



VOLUME FIVE

HANDBOOK OF
PHARMACEUTICAL
MANUFACTURING FORMULATIONS
THIRD EDITION

OVER-THE-COUNTER PRODUCTS

Sarfaraz K. Niazi



CRC Press
Taylor & Francis Group

Handbook of Pharmaceutical Manufacturing Formulations

Volume Five, Over-the-Counter Products



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To the memory of Dean Allen I. White

Dean Allen I. White passed away in 2002; he gave me the opportunity to enter the graduate school at Washington State University, where he served from 1940 to 1979.



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Preface to the Series—Third Edition

I am humbled by the wide praise and acceptance of the last two editions of the *Handbook of Pharmaceutical Formulations*, a six-volume series that found home in the R&D laboratories of just about every pharmaceutical company, both generic and branded, and in the classrooms of pharmaceutical technology; and the regulatory agencies used this treatise to compare the quality of pharmaceutical products. In creating this work, back in 2004, my primary objective was to provide a ready source of safe and scalable generic and new pharmaceutical formulations that take a long time to develop and incur a substantial cost, to enable the availability of affordable medicines.

Each of the six volumes in the series has a structured content. Part I includes regulatory guidance, formulation steps, references to active ingredients and excipients, and a self-audit guidance for cGMP compliance. Chapters of common interest to all volumes are distributed across the six volumes, such as the formulations for coating solutions are presented in Volume 5 (OTC), though they are also pertinent to Volume 1 (Compressed Dosage Forms), and global bioequivalence testing guidelines are provided in Volume 4 (Semisolids), though they apply to all volumes. Part II includes scalable formulations and Part III, where applicable, other general formulations. The appendices include a listing of excipients used in FDA approved products and a cGMP compliance self-testing tool. Whereas the main focus of the guidance provided in the handbook pertains to compliance with FDA requirements, these apply equally to EU requirements, and, as a result, to any global agency.

The third edition also gets several significant additions; now each volume includes a self-audit template, several chapters advising how to stay cGMP compliant, including a listing of most common FDA citations to look out for in the audits, a global regulatory focus and an updated list of excipients and the level of their incorporation in the FDA-approved products. The number of formulations is also increased, and the OTC

volume now contains several cosmetic formulations, and the semisolid product volume also includes details on chewing gum delivery systems.

The updating of formulations is always cumulative as there is little need to remove any formulation provided previously—if it was right then, it shall remain good now. However, a variety of new drug delivery systems have evolved since the second edition was published, so I have included more details on these formulations, although some of these may not be available to practice due to possible limitations on the intellectual property.

As always, I advise the formulators to be aware of any intellectual property infringements as I cannot provide a guarantee to this effect.

Finally, I wish to acknowledge the leaders of the pharmaceutical world, to whom each of the volumes is dedicated. I have made a few changes to those whom the volumes are dedicated, to recognize those who have since passed away; they provided a role model to me and thousands of leaders and students of pharmacy over the decades of their careers. They are gone, but not without leaving an indelible mark on the profession.

I also consider myself fortunate to have the sponsorship and assistance of the great folks at the CRC Press, more particularly Jessica Poile and Hilary LaFoe. The teams at the CRC Press were very kind to put up with my redundant changes to the manuscript and were extremely generous in their advice in balancing the scientific and practical knowledge and, above all, making sure that the book was framed and published in the highest professional presentation. As always, I take responsibility for any mistakes and errors in my writing, and I am always open to suggestions by the readers to make future editions. I can be contacted at niazi@niazi.com.

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Preface to the Series—Second Edition

The science and the art of pharmaceutical formulation keeps evolving as new materials, methods, and machines become readily available to produce more reliable, stable, and release-controlled formulations. At the same time, globalization of sourcing of raw and finished pharmaceuticals brings challenges to regulatory authorities and results in more frequent revisions to the current good manufacturing practices, regulatory approval dossier requirements, and the growing need for cost optimization. Since the publication of the first edition of this book, a lot has changed in all of these areas of importance to pharmaceutical manufacturers. The second edition builds on the dynamic nature of the science and art of formulations and provides an evermore useful handbook that should be highly welcomed by the industry, the regulatory authorities, as well as the teaching institutions.

The first edition of this book was a great success as it brought under one umbrella the myriad of choices available to formulators. The readers were very responsive and communicated with me frequently pointing out to the weaknesses as well as the strengths of the book. The second edition totally revised attempts to achieve these by making major changes to the text, some of which include:

1. Complete, revised errors corrected and subject matter reorganized for easy reference. Whereas this series has six volumes differentiated on the basis of the type of dosage form and a separate inclusion of the U.S. OTC products, ideally the entire collection is needed to benefit from the myriad of topics relating to formulations, regulatory compliance, and dossier preparation.
2. Total number of pages is increased from 1684 to 2726.
3. Total number of formulations is expanded by about 30% with many newly approved formulations.
4. Novel formulations are now provided for a variety of drugs; these data are collected from the massive intellectual property data and suggest toward the future trend of formulations. While some of these formulations may not have been approved in the United States or Europe, these do provide additional choices, particularly for the NDA preparation. As always, it is the responsibility of the manufacturer to assure that the intellectual property rights are not violated.
5. A significant change in this edition is the inclusion of commercial products; while most of this information is culled out from the open source such as the FOIA (<http://www.fda.gov/foi/default.htm>), I have made attempts to reconstruct the critical portions of it based on what I call the generally acceptable standards. The drug companies are advised to assure that any intellectual property rights are not violated

and this applies to all information contained in this book. The freedom of information act (FOIA) is an extremely useful conduit for reliable information and manufacturers are strongly urged to make use of this information. Whereas this information is provided free of charge, the process of obtaining the information may be cumbersome, in which case, commercial sources of these databases can prove useful, particularly for the non-U.S. companies.

6. Also included are the new Good Manufacturing Guidelines (2007) with amendments (2008) for the United States and similar updates for European Union and WHO; it is strongly urged that the companies discontinue using all old documents as there are significant changes in the revised form, and many of them are likely to reduce the cost of GMP compliance.
7. Details on design of clean rooms is a new entry that will be of great use to sterile product manufacturers; whereas the design and flow of personnel and material flow is of critical nature, regulatory agencies view these differently and the manufacturer is advised always to comply with most stringent requirements.
8. Addition of a self-auditing template in each volume of the series. While the cGMP compliance is a complex issue and the requirements diversified across the globe, the basic compliance remains universal. I have chosen the European Union guidelines (as these are more in tune with the ICH) to prepare a self-audit module that I recommend that every manufacturer adopt as a routine to assure GMP compliance. In most instances reading the template by those responsible for compliance with keep them sensitive to the needs of GMP.
9. OTC products cross-referenced in other volumes where appropriate. This was necessary since the regulatory authorities worldwide define this class of drug differently. It is important to iterate that regardless of the prescription or the OTC status of a product, the requirements for compliance with the cGMP apply equally.
10. OTC monograph status is a new section added to the OTC volume and this should allow manufacturers to choose appropriate formulations that may not require a filing with the regulatory agencies; it is important to iterate that an approved OTC monograph includes details of formulation including the types and quantities of active drug and excipients, labeling, and presentation. To qualify the exemption, the manufacturer must comply with the monograph in its entirety. However, subtle modifications that are merely cosmetic in nature and where there is an evidence that

the modification will not affect the safety and efficacy of the products can be made but require prior approval of the regulatory agencies and generally these approvals are granted.

11. Expanded discussion on critical factors in the manufacturing of formulations provided; from basic shortcuts to smart modifications now extend to all dosage forms. Pharmaceutical compounding is one of the oldest professions and whereas the art of formulations has been relegated to more objective parameters, the art nevertheless remains. An experienced formulator, like an artist, would know what goes with what and why; he avoids the pitfalls and stays with conservative choices. These sections of the book present advice that is time tested, although it may appear random at times; this is intended for experienced formulators.
12. Expanded details on critical steps in the manufacturing processes provided but to keep the size of the book manageable, and these are included for prototype formulations. The reader is advised to browse through similar formulations to gain more insight. Where multiple formulations are provided for the same drug, it is intended to show the variety of possibilities in formulating a drug and whereas it pertains to a single drug, the basic formulation practices can be extended to many drugs of same class or even of diversified classes. Readers have often requested that more details be provided in the Manufacturing Direction sections. Whereas sufficient details are provided, this is restricted to prototype formulations to keep the size of the book manageable and to reduce redundancy.
13. Addition of a listing of approved excipients and the level allowed by regulatory authorities. This new section allows formulators a clear choice on which excipients to choose; the excipients are reported in each volume pertaining to the formulation type covered. The listing is drawn from the FDA-approved entities. For the developers of an ANDA, it is critical that the level of excipients be kept within the range generally approved to avoid large expense in justifying any unapproved level. The only category for which the listing is not provided separately is the OTC volume since it contains many dosage forms and the reader is referred to dosage form-specific title of the series. The choice of excipients forms keeps increasing with many new choices that can provide many special release characteristics to the dosage forms. Choosing correct excipients is thus a tedious exercise and requires sophisticated multivariate statistical analysis. Whereas the formulator may choose any number of novel or classical components, it is important to know the levels of excipients that are generally allowed in various formulations to reduce the cost of redundant exercises; I have therefore included, as an appendix to each volume, a list of all excipients that are currently approved by the U.S. FDA along their appropriate levels. I suggest that a formulator consult this table before deciding on which level of excipient to use; it does not mean that the excipient cannot be used outside this range but it obviates the need for a validation and lengthy justification studies in the submission of NDAs.
14. Expanded section on bioequivalence submission was required to highlight the recent changes in these requirements. New entries include a comprehensive listing of bioequivalence protocols in abbreviated form as approved by the U.S. FDA; these descriptions are provided in each volume where pertinent. To receive approval for an ANDA, an applicant must generally demonstrate, among other things, equivalence of the active ingredient, dosage form, strength, route of administration and conditions of use as the listed drug, and that the proposed drug product is bioequivalent to the reference listed drug [21 USC 355(j)(2)(A); 21 CFR 314.94(a)]. Bioequivalent drug products show no significant difference in the rate and extent of absorption of the therapeutic ingredient [21 U.S.C. 355(j)(8); 21 CFR 320.1(e)]. BE studies are undertaken in support of ANDA submissions with the goal of demonstrating BE between a proposed generic drug product and its reference listed drug. The regulations governing BE are provided at 21 CFR in part 320. The U.S. FDA has recently begun to promulgate individual bioequivalence requirements. To streamline the process for making guidance available to the public on how to design product-specific BE studies, the U.S. FDA will be issuing product-specific BE recommendations (www.fda.gov/cder/ogd/index.htm). To make this vital information available, an appendix to each volume includes a summary of all currently approved products by the U.S. FDA where a recommendation on conducting bioequivalence studies is made available by the U.S. FDA. When filing an NDA or an ANDA, the filer is faced with the choice of defending the methods used to justify the bioavailability or bioequivalence data. The U.S. FDA now allows application for waiver of bioequivalence requirement; a new chapter on this topic has been added along with details of the dissolution tests, where applicable, approved for various dosage forms.
15. Dissolution testing requirements are included for all dosage forms where this testing is required by the FDA. Surrogate testing to prove efficacy and compliance is getting more acceptance at regulatory agencies; in my experience, a well-designed dissolution test is the best measure of continuous compliance. Coupled with chapters on waivers of bioequivalence testing, this information on dissolution testing should be great value to all manufacturers; it is recommended that manufacturers develop their own in-house specifications, more stringent than those allowed in these listings and the USP.

16. Best-selling products (top 200 prescription products) are identified with an asterisk and a brand name where applicable; in all instances, composition of these products is provided and formulation of generic equivalents. Despite the vast expansion of pharmaceutical sales and shifting of categories of blockbuster drugs, basic drugs affecting gastrointestinal tract, vascular system, and brain remain most widely prescribed.
17. Updated list of approved coloring agents in the United States, Canada, European Union, and Japan is included to allow manufactures to design products for worldwide distribution.
18. Tablet-coating formulations that meet worldwide requirements of color selection are included in the Volume 1 (compressed solids) and Volume 5 (OTC) because these represent the products often coated.
19. Guidelines on preparing regulatory filings are now dispersed throughout the series depending on where these guidelines are more crucial. However, the reader would, as before, need access to all volumes to benefit from the advice and guidelines provided.

As always, comments and criticism from the readers are welcomed and these can be sent to me at Niazi@pharmsci.com or Niazi@niazi.com. I would try to respond to any inquiries requiring clarification of the information enclosed in these volumes.

I would like to express deep gratitude to Sherri R. Niziolek and Michelle Schmitt-DeBonis at Informa, the publisher of this work, for seeing an immediate value to the readers in publishing the second edition of this book and allowing me enough time to prepare this work. The diligent editing and composing staff at Informa, particularly Joseph Stubenrauch, Baljinder Kaur and others are highly appreciated. Regardless, all errors and omissions remain altogether mine.

In the first edition, I had dedicated each volume to one of my mentors; the second edition continues the dedication to these great teachers.

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Preface to the Series—First Edition

No industry in the world is more highly regulated than the pharmaceutical industry because of potential threat to a patient's life from the use of pharmaceutical products. The cost of taking a new chemical entity (amortized over the cost of all molecules racing) to final regulatory approval is a staggering \$800 million, making the pharmaceutical industry one of the most research-intensive industries in the world. In the year 2004, it is anticipated that the industry will spend about \$20 billion on research and development. The generic market of drugs as the new entities come off patent is one of the fastest growing segments of the pharmaceutical industry, with every major multinational company having a significant presence in this field.

Whereas many stages of new drug development are inherently constrained with time, the formulation of drugs into desirable dosage forms remains an area where expediency can be practiced with appropriate knowledge by those who have mastered the skills of pharmaceutical formulations. The *Handbook of Pharmaceutical Manufacturing Formulations*—is the first major attempt to consolidate the available knowledge about formulations in a comprehensive, and by nature a rather voluminous, presentation.

The book is divided into six volumes, based strictly on the type of formulation science involved in the development of these dosage forms: sterile products, compressed solids, uncompressed solids, liquid products, semisolid products, and OTC products. The separation of OTC products, even though they may easily fall into one of the other five categories, is made to comply with the industry norms of separate research divisions for OTC products. Sterile products require skills related to sterilization of product, and of less importance is the bioavailability issue, which is an inherent problem of compressed dosage forms. These types of

considerations have led to the classification of products into these six categories.

Each volume includes a description of regulatory filing techniques for the formulations described. Also included are the current regulatory guidelines on cGMP compliance specific to the dosage form. Advice is offered on how to scale up the production batches.

It is expected that formulation scientists will use this information to benchmark their internal development protocols and cut the race to file short by adopting formulae that have survived the test of time. Many of us who have worked in the pharmaceutical industry suffer from a close paradigm when it comes to selecting formulations—"not invented here" perhaps reigns in the mind of many seasoned formulations scientists subconsciously when they prefer to choose only a certain platform for development. It is expected that with the quick review of possibilities available to formulate made available in this book, scientists will benefit from the experience of others.

For the teachers of formulation sciences, this series offers a wealth of information. Whether it is a selection of a preservative system or the choice of a disintegrant, the series offers a wide choice to study and rationalize.

Many have assisted me in the development of this work that has taken years to compile, and I thank scores of my graduate students and colleagues for their help. A work of this size cannot be produced without errors, although I hope that these errors do not distract the reader from the utility of the book. I would sincerely appreciate if readers point out these mistakes for corrections in future editions.

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Preface to the Volume—First Edition

The *Handbook of Pharmaceutical Manufacturing Formulations OTC Drugs* is written for the pharmaceutical scientist and others involved in the regulatory filing and manufacturing of new OTC products. Because of the wide variety of products involved, from those bordering on cosmetics to proton pump inhibitors, the OTC products are manufactured by the most sophisticated global manufacturers as well as small one-room makeshift manufacturing houses.

The OTC products comprise a special category of health-care products in that they can be dispensed without prescription; the rationale being that the use of these products does not expose patients to serious risks associated with side effects even if some misuse or overuse of these products occurs. The OTC category includes three types of products:

Products that require full filing with the U.S. Food and Drug Administration (FDA) for marketing approval (the NDA/NADA or ANDA/ANADA process) including products or compositions not included in the monographs (see below) or administered in controlled release formulations.

Products that do not require filing with the U.S. FDA because they comply with the monographs issued by the U.S. FDA in its Code of Federal Regulations (CFR).

Products that fall under the category of grandfather products which have been in use prior to the 1960s and have not been specifically excluded by the FDA; not all grandfather products fall under the OTC category—only those that are generally regarded as safe (GRAS).

The U.S. FDA provides excellent support through its OTC website (<http://www.fda.gov/cder/otc/index.htm>) and formulators are highly encouraged to make use of the information available, particularly the updates in the monograph label requirements and withdrawal of approvals of formulations.

With the safety of consumers in mind, the U.S. FDA is in the process of establishing guidelines for all OTC products. Although the U.S. FDA began this work over three decades ago, much remains to be done. The U.S. FDA process begins with the issuance of Proposed Rules; this notification is like a warning (or advice) to the industry that this category of products is now under the U.S. FDA watch. Often years go by before Proposed Rules are published in the Code of Federal Regulations. The Proposed Rules include not only identification of approved active ingredients but also inactive ingredients that are deemed compatible with the active ingredients and safe for consumers. The Proposed Rules are subject to criticism by the industry health-care practitioners and consumers. After receiving these comments over what can be a period of several years, the U.S. FDA issues Final Rules on a specific category of products; these become official on the date of publication in the Code of Federal Regulations. In many cases, however, the U.S. FDA issues subsequent rules either to delay application of Final Rules or to modify the Final Rules if new information has become available.

The Final Rule requirements have primarily been applied to products on the market and a newcomer is well advised to study competitor products for market leaders as ample opportunities are available to innovate these products. Examples include the Tylenol® Hot Therapy products and loratidine tablets that dissolve in the mouth and do not require water. I foresee more such products entering into the ever-competitive OTC market.

It is imperative that any prospective entry into the OTC market should begin with a thorough consultation of the Final Rules; an examination of Proposed Rules and notifications to issue Proposed Rules is also helpful in determining what rules are about to become Final Rules. Reviewing the discussions about Proposed Rules that have affected their finalization can be very helpful in understanding the relevant issues of safety, efficacy, and labeling. Because the marketing of OTC products requires a large investment in marketing efforts, it is prudent to develop a clear understanding of the legality of formulations and claims made in the initial phases of product development.

A large number of products on the market today are not covered by the U.S. FDA monographs but does that make them legitimate? This is the often-asked question. The U.S. FDA has limited resources to tackle everything that is out there on the market. When emergencies arise, however, the U.S. FDA reacts immediately as it did in the case of phenylpropanolamine, pseudoephedrine, and recently, kava. Here are some broad guidelines adopted by the U.S. FDA for the most commonly abused categories of products:

No treatments are approved for hair growth except for minoxidil.

No treatments are approved for enhancing sexual performance except for sildenafil citrate (and that only in MED).

The few treatments approved for weight loss include orlistat, phentermine, and sibutramine (phenylpropanolamine is no longer a recommended compound).

It is noteworthy that the U.S. FDA does not differentiate between botanical products and chemical-based products. If a product bears an efficacy claim, it must be governed by the U.S. FDA rules; however, a product that falls into a drug category that makes nutritional claims falls under a food category with its own set of detailed rules. Vitamins and minerals fall under food labeling guidelines; however, a single-entity vitamin product with specific claims to treat or ameliorate a disease is a drug product. These definitions do not necessarily coincide with the rulings of regulatory authorities worldwide. In many countries nutritional products are controlled as drugs and require prescriptions; these same products would be considered nonprescription items in the United States.

On the other hand, a number of highly active drugs are available without prescription in many countries such as the Traditional Chinese Medicine (TCM) in China and Ayurvedic and Unani medicines in South Asia.

A reclassification of a drug to OTC status can be requested by drug manufacturers. Recent examples of such a prescription-to-OTC switch include ibuprofen (200 mg), ranitidine hydrochloride (75 mg), and loratidine (10 mg). Note that specific strengths, not necessarily the chemical entity itself, are made OTC. In other words, it is not necessary to have an official monograph to secure OTC status for a drug. The decision to request reclassification of a drug as OTC is always a well-calculated business decision. Generally, drugs with an OTC status will not qualify for medical reimbursement by insurance companies or federal assistance programs in the United States. This can substantially reduce sales of the product; on the other hand, ease of availability to a greater number of patients can easily compensate for this loss. The most lucrative opportunities arise when one strength is made OTC while other strengths remain available by prescription only.

It is noteworthy that the decision to allow a switch from prescription to OTC by the U.S. FDA is primarily driven by the side effects or toxicity of the drug. For example, in Australia a Roche request for a prescription-to-OTC switch for its weight-loss drug orlistat (Xenical®) was recently turned down because of extensive side effects associated with the use of Xenical. The drug itself is very safe as it does not enter the body and acts only locally to partially block absorption of fat. The unabsorbed fat produces many gastrointestinal symptoms which though temporary were sufficient to disallow the status switch. Obviously, Roche would have been best advised to develop an OTC formulation with fewer side effects before requesting this switch. (In the case of orlistat, the solution was simple as described in U.S. Patent No. 6,251,421 by this author wherein combining orlistat with a natural fiber reduced the side effects by 70%.)

The OTC category of products represents a wide range of dosage forms. These formulations have much in common with their prescription counterparts but are presented in this volume of the *Handbook of Pharmaceutical Manufacturing Formulations* because of the development approach taken, labeling considerations, and support available from suppliers of ingredients in designing these products. Because the consumer is inevitably involved in the selection of these products, packaging considerations are much more important than in the prescription category of products. Additional considerations include ease of administration, palatability, and stability in storage as consumers are likely to keep leftovers around for a long time. Additionally, price constraints often make it difficult to enjoy some freedom of choice in formulations, especially if the innovator company faces the competition of house brands. All of these considerations taken together make the OTC category one that should be presented in a single volume of this series of books.

Formulating OTC products is generally easier than formulating prescription products if the product is described in U.S. FDA monographs (either as Proposed Rules or Final Rules);

such formulations become merely an exercise in mechanics. Whereas a manufacturer is not bound by these rules, complying with them reduces the costs and time involved securing approval from regulatory authorities. The multibillion-dollar market of OTC products has attracted major chemical suppliers to develop support ingredients that are much easier to use; they have also developed typical formulations for hundreds of these products.

The most notable industry leaders include

Amerchol, American Colloid, Aqualon, BASF, BF Goodrich, Calgon, Colorcon, Croda, Dow Corning, FMC, Gattefosc, General Electric, Henkel, Hormel, Huls America, ICI Americas, Inolex, International Sourcing, International Specialty, Laboratoires Serobiologique, Lonza, NIPA, PPG Industries, R.I.T.A., Reheis, Rheox, Rhone-Poulenc, Rohm and Haas, Southern Clay, Sutton, and Vanderbilt.

The formulations recommended by these and other companies have acquired almost a universal appeal; throughout this book you will find formulations recommended by these laboratories, as acknowledged by the listing of a brand name in the formula. The best way to connect to these companies is to search the Internet for contact information; it is no longer necessary to reproduce such information here. Whereas many companies prefer to use generic components in the dosage form, it has been found that the use of proprietary components can indeed reduce costs in the long run.

The choice of color is a highly sensitive issue in the formulation of OTC products; only FDC colors are allowed. Whereas there is a great need to make the products attractive and appealing, the choices of safe colors are dwindling quickly, such as for red colors. The formulator is encouraged to review the status of approved colors around the world before committing to a specific color.

Many OTC solid dosage forms are available in coated form. Sugar coatings have yielded to film coatings, and this book contains a large number of sugar-coating, seal-coating, subcoating, film-coating, and polish-coating formulations that can be easily adapted to various dosage form sizes. The use of organic solvent-based coatings has become prohibitive because of environment considerations, but in those cases where formulations are extremely sensitive to moisture, organic coatings may still offer a valid choice. A few companies offer ready-made coating formulations, and these are worth considering. The Appendix to this book includes a large number of formulations of coatings of solid dosage forms. A keen formulator will have no difficulty based on these formulations in adopting a coating system that will provide the necessary protection and offer esthetic appeal as well. Solid dosage forms are coated for many reasons, including masking the taste, making them easier to swallow, and providing protection against the environment.

Stability considerations remain paramount, and the data in the final packaging must be evaluated carefully before adjusting formulae for excesses; in this book, most formulations are provided without this consideration. A strip or blister dosage form is more popular around the world, but the plastic bottle is the most popular final form in the United States.

The development of OTC products is similar to the development of prescription dosage forms; as a result, cGMP and Good Laboratory Practice (GLP) considerations apply equally. The first chapter describes in greater detail the cGMP considerations. An appendix to chapter 1 provides a comprehensive checklist of items to review to ensure that a manufacturing facility is in compliance with cGMP standards. Appropriate identification is made in this checklist of those items that comply with EC guidelines. The U.S. FDA guidelines are available from the U.S. FDA website: <http://www.fda.gov>. The World Health Organization (WHO) provides GMP guidelines that are less stringent than those of the U.S. FDA and EC, and formulators should be aware of the fact that all of these are simply guidelines. One should be fully cognizant of the fact that no agencies are bound by these guidelines, particularly the U.S. FDA. Manufacturers cannot take refuge in the defense that they have complied with these guidelines. It is further worthwhile remembering that all of these guidelines are continuously revised, and the “c” in the cGMP does refer to current.

The second chapter deals with the most popular category of dosage forms encountered in OTC offerings—solids. Issues specific to manufacturing of these dosage forms are described from a practical viewpoint, indicating the problem areas frequently encountered in manufacturing practice.

The third chapter deals with liquids and suspensions and includes, like the chapter above, practical advice on how to bring manufacturing practices into compliance with regulatory requirements.

The fourth chapter offers highlights of cleaning validation, a topic often ignored by OTC manufacturers as not being significant because of the safety of ingredients used. It is true that the same stringent standards may not apply, but compliance with cleaning standards and validation of processes go a long way toward ensuring overall compliance.

The first four chapters were drawn from the advice which the U.S. FDA gives to its inspectors before they inspect a manufacturer. The CFR includes complete details of what is considered acceptable by the U.S. FDA; this advice is of a practical nature, and I find it to be extremely helpful in enhancing awareness of the guidelines of regulatory authorities. It is noteworthy that EC guidelines, particularly in light of the harmonization of specifications, are somewhat identical to the U.S. FDA guidelines; in chapter 1, specific references are made to EC guidelines. The Appendix includes formulations of coating solutions; these should prove useful for the pharmaceutical formulation teams.

The formulations in this book generally fall into three categories. Some formulations are presented in greater detail, including indications of where quality assurance (QA)/quality control (QC) sampling is to be done and describing the tooling and in-process and finished product specifications. The other extreme is a mere listing of components with a bare minimum of manufacturing methods. This was necessary for two reasons: first, to contain the size of this book, and second, to keep from presenting superfluous information, as formulators would eventually adopt such a formula to their own delivery forms. Also, at times the various strengths are merely achieved through adjustment of dosage size, so it was considered unnecessary to reproduce manufacturing steps where they are obvious.

The primary source of these formulations is publicly available knowledge about formulae that have proven to provide stable products. No representation is made that these formulations meet U.S. FDA monographs or any other regulatory guidelines for safety of inert ingredients. The formulator is advised to determine guideline compliance before adopting any of the formulations given in this book. Those interested in obtaining detailed information about these formulations are encouraged to contact the author at <http://www.pharmsci.com>. Because of the wide variety of sources from which the information has been gathered in the book, the format of formulations also varies. For example, in some instances scale is provided, whereas in others a percentage by weight is described. In still other instances, quantities for a specific batch size are provided. Obviously, it would be desirable to convert these formulations into a uniform format, but the task would be daunting and inevitably would lead to inclusion of errors. Professional formulators should not encounter any difficulty in adapting these formulations to their own system.

As mentioned before, not all formulations contain the required overages for stability considerations and losses during manufacturing; formulators are expected to develop these based on the final packaging chosen for the product. The author would appreciate being notified of any special problems encountered in adopting these formulations or of any errors (niazi@pharmsci.com). Whereas much care has gone into ensuring the accuracy of quantities and proper identification of ingredients, such errors shall remain in a work as large as that presented here.

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Sarfaraz K. Niazi has been teaching and conducting research in the pharmaceutical industry for over 40 years. He has authored hundreds of scientific papers and scores of textbooks, handbooks, and literary books on the topics of pharmaceutical formulation, biopharmaceutics, pharmacokinetics, bioprocessing, and recombinant engineering, as well as poetry and philosophy.

He is also an inventor, with 100+ patents in the fields of bioprocessing, technology, and drug and dosage form delivery systems; he is also licensed to practice law before the U.S. Patent and Trademark Office. He has formulated hundreds of products, ranging from the most popular consumer products to complex generics and biotechnology-derived products. Dr. Niazi advises regulatory agencies and the pharmaceutical industry on making safe and effective drugs affordable (www.pharmsci.com). He can be contacted at niazi@niazi.com.

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Part I

Regulatory Guidance



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1 European Directorate for the Quality of Medicines (EDQM) Certification

European legislation does not require mandatory routine good manufacturing practice (GMP) inspections for active substance manufacturers. The responsibility for using only active substances that have been manufactured in accordance with GMP is placed on the holders of a manufacturing authorization. Art. 111 Directive 2001/83/EC (Art. 80 Directive 2001/82/EC for veterinary medicinal products), however, makes provision for GMP inspections of active substance manufacturing sites to be carried out at the request of the manufacturer itself. The request for the inspection should be made to the European Economic Area (EEA) competent authority where the site is located or, in case of sites located in third countries, to a competent authority where the active substance is used as a starting material in the manufacture of medicinal products. If this is not the case, any EEA authority can be approached. There is no guarantee that such a request will be fulfilled, as the competent authorities need to balance such requests with other priorities. It should also be borne in mind that an inspection does not replace the responsibility of the manufacturing authorization holder using the active substance in question as a starting material and will not be accepted alone as adequate assurance that the manufacturing authorization holder has fulfilled its responsibilities.

Manufacturing authorization holders sometimes confuse the role of inspectorates with their own obligations, but nevertheless, when inspection reports or GMP certificates issued by the EEA, Medicines and Healthcare Products Regulatory Agency (MHRA) partners, or other recognized authorities are available, these can provide useful information to manufacturing authorization holders. However, these alone cannot fulfill the statutory obligations of the manufacturing authorization holder or the requirements of section 5.25 of the GMP Guide, but the results of inspections may be used together with other supporting information in a risk-based approach by the manufacturer in establishing priorities for its own audit program of active substance suppliers.

A GMP certificate is a certificate issued, following a GMP inspection, by the competent authority responsible for carrying out the inspection to confirm the GMP compliance status of the inspected site. GMP certificates are site specific but can be restricted to particular activities depending on the scope of the inspection (e.g., manufacturing activities related to a specific product). Directives 2001/82/EC and 2001/83/EC, as amended, state that after every GMP inspection, and within

90 days of the inspection, a GMP certificate shall be issued to a manufacturer if the outcome of the inspection shows that the manufacturer complies with GMP.

Certificates of a medicinal product (CMPs) are product-specific certificates issued by the competent authority that granted the marketing authorization (the European Medicines Agency [EMA] issues CMPs on behalf of the European Commission for centrally authorized products), in the context of the World Health Organization (WHO) certification scheme on the quality of pharmaceutical products moving in international commerce, to confirm the marketing authorization status of the products. These certificates also confirm the GMP compliance status of the manufacturing site(s). CMPs are mainly used by companies to support applications to export their pharmaceutical products to countries with less developed regulatory systems.

CEPs are certificates issued by the European Directorate for the Quality of Medicines (EDQM) to confirm that a certain active substance is produced according to the requirements of the relevant monograph of the European Pharmacopoeia or of the monograph on transmissible spongiform encephalopathy (TSE). Certificates of Suitability to the monographs of the European Pharmacopoeia (CEPs) can be used by companies when submitting an application for marketing authorization and replace much of the documentation required for the active substance in the marketing authorization dossier. GMP inspections of active substance manufacturers can be requested by EDQM in the context of the CEP certification scheme.

EMA does not perform inspections; they are carried out on its behalf by the national competent authorities of the member states of the EEA in connection with products under the centralized marketing authorization procedure. The competent authority responsible for carrying out the inspection issues the GMP certificate or makes an entry of noncompliance into the EudraGMP Database.

The EDQM allows raw material manufacturers to submit and secure approval for their active pharmaceutical ingredients (APIs) besides the approval of the finished products; such approvals are not available in the jurisdictions of the FDA. Given in the following is a submission requirement that can be used by the manufacturers to audit for the quality of the API in those instances where such certificates and/or DMF are not available.

1.2.3.S DRUG SUBSTANCE

A.2.3.S.1 GENERAL INFORMATION

Use of the substance: Route(s) of administration, maximum daily dose.

Commercialization history: Summarize the history based on the table in application form.

Declarations: Summarize the declarations appended to the application form:

- Manufacture of the substance in accordance with International Conference for Harmonisation (ICH) Q7A GMP rules
- Commitment by the manufacturer to keep the proposed holder informed of any changes to the documentation
- If applicable: manufacturer's authorization for X to act as representative
- Willingness to be inspected (holder, manufacturers)
- Nonuse/use of materials of human or animal origin in the process

1.2.3.S.1.1 Nomenclature

- (a) Recommended international nonproprietary name (INN)
- (b) Chemical name(s)
- (c) Company or laboratory code
- (d) Other nonproprietary name(s) (e.g., national name, United States Adopted Name [USAN], British Approved Name [BAN])
- (e) CAS No.: Molecular Formula, MW

1.2.3.S.1.2 General Properties

Give summarized data on

- (a) Physical description (e.g., appearance, color, physical state ...)
- (b) Physical form (e.g., polymorphic form, solvate, hydrate): to be commented especially if requested as grade
- (c) Solubility and other properties as necessary
- (d) Particle size: for example, nonmicronized, micronized, or any grade claimed as subtitle

2.3.S.2 MANUFACTURE

2.3.S.2.1 MANUFACTURER(S) (NAME, MANUFACTURER) AND SITES INVOLVED IN THE ENTIRE PROCESS

Give the name, address, and responsibility of each manufacturer, including contractors and manufacturer, and each proposed production site or facility involved in manufacture.

2.3.S.2.2 DESCRIPTION OF MANUFACTURING PROCESS AND PROCESS CONTROLS

- (a) Give a brief narrative step-by-step description of the manufacturing process(es), and provide reference to detailed description in the documentation. Confirm the maximum batch size.
- (b) If applicable, summarize alternate processes and give a short explanation of their use.
- (c) Comment briefly on recovery of materials (solvents, reagents, and mother liquor) together with reprocessing steps, and give a brief justification.

2.3.S.2.3 CONTROL OF MATERIALS

- (I) Starting material(s)
 - (a) Give summarized specifications (including impurities profile) including their justification based on studies of carryover.

NB: If starting material is obtained by fermentation or is of herbal origin, summarize the information related to the nature of this material.

- (II) Reagents and solvents

Summarize the quality and controls of the materials (e.g., raw materials, solvents pure and/or recovered, reagents, and catalysts) used in the manufacture of the drug substance.

2.3.S.2.4 CONTROLS OF CRITICAL STEPS AND INTERMEDIATES

Summary of the controls performed at critical steps of the manufacturing process and on intermediates; compare analytical procedures used for intermediates and final substance.

2.3.S.2.5 PROCESS VALIDATION AND/OR EVALUATION

For aseptic processing and sterilization, only give the summary of process validation and/or evaluation studies.

2.3.S.3 CHARACTERIZATION

2.3.S.3.1 IMPURITIES

- (I) Related substances
 - (a) Fill in the following table identifying related substances, their origin, and distinguishing between potential and actual impurities and comparing with impurity section of the monograph.

Chemical Name	Ph.Eur. Impurity	Applicant's Specifications	Ph.Eur. Specifications	Levels of Origin Found	LOD of the Method	LOQ of the Method

- (b) *Justify these specifications based on data* observed for impurities in relevant batches.
- (c) Discuss briefly the *suitability of the monograph* to control the potential impurities present in the substance (residual starting materials, reactants, reagents, etc.).
- (d) *Specific discussion on possible genotoxic impurities*: Give a brief discussion on impurities with potential genotoxicity based on the requirements of the guideline.

(II) Residual solvent(s)/reagent(s)/catalyst(s)

- (a) Fill in the following table.

Solvent/ Reagent/ Catalyst	Used in Step X/Y	ICH Applicant's Class/ Limit	LOD Levels of the Method	LOQ of the Method

- (b) Discuss briefly the basis for setting the specification.

2.3.S.4 CONTROL OF THE DRUG SUBSTANCE

2.3.S.4.1 SPECIFICATION

Give a table summarizing the proposed specifications.

2.3.S.4.2 ANALYTICAL PROCEDURES

- (a) Summarize the analytical procedures.

2.3.S.4.3 VALIDATION OF ANALYTICAL PROCEDURES

Give the summary of the validation information for any in-house tests, and compare briefly with the method(s) described in the monograph (cross-validation).

2.3.S.4.4 BATCH ANALYSES

- (a) Give a short description of the batches: batch number, batch size, date, and site of production.

- (b) Summarize the results for relevant batches (according to specifications and showing equivalence of any alternative supplier, process, etc.).

2.3.S.4.5 JUSTIFICATION OF SPECIFICATION

Justify the drug substance specification.

2.3.S.5 REFERENCE STANDARDS OR MATERIALS

- (a) Give the source of primary reference standards or reference materials (e.g., Ph.Eur.) for final substance and its impurities where relevant.
- (b) Summarize characterization and evaluation of in-house standards.

2.3.S.6 CONTAINER CLOSURE SYSTEM

- (a) Describe briefly the container closure system(s) for the storage and shipment of the drug substance, as it has to be mentioned on the CEP in case a retest period is requested (i.e., in a clear and understandable manner).
- (b) Summarize the specifications (description + identification).

2.3.S.7 STABILITY

State retest period claimed for the substance and storage recommendations, if any.

2.3.S.7.1 STABILITY SUMMARY AND CONCLUSIONS

- (a) Summarize accelerated and long-term testing (e.g., studies conducted, protocols used, and results obtained).
- (b) Justify the retest period claimed based on data available.

2.3.S.7.2 POSTAPPROVAL STABILITY PROTOCOL AND STABILITY COMMITMENT

Give the stability protocol for commitment batches.



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2 Solid Oral Dosage Forms Validation

I. INTRODUCTION

The *Validation Guidelines* issued by the Food and Drug Administration (FDA) in 1987 defines process validation as establishing documented evidence that provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes. The three components of this definition are

- Documented evidence
- Consistency
- Predetermined specifications

Documented evidence includes the experiments, data, and analytical results that support the master formula, the in-process and finished product specifications, and the filed manufacturing process.

With regard to consistency, several batches would have to be manufactured, using the full-scale batch size, to demonstrate that a process meets the consistency test. At least three batches are needed to demonstrate consistency.

The development of a product and its manufacturing process and specifications, the design of the validation protocol, and the demonstration (validation) runs of the full-scale manufacturing process require scientific judgment based on good scientific data. The FDA expects that in-process control and product specifications will be established during the product development process, with the test batch serving as the critical batch used for the establishment of specifications.

Specifications, such as hardness and particle size, should be established prior to validation of the process; these specifications should be included in the validation protocol. Problems often arise when the product development runs of the process are used both to establish specifications and to demonstrate that the system is validated. In these cases, more in-depth inspection and evaluation will be required; some of these process runs often produce failing product because the product specifications have not been fully established and tested.

II. BACKGROUND

Two common complaints regarding validation issues have frequently been raised. The first concerns the misconception that the 1987 *Validation Guidelines* represents a new requirement. The second concerns the lack of specificity in the FDA's guides. In 1978, however, the current good manufacturing practice regulations (cGMPs) were revised and provided for process validation, so this guideline does not represent a new requirement.

Both the FDA and the industry have recognized the need to establish general guidance for the validation of manufacturing

processes, and the FDA published a draft guideline in 1983. However, this draft guideline was a very general document that addressed general principles and was applicable to both sterile and nonsterile drugs and devices. In 1984, the guideline was reissued as a draft guideline, and it was finalized in 1987. The 1987 *Validation Guidelines* merely points out the need to adequately develop and control manufacturing processes. It discusses microbiological issues and provides few specific and practical applications for the validation of manufacturing processes for a marketed solid oral dosage form.

The issue of retrospective validation and its application to marketed products is frequently encountered. This concept of using historical data (test results) along with process control and process specificity was of value until more scientific methods for demonstrating process validation evolved. It should be pointed out that retrospective validation is not merely the review of test results. It also requires that the manufacturing process be specific and the same each time a batch is manufactured. Thus, specific raw material specifications (including particle size when necessary), in-process specifications (tablet hardness, etc.), and specific manufacturing directions are required. Obviously, any failing batches attributed to the process would necessitate the conclusion that the process is not validated and is inadequate.

Prospective process validation is required, particularly for those products introduced in the last 7 to 8 years or those for which manufacturing changes have been made; however, in some cases where older products have been on the market without sufficient premarket process validation, it may be possible to validate, in some measure, the adequacy of the process by examination of accumulated test data on the product and records of the manufacturing procedures used.

III. PRODUCT DEVELOPMENT

A. PRODUCT DEVELOPMENT REPORTS

No statute or regulation specifically requires a product development report, although companies are required to produce scientific data that justify the formulation and the manufacturing and control processes. Most companies use product development reports, technology transfer reports, and others to summarize the scientific data that justify the product and process. The product development report should satisfy the needs of the company. No specific format is required for the contents of the report.

It is suggested that a company develop a product development standard operating procedure (SOP) that describes the development process, the documentation requirements, and the individuals responsible for approving the filed process. This SOP can be brief, and again, no legal requirement exists

stating that companies must produce such an SOP. Failure to have a formal development report is not a GMP deficiency, nor is it a filing requirement to have a formal development report; however, where such reports *are* written, the development data found in these reports should include the following.

1. Drug Substance Characterization

Characterization of the chemical and physical properties of the drug substance is one of the most critical steps in the development of a solid dosage form. Chemical properties, especially the identification of impurities, are very important. In addition, the physical properties of the active pharmaceutical ingredient (API), such as solubility, polymorphism, hygroscopicity, particle size, density, etc., must be addressed. The literature and actual experience demonstrate that the physical quality (e.g., particle size of raw materials) can sometimes have a significant impact on the availability and clinical effect of a dosage form drug; therefore, it is appropriate that the physical characteristics of a drug substance be characterized, that the impact of the physical characteristics be determined, and that a specification for the bulk drug product be established, if necessary.

Development data will vary between new drugs and generics (e.g., characterization and establishment of specifications for the drug substance). In most cases, the manufacturing process for a new drug substance (new chemical entity) is developed and scaled up before the dosage form. In early development stages, very little information is available regarding polymorphic forms, solubility, etc. Consequently, changes to the manufacturing process for the drug substance may change the purity profile or physical characteristics and thus, cause problems with the finished dosage form. Although these types of problems are expected, the firm must investigate and document batch failures for the API and dosage form product.

On the other hand, generic manufacturers usually purchase drug substances from API manufacturers who may not be willing to supply information regarding the synthesis or analysis of the drug substance; therefore, the manufacturer of the finished dosage form must perform the appropriate tests to characterize the drug substance chemically and physically and establish appropriate specifications. This may require developing analytical methods to identify impurities. In some cases, this information can be obtained from literature searches.

In either case, it is important that each firm compare the drug substance used to manufacture the biobatch or clinical batch(es) and the drug substances used for the commercial batches, including specifications, analytical methods, and test results for the lots of each drug substance. Remember that the safety of the drug may be based upon the type and level of impurities, and different physical characteristics may affect dissolution or content uniformity. This is particularly important for those drug substances that are poorly soluble in water.

For those products on which biostudies have been conducted, the physical characteristics of the drug substance

used for the study should serve as the basis for the physical specifications.

It is widely recognized that when discussing *in vivo* release rates and drug absorption rates, fast and immediate release is not always best. For some “immediate”-release drug products, such as carbamazepine tablets, a slower release is desired; therefore, it is frequently desirable to have minimum and maximum particle size specifications to control the release rate. For example, micronizing or milling a drug substance to provide a greater surface area of the substance may also result in faster dissolution and possibly, faster absorption and higher blood levels. Such changes to improve the dissolution may not always be desired.

In addition to release or dissolution, variation in particle size, particle shape, and/or bulk density can also have an effect on the uniformity of dosage forms, particularly those manufactured by direct compression or direct encapsulation.

Particulate solids, once mixed, have a tendency to segregate by virtue of differences in the shape, size, and density (other variables are also important) of the particles of which they are composed. This process of separation occurs during mixing as well as during subsequent handling of the completed mix. Generally, large differences in particle size, density, or shape within the mixture result in instability in the mixture. The segregation process normally requires energy input and can be reduced following mixing by careful handling.

Some manufacturers establish wide ranges for specifications. These must be established based on a GMP and validation perspective. Even though a wide range for a physical specification, such as particle size or surface area, may be established in a filing, it is expected that such ranges will be verified during validation of the process. In a recent court decision, the judge ruled that companies cannot hide behind approval of processes listed in an application when these processes do not work. In other words, the approval of a filing has no impact on processes that do not perform consistently. For example, in a particular filed process, it was determined that particle size would have no effect on drug absorption and dissolution, and a wide-range particle size specification was established; however, during the GMP review, it was found that variation in particle size did have a major effect on content uniformity. Therefore, a tighter particle size specification had to be established.

Control of the physical characteristics of the excipient is also important, because variations in such characteristics may also affect the performance of the dosage form. Changes in particle size of some excipients, for example, may affect content uniformity. In other cases, a change in the supplier of an excipient or lubricant may affect dissolution or bioavailability. In fact, the release of the active ingredients in some products is timed by varying lubricant blending time and concentration. The literature contains many examples of lubricant processing causing major changes. Such changes in excipients illustrate deficiencies in the utilization of retrospective validation; for such validation to be satisfactory, control of all parameters and key steps in the process is necessary.

The control of mixing times and physical characteristics of all ingredients is critical to successful validation of all formulations and processes. A major question that must be addressed is the need for testing physical characteristics (particle size) for each batch of excipient. For many single-source excipients, particle size is a supplier specification and is usually tightly controlled. Having established a specification and not testing each lot of excipient upon receipt may be satisfactory in such cases; however, for some multisource excipients, and where the dosage formulator expects to shift sources of supply, some resulting differences in physical characteristics (particle size) may have an effect on dose uniformity and dissolution. A definite justification should exist for not testing lots of excipients for physical characteristics.

2. Manufacturing Procedures

Procedures used to manufacture development batches must be specific and well documented. This is necessary for scale-up and subsequent comparison with the commercial process. This is another area where differences between new drug application (NDA)/new animal drug application (NADA) and abbreviated new drug application (ANDA)/abbreviated new animal drug application (ANADA) products arise. In the case of the NDA/NADA, there will be several clinical and/or test batches manufactured over a period of time showing changes in the process as more is learned about the drug and the process. The level of documentation should increase as the process becomes more defined and the firm begins phase II and III studies.

The generic product focus is on the biobatch. Again, the process used to manufacture the biobatch must be well defined and well documented; test batches must be manufactured to establish that biobatch manufacture is reproducible.

3. In-Process Testing

Specific specifications required to control the manufacturing process must be established and justified. Doing so will require granulation studies, including blend uniformity, sieve analysis, and moisture.

4. Finished Product Testing

Testing for standards given in FDA monographs, such as content uniformity (when a specification applies), assay, hardness, friability, dissolution, and others, is essential.

5. Dissolution Profile

The dissolution profiles for the biobatch or pivotal clinical batches should be evaluated in the product development report. A good correlation should exist between the dissolution specifications and test results for the biobatch/clinical test batches and the full-scale commercial process.

6. Stability

The Center for Drug Evaluation and Research (CDER) conducts an evaluation of stability data and approves proposed expiration dates. The product development report should

contain an evaluation of the stability data that have been obtained. During postapproval inspections, stability data are reviewed by the field. An FDA inspection, therefore, inevitably includes an audit of underlying raw data and analytical worksheets to ensure the accuracy and authenticity of stability data contained in summary reports.

B. PREAPPROVAL INSPECTIONS

Validation of three full-size commercial lots is not required for approval of the marketing application; however, the firm must have data that justify the full-scale commercial process filed in the NDA/ANDA or NADA/ANADA application. In other words, the firm should have sufficient research on the test batches to establish specifications for the manufacturing and control procedures listed in the application. These data and specifications form the basis for the validation protocol that may be developed following approval of the application. The final step in the process is demonstration (validation) runs to prove that the process will perform consistently. Firms should validate the process using the specifications listed in the filing. To evaluate the proposed manufacturing process, the following areas must be covered during the preapproval inspection.

1. Master Formula

This document must include specific manufacturing directions for the full-scale commercial process, including in-process and finished product specifications. Make sure that the process filed in the application complies with the process used to manufacture the bio/clinical batch. In some cases, the process may be different after scale-up. This is acceptable if the firm has data showing that the product produced by this process will be equivalent. Data such as granulation studies, finished product test results, and dissolution profiles are used to document that the two processes are equivalent.

2. History Section of the Application

This section of the application is used to identify the biobatch or batches used for pivotal clinical studies. Any batches in which in vivo studies were carried out, particularly those for which in vivo studies showed a lack of equivalency, are subject to review.

3. Development Data (Product Development Report)

The firm cannot logically proceed to the validation step without some prior evaluation of the process. During the development phase, the critical process parameters must be identified and specifications established. These predetermined specifications must be established during the development of the process, with the biobatch or pivotal clinical batch serving as the reference batch.

The development of a solid dosage form will vary from firm to firm and will be dependent upon the specific product and process; however, the formula ranges, physical and chemical specifications of the drug substance and excipients,

in-process variables, and interaction effects of the dosage form ingredients under normal and stress aging conditions should be confirmed by limited challenge in pilot-scale and production-size batches.

Such development data serve as the foundation for the manufacturing procedures, specifications, and validation of the commercial process. In some cases, manufacturers establish specifications such as hardness and particle size during validation; however, as the validation definition states, specifications must be determined prior to validation of the process.

When a manufacturer files a manufacturing process in an application, the FDA expects that the process will yield a product that is equivalent to the product on which the bio study or pivotal clinical study was conducted; therefore, it is important that the development and scale-up of the process be well documented, so that a link between the bio/clinical batches and the commercial process can be established. The firm should have data such as granulation studies, finished product test results, and dissolution profiles that may be used to document that the two processes are equivalent.

In most cases, *in vitro* data alone will not be sufficient to document equivalency. The bioequivalency evaluation must be made by qualified individuals, and the firm should have a signed statement documenting that the processes are equivalent.

4. Inspection of the Facilities

The FDA inspectors physically inspect the facility to ensure that the area and ancillary equipment such as air handling and water systems are suitable for the proposed manufacturing process. Construction of new walls, installation of new equipment, and other significant changes must be evaluated for their impact on the overall compliance with GMP requirements. These inspections include facilities used for development batches and to be used for full-scale production batches.

5. Raw Materials

The FDA inspectors review the information contained in the raw materials section of the product development report. Inventory records are a good source for identification of batches used for product development and bio studies.

6. Laboratory

The regulatory inspection of a laboratory involves observations of the laboratory in operation and of the raw laboratory data to evaluate compliance with GMPs and to specifically carry out the commitments in an application or Drug Master File (DMF). The raw laboratory data, laboratory procedures and methods, laboratory equipment, and methods validation data must be periodically reviewed to ensure overall quality of the laboratory operation and the ability to comply with GMP regulations.

It is not uncommon for the FDA inspecting team to identify foreign peaks and impurities not filed or discussed in applications. Also, many inspections reveal laboratory test methods that are not validated. The transfer of laboratory methods and technology from the research and development department to

the quality control department should be firmly established. Be aware that FDA inspectors are not bound by any rules to restrict their investigation to particular product files. They can and often do pick up data files, charts, and recordings that are lying around in the area and will raise queries. It is a good idea to keep these records properly secured to avoid unnecessary distractions in the inspection process.

7. Equipment

At the time of the preapproval inspection, the FDA expects that the equipment will be in place and qualified. New products, particularly potent drug products, can present cleaning problems for existing equipment. Manufacturers must validate their cleaning processes for the new drug/dosage form.

IV. VALIDATION PROTOCOLS

Validation protocols are developed from the information obtained during product development research. These protocols list the specific manufacturing process and specifications that will be tested during the demonstration runs. Validation protocols are not required for the preapproval inspection but are required for postapproval inspections. Key processes and control specifications should have been established during product development research and should be carefully listed in the validation protocol.

V. DEMONSTRATION RUNS (VALIDATION OF THE PROCESS)

A. TEST BATCH RELATIONSHIPS

A validated process should produce a dosage form that is directly related to the dosage form on which equivalency and/or efficacy and safety data were determined. This is usually the test batch; therefore, ensure that the process used to make the test batch has been used for routine full-scale production batches. These processes and specifications must be equivalent, and the importance and need for good control of the manufacturing process used to produce the test and clinical batches cannot be overemphasized. Typically, the control of test batches includes, among other components, drug substance characterization, granulation analyses, and dose uniformity and dissolution profiles. The validation report should compare the manufacturing processes and specifications for the test batches with those for the full-scale batches; however, such findings may be contained in other documents, such as bioequivalency reports, and should be readily available.

B. POSTAPPROVAL PROSPECTIVE VALIDATION INSPECTIONS

In the postapproval, premarketing phase, the FDA reviews the validation protocol and validation report. Obviously, a validation protocol that lists all the variables and parameters that should be controlled when the process is validated cannot be written until the variables are identified in the development phase. In many of the FDA's postapproval, premarketing inspections, validations

(and consistency) are often not well established. Failures of production-size batches include dissolution, lack of content uniformity, and variable potency. Validation reports on batch scale-ups may also reflect selective reporting of data. Several parameters must be considered when ensuring validation of the manufacturing process for an oral solid dosage form. For example, at least eight major areas must be evaluated:

- Biobatch relationship
- Raw materials
- Manufacturing procedures and equipment
- Granulation/mix analysis
- In-process controls
- Test results with validated methods
- Investigations/product failures
- Site review

1. Raw Materials

Physical characteristics of raw materials can vary among manufacturers of drug substances and on occasion, have varied from lot to lot from the same manufacturer. The examination of retained samples of the lots of raw materials can reveal physical differences between the two lots and thus should become a routine measure. Quantitative compliance must be present for the raw material inventory records to evaluate the use of the drug substance in biobatch, clinical, and/or test batches. Make sure to account for the quantities and sources of materials used and the testing performed. Physical specifications for drug substances should be well established. If no such specifications, or only a very vague specification, are available, support data should exist to demonstrate that dissolution profiles and content uniformity will be satisfactory over a wide range of particle sizes. For example, a manufacturer may establish a specification that 90% of the particles must be less than 300 microns. For validation of this process, one would expect the use of micronized as well as nonmicronized material with particles close to 300 microns in size.

2. Manufacturing Procedures and Equipment

Regardless of the nature of the specificity of the manufacturing directions contained in the application, a detailed master formula with specific manufacturing directions and specifications must have been developed before any validation protocol is prepared and before the validation process begins. The basic premise of validation of a process is that a detailed process already exists that, it is hoped, will be shown to perform consistently and produces products in compliance with predetermined specifications; therefore, detailed manufacturing directions specifying equipment and operating parameters must be specified in the master formula.

The importance of specific written directions and specifications cannot be overemphasized. For example, problem areas include

- Failure to specify the amount of granulating solution, resulting in overwetting and dissolution failures of aged batches

- Failure to specify the encapsulation machine and operating parameters, such as dosing discs, resulting in weight variation failures
- Failure to specify the compression machine(s) and operating parameters, resulting in content uniformity failures

In addition to the concern about specific manufacturing directions, equipment presents its own set of unique problems that have to be considered in the control of the manufacturing and the validation processes. The following is a brief description of some issues associated with equipment.

a. Blenders

Many solid oral dosage forms are made by direct compression. The two types of mixers are low energy and high energy. The low-energy mixers represent the classical type of slow mixers, such as ribbon blenders, tumblers, and planetary pony pan; the high-energy mixers include some basic features of the low-energy mixers but also contain some type of high-speed blade, commonly termed an *intensifier bar* or *chopper*. The various types of mixers can be described as follows.

1. *Pony pan type*. This mixer has historically been used for the manufacture of wet granulations. Because of its open pan or pot, granulating agents such as starch paste can be added while mixing. Because the pan is open at the top to allow the mixing blades to penetrate the powder, mixing operations are usually dusty and can lead to potential cross-contamination problems. The usefulness of these mixers is limited to wet granulating. This type of mixer provides good horizontal (side-to-side) blending; however, vertical (top-to-bottom) mixing does not occur. Powder placed in the mixer first will be poorly mixed. Segregation or unmixing is also a recognized problem. To minimize this problem, some manufacturers have emptied the pan contents halfway through the mixing cycle in an attempt to turn the powder over at the bottom of the mixer. To alleviate the problem of the lack of mixing along the sides or walls of the pan, manufacturers have used a hand-held steel paddle at various times during mixing. This type of mixing is difficult to control and reproduce; thus, it would be difficult to validate.

The potential for segregation and poor mixing along the sides and particularly the bottom of the pony blender makes this type of blender less desirable for the dry blending of granulations of drug products; consequently, whenever such dry blending is encountered, investigators will look for potential problems with blending validation and content uniformity. Whenever in-process samples of the granulation are collected as part of an investigation or inspection, the formula card and the weight of the dosage unit to be manufactured are needed for the calculations.

2. *Ribbon blender.* In the ribbon blender, powder is mixed both horizontally and vertically. Loading operations can be dusty, but during the actual blending the unit is enclosed, thereby limiting the amount of dust released to the environment. The major and potentially the most serious problem with the ribbon blender is the “dead spot” or zone at the discharge valve in some of these blenders. To compensate for this dead spot, manufacturers have to recycle the powder from this area at some point during the mixing process. Obviously, adequate and very specific directions and procedures should be available to ensure that this critical step is performed. Another concern with this mixer is the poor mixing at the ends of the center horizontal mixing bar and at the shell wall because of blade clearance. The level of powder placed in this mixer is normally at the top of the outer ribbon blade, and as with other mixers, care must be taken not to overfill the mixer. Cleaning problems, particularly at the ends of the ribbon blender where the horizontal bar enters the blender, have been identified. Manufacturers who do not disassemble and clean the seals/packing between batches should have data to demonstrate the absence of foreign contaminants between batches of different products processed in the blender.
3. *Tumbler blender.* Common mixers of this type include the twin shell and double cone. These mixers exert a gentle mixing action; because of this mild action, lumps of powder will not be broken up and mixed. Powders may also clump due to static charges, and segregation can occur. Low humidity can contribute to this problem. Blending under very dry conditions has been found to lead to charge buildup and segregation, while blending of some products under humid conditions has led to lumping. More so than with other mixers, powder charge levels should not exceed 60% to 65% of the total volume of the mixer. Fabricators of tumbler-type blenders identify the volume as the actual working capacity and not the actual volume of the blender. It is important to correlate the bulk density of the granulation with the working capacity of the blender.
4. *High-shear (high-energy) mixers.* The fabricators of these mixers include GRAL, Diosna, and Littleford/Lodge. These mixers are highly efficient and ideally suited for wet granulations. End points of wet granulations can be determined by measurements on a gauge of the work required to agitate the blend. The mixing vessel is enclosed, and dust only enters the environment when loading. One of the problems associated with these mixers is the transfer or conversion of products blended in the older types of mixers to these blenders. Mixing times are going to be different, and the physical characteristics of the blend may also be different. These mixers are very efficient. For wet granulations, it is important to control the rate and amount of addition of the

solvent. Because of their efficiency, drug substance may partially dissolve and recrystallize upon drying as a different physical form. An intensifier bar in the center of the blender rotates at very high speeds to break down the smaller, harder agglomerates. A major disadvantage of this type of blender is that the extremely high speed of the intensifier bar generates considerable heat, which can sometimes result in charring of some sugar-based granulations. It should be pointed out that these same comments are applicable to other high-energy mixers that also rely on high-speed choppers to disperse powders. Also, cleaning of the blender requires disassembly of the intensifier bar between products.

5. *Plastic bag.* Any discussion of mixers would not be complete without addressing the plastic bag. Firms have resorted to the blending or manufacture of a trituration in a plastic bag. Obviously, it is very difficult to reproduce such a process, and there is the potential for loss of powder as a result of breakage or handling. The use of a plastic bag cannot be justified in the manufacture of a pharmaceutical product. When the plastic bag has been used, directions are usually not specific, and one would not know by reading the directions that a plastic bag was employed. Some companies have been known to hide the use of plastic bags by indicating in the manufacturing records that a blender was used; these bags are easy to spot during an inspection, and the practice is highly discouraged.

b. Dryers

The two basic types of dryers are the oven dryer, in which the wet granulation is spread on trays and dried in an oven, and the fluid-bed dryer, in which the wet granulation is “fluidized” or suspended in air. Generally, the fluid-bed dryer yields a more uniform granulation with spherical particles; however, this may result in compression problems that may require additional compression force. It is not unusual to see manufacturers change from an oven dryer to the fluid-bed dryer; however, such a change should be examined for equivalency with *in vitro* testing such as hardness, disintegration, and comparative dissolution and stability testing.

Other issues of concern with drying include moisture uniformity and cross-contamination. Tray dryers present more moisture uniformity problems than fluid-bed dryers. Obviously, a dryer should be qualified for heat uniformity and a program developed to ensure moisture uniformity in granulations at the end point of drying. With respect to fluid-bed dryers, moisture problems can occur if the granulation is not completely fluidized.

In regard to cross-contamination, oven dryers, particularly those in which air is recirculated, present cross-contamination problems, because air recirculates through a common filter and duct. For fluid-bed dryers, the bag filters present cross-contamination problems. In order to minimize such problems, manufacturers should use product-dedicated bags.

c. Tablet and Capsule Equipment

Another important variable in the manufacturing process is the tablet press or encapsulating machine. The newer dosage form equipment requires granulations with good flow characteristics and good uniformity. The newer tablet presses control weight variation by compression force and require a uniform granulation to function correctly. The setup of the microprocessor-controlled tablet press usually includes some type of challenge to the system. For example, a short punch is sometimes placed among the other punches. If the press is operating correctly, it will alarm when a lower- or higher-weight tablet is compressed.

Different tablet compression equipment can cause dose uniformity, weight uniformity, and hardness problems. For example, vibrations during tablet compression can cause segregation of the granulation in the feed hopper. The speed of the machine can affect the fill of the die and tablet weight; therefore, as previously noted, it is important to have specific operating directions.

Many unit operations now provide for blending in totes with direct discharge of the tote into the tablet compression equipment. Because of segregation problems at the end of the discharge, tablets from the end of the compression should be tested for content uniformity. The use of inserts in totes has been shown to minimize segregation.

With regard to the newer computer-controlled tablet compression equipment, buckets of tablets are often rejected because of potential weight variation problems. The disposition of these tablets, as well as the granulation and tablets used to set up the press, should be documented, and reworking processes must be validated.

With regard to encapsulation operations, the hygroscopic nature of gelatin capsules and some of the granulations require humidity controls for storage of the empty capsules and their subsequent filling. The scale-up of capsule products has also presented some problems because of the different types of encapsulation equipment. Older equipment that operated on gravity fill, such as Lilly and Parke-Davis machines, was commonly used for manufacturing capsules in clinical manufacturing areas. When formulations were scaled up to high-speed encapsulation equipment, flow problems and weight variation resulted. Additionally, some of the newer equipment provides for the formation of a slug, which could have an impact on dissolution.

Many firms, in order to recondition (rework) batches, pass those particular batches through a sorter, such as the MOCON VERICAP®. This machine works on the principle of current (dielectric constant), and moisture variation in the filled capsules can cause inaccurate results. Manufacturers should qualify equipment and examine equipment logs for these sorting machines to identify batches with weight problems. Data supporting the accuracy of equipment in regard to rejecting low- or high-weight capsules should be available during an FDA inspection.

d. Coating Equipment

Many tablets are now coated with an aqueous film coat, which is usually very soluble. Current technology provides for fixed

sprays of the coating solution. The volume of coating solution, rate, and temperature can be controlled by some of the more highly automated operations; however, for many sugar-coated, enteric-coated, and delayed-release products, some components of the coating are not highly soluble, and that part of the process is performed manually. Generally, the shellac undercoat used for sugar-coated tablets has presented disintegration/dissolution problems, particularly in aged samples.

With respect to poor disintegration, the example of ferrous sulfate tablets probably represents the classical example. Over the years, many different manufacturers have issued recalls for poor disintegration of coated ferrous sulfate tablets; likewise, problems with poor dissolution have been attributed to the coating process. Again, the shellac undercoat hardens and even sometimes cracks, resulting in poor dissolution.

On many occasions, the coating process has not been validated. The number of applications of coats, volume of coating solution in a specific application, and temperature of the solution during application are all parameters that must be addressed. For example, the temperature of application and even heat during drying have been found to cause dissolution failures in aged tablets.

Another problem associated with the coating process concerns heat applied to products that are sensitive to heat. For example, it has been shown that estrogen tablets are heat sensitive and have exhibited stability problems; thus, it is important to control this phase of the process.

For a few products, such as some of the antihistamine tablets or multivitamin tablets containing folic acid or cyanocobalamin, the drug substance is applied during the coating process. Some products require the active drug substance to be applied as a dust on tacky tablets as part of the coating process; for these products, it is particularly important to apply the drug in the coating solution through controlled applications. Again, it is important as part of the validation of these processes to demonstrate dose uniformity and dissolution and to control the parameters of the coating process.

3. Granulation/Mix Analysis

A critical step in the manufacture of an oral solid dosage form is the blending of the final granulation. If uniformity is not achieved at this stage, then one could assume that some dosage units would not comply with uniformity requirements. The major advantage of blend analysis (from a uniformity perspective) is that specific areas of the blender that have the greatest potential to be nonuniform can be sampled. This is particularly true of the ribbon-type blender and planetary or pony-type mixers.

In some cases, such as for large or tumbler-type blenders, it is impractical to sample from the blender directly. In such cases, granulations or blends could be sampled at the time of blender discharge or directly from drums. If sampling from drums, samples from the top, middle, and bottom of each drum should be collected.

In most cases, sampling thieves are readily available for sampling the small quantities that need to be taken from key areas of the blender or the drums. If samples larger than one

dosage unit must be collected, however, adequate provisions must be made to prevent excessive handling manipulation between the time of sampling and the time of analysis.

Good science and logic would seem to dictate that sample sizes of the approximate equivalent weight of the dosage unit should be sampled in order to test for uniformity. Many industrial pharmacy and engineering texts confirm this approach. Large granulation sample sizes (e.g., 1 oz) will provide little information with respect to uniformity. Generally, further mixing after sampling and prior to analysis can yield misleading results.

The acceptance criteria for granulation dose uniformity testing must be established. Although many firms evaluate dose uniformity using the compendial dose uniformity specifications (85% to 115% with a relative standard deviation [RSD] of 6 to 7.8), such specifications should be tighter where supported by the firm's historical data on the level of blend uniformity with its equipment for a given product. In many cases, compendial assay limits for the finished product (90% to 110% of label claim) are broad enough for this purpose, and most firms should be able to demonstrate blend assay results well within these limits. If larger sample sizes are taken for assay to evaluate total composite assay, then the specific U.S. Pharmacopeia (USP) or filed criteria for assay should be used.

In addition to analysis of blends for dose uniformity and potency, blends are tested for physical characteristics. A major physical parameter used to demonstrate equivalence between batches is the particle size profile. This is particularly important for comparison of the biobatch with production batches and also when processes are modified or changed. The particle size profile will provide useful information for demonstrating comparability.

Particle size profiles are particularly important for tablets made by a wet granulation process. The size and even the type of granule can affect the pore size in a tablet and have an effect on dissolution. For example, a recent dissolution failure was attributed to a change in the milling screen size, yielding a granulation with larger granules. It was a coated tablet, and the larger pores permitted increased penetration of the coating solution into the tablet, resulting in slower dissolution.

Another test that is typically performed in regard to granulation, particularly when the wet granulation process is used, is loss on drying (LOD) and/or moisture content. If organic solvents are employed, then residual solvent residues are also tested. To validate a drying process, LOD levels are determined prior to, during, and after drying in order to demonstrate times and levels. As with processing variables, levels (specifications) are established in the development phase, with the validation phase being used to confirm the adequacy of the process.

4. In-Process Testing

In-process testing is testing performed on dosage forms during their compression/encapsulation stages to ensure consistency throughout these operations. For tablets, individual tablet

weight, moisture, hardness (compression force), and disintegration tests are performed. For capsules, individual weight and moisture tests are performed. In many of the validation reports, it has been found that manufacturers have neglected to supply results of individual (not composite) dosage unit weight tests that should be performed throughout compression/encapsulation. Such testing is particularly important for capsule products, which may exhibit weight variation problems. If not part of the validation reports, the individual dosage unit weights should be recorded and be available for FDA inspectors to review.

With regard to individual capsule weights, a major question that arises concerns acceptable levels. Because most USP assay limits are 90% to 110%, it would seem reasonable that each unit manufactured complies with these specifications. It should be pointed out that 85% to 115% limits are established by the USP for variability in both blending and compression or encapsulation operations.

Because hardness and disintegration specifications are established during development and biobatch production, testing is performed to demonstrate both equivalency (comparability) and consistency.

With regard to moisture, some tablets set up upon aging as a result of poor moisture control and inadequate specifications. For example, this has been shown to be a major problem with carbamazepine tablets and often for ferrous sulfate tablets.

5. Test Results

Finished product testing, particularly assay, content uniformity, and dissolution, should be carefully recorded. With regard to dissolution, it is important to establish dissolution profiles. Validation batches with dissolution profiles not comparable to biobatches indicate nonequivalency of the manufacturing process. Depending on the discriminating nature of the dissolution test, it may also indicate lack of equivalence of the dosage forms made during validation with the biobatch. In the review of dissolution test results, it is important to eventually see results very close to 100% dissolution. In some cases, manufacturers will profile the dissolution results only to the specification; however, if lower but still acceptable results are obtained (such as 85%), it is important to continue the test by increasing the speed of the apparatus. If a product completely dissolves, yet only results in a value of 85%, it may indicate some problem with the test. Likewise, high dissolution results (115%) also indicate some problem with the test. Obviously, unusual or atypical results should be explained in the validation report.

6. Investigations and Product Failures

In any process validation exercise, a basic objective is to prove that a process is satisfactory; unfortunately, some processes are unsatisfactory and may sometimes yield unacceptable results. It is important, therefore, that when the final validation report is reviewed, all results, including failing results, are discussed and evaluated. Historically, reviews of

manufacturing processes typically show that one out of every eight batches manufactured has failed content uniformity testing. Manufacturers often recognize that the process is unsatisfactory and not validated but fail to draw this conclusion in the written validation report. This is a dangerous procedure and is often easily identified during FDA inspections.

7. Site Review

A major aspect and possibly the most critical phase of process validation is the review of data to ensure that failing batches were not omitted without justification. Additionally, manufacturers must ensure that the raw data, including analytical raw data, are accurate.



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3 Current Regulatory Status of Over-the-Counter Products

BACKGROUND

Over-the-Counter (OTC) drug products are those drugs that are available to consumers without a prescription. There are more than 80 classes (therapeutic categories) of OTC drugs, ranging from acne drug products to weight control drug products. As with prescription drugs, the Center for Drug Evaluation and Research (CDER) oversees OTC drugs to ensure that they are properly labeled and that their benefits outweigh their risks.

OTC drugs play an increasingly vital role in America's health-care system by providing easy access to certain drugs that can be used safely without the help of a health-care practitioner. This enables consumers to take control of their own health care in many situations. There are more than 100,000 OTC drug products marketed, encompassing about 800 significant active ingredients. Most OTC drug products have been marketed for many years, prior to the laws that require proof of safety and effectiveness before marketing. For this reason, the Food and Drug Administration (FDA) has been evaluating the ingredients and labeling of these products as part of "The OTC Drug Review Program." The goal of this program is to establish OTC drug monographs for each class of products. OTC drug monographs are a kind of "recipe book" covering acceptable ingredients, doses, formulations, and labeling. Monographs will continually be updated adding additional ingredients and labeling as needed. Products that conform to a monograph may be marketed without further FDA clearance, while those that do not must undergo separate review and approval through the "new drug approval system." The new drug application (NDA) system—and not the monograph system—is also used for new ingredients entering the OTC marketplace for the first time. For example, the newer OTC products (previously available only by prescription) are first approved through the NDA system, and their "switch" to OTC status is approved via the NDA system.

FDA's review of OTC drugs is primarily handled by CDER's Division of Over-the-Counter Drug Products in the Office of Drug Evaluation V. However, scientists and regulators throughout CDER, the Office of General Counsel, and other centers within FDA are routinely asked to assist in this massive effort. There is also an advisory committee, "The Nonprescription Drug Advisory Committee," which meets

regularly to assist the agency in evaluating issues surrounding these products.

REGULATORY DEFINITIONS

An OTC drug product is a drug product marketed for use by the consumer without the intervention of a health-care professional in order to obtain the product. Two post-1938 regulatory pathways exist for the legal marketing of such products: (a) marketing in compliance with an OTC drug monograph and (b) marketing under the authority of an approved product-specific NDA or an abbreviated new drug application (aNDA). The OTC drug review was established to evaluate the safety and effectiveness of OTC drug products marketed in the United States before May 11, 1972. It is a three-phase public rulemaking process (each phase requiring a *Federal Register* publication) resulting in the establishment of standards (monographs or nonmonographs) for an OTC therapeutic drug category. The first phase was accomplished by advisory review panels. The panels were charged with reviewing the ingredients in nonprescription drug products to determine whether these ingredients could be generally recognized as safe and effective for use in self-treatment. They were also charged with reviewing claims and recommending appropriate labeling, including therapeutic indications, dosage instructions, and warnings about side effects and preventing misuse. According to the terms of the review, the panels classified ingredients into three categories as follows:

- Category I: generally recognized as safe and effective for the claimed therapeutic indication
- Category II: not generally recognized as safe and effective or unacceptable indications
- Category III: insufficient data available to permit final classification

The second phase of the OTC drug review was the agency's review of ingredients in each class of drugs based on the panel's findings, on public comment, and on new data that may have become available. The agency, in turn, publishes its conclusions in the *Federal Register* in the form of a tentative final monograph. After publication of the tentative final monograph, a period of time is allotted for objections to the

agency's proposal or for requests to be submitted for a hearing before the Commissioner of FDA.

The publication of final regulations in the form of drug monographs is the third and last phase of the review process. The monographs establish conditions under which certain OTC drug products are generally recognized as safe and effective.

The term *human drug application* means an application for approval of a new drug submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) or approval of a new drug submitted under section 505(b)(2) of the FD&C Act or approval of an abbreviated new drug application under section 505(j) of the FD&C Act or licensure of certain biological products under section 351 of the Public Health Service Act. A 505(b)(1) application is an application

that contains full reports of investigations of safety and effectiveness. The investigations the applicant relied on for approval were conducted by, or for, the applicant, or the applicant has obtained a right of reference or use for the investigations.

Appendix I to this chapter is a listing of OTC ingredients and their respective recommended uses and classification.

The U.S. FDA has recently issued guidance on unproven safety of OTC drug components (current as of April 2008) (CITE: 21CFR310.545). A number of active ingredients have been present in OTC drug products for various uses, as described later. However, based on evidence currently available, there are inadequate data to establish general recognition of the safety and effectiveness of these ingredients for the specified uses. These ingredients are listed as Appendix II to this chapter.

APPENDIX I OTC INGREDIENT LIST

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
2-Ethylhexyl-4-phenylbenzophenone-2-carboxylic acid					
Topical analgesic	Sunscreen	Sunscreen	IISE	IISE	Pending
Acetaminophen					
Internal analgesic	Internal analgesic	Analgesic	I	I	Pending
Internal analgesic	Internal analgesic	Antipyretic	I	I	Pending
Internal analgesic	Internal analgesic	Antirheumatic	IIE	Not OTC	n/a
Miscellaneous internal	Menstrual/diuretic	Analgesic	I	I	Pending
Miscellaneous internal	Overindulgence in alcohol/food	Overindulgence remedies (hangover)	I	I	Pending
Sedative	Nighttime sleep aid	Sleep aid	IIE	IIE	[54 FR 6826]
Sedative	Daytime sedative	Sedative	IISE	IISE	310.519(a)
Acetanilide					
Internal analgesic	Internal analgesic	Analgesic	IIS	IIS	Pending
Internal analgesic	Internal analgesic	Antipyretic	IIS	IIS	Pending
Internal analgesic	Internal analgesic	Antirheumatic	IISE	not OTC	n/a
Acetic acid					
	Otic	Swimmer's ear prevention	n/a	IIIE	310.545(15)(i)
Contraceptive/vaginal	Vaginal	Alters vaginal pH	IIIE	Withdrawn	n/a
Miscellaneous external	Wart remover	Wart remover	IIISE	IIISE	[55 FR 33254]
Acetic acid, glacial					
Miscellaneous external	Wart remover	Wart remover	IIIE	IIISE	[55 FR 33254]
Miscellaneous external	Corn/callus remover	Corn/callus remover	IIIE	IIISE	[55 FR 33261]
Acetone					
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(18)(ii)
Acidulated phosphate fluoride (sodium fluoride/sodium phosphate/phosphorous acid)					
Dental	Anticaries	Anticavity dental rinse	I	I	355.10(a)(2)(ii)
Acidulated phosphate fluoride (sodium fluoride/hydrogen fluoride)					
Dental	Anticaries	Anticavity dental rinse	IIS	IIS	355.10(a)(2)(ii)
Acidulated phosphate fluoride (sodium fluoride/sodium phosphate dibasic/phosphorous acid)					
Dental	Anticaries	Anticavity dental rinse	I	I	355.10(a)(3)(ii)
Agar					
Laxative	Laxative	Bulk laxative	IIIE	IIIE	310.545(12)(i)
Alanine					
Miscellaneous internal	Benign prostatic hypertrophy	Benign prostatic hypertrophy	IIE	IIISE	310.532(a)
Alcloxa					
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(1)
Antimicrobial II	Antifungal	Antifungal	IIIE	IIIE	310.545(22)(ii)
Hemorrhoidal	Anorectal	Keratolytic (external)	I	I	346.20(a)
Hemorrhoidal	Anorectal	Keratolytic (intrarectal)	I	I	346.20(a)
Alcohol					
Miscellaneous external	Alcohols (topical)	Antiseptic	I	Defer	n/a

(Continued)

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Mercury	First aid antiseptic	n/a	I	Pending
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	Defer	n/a
Miscellaneous external	External analgesic	Insect bite/sting	IISE	IISE	310.545(a)(10)(vi)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(18)(v)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(18)(vi)
Miscellaneous external	Skin protectant	Fever blister (topical)	IISE	IISE	Pending
Miscellaneous internal	Digestive aid	Digestive aid (immediate postprandial upper abdominal distress [ippuad])	n/a	n/a	310.545(a)(18)(ii)
Miscellaneous internal	Menstrual/diuretic	Analgesic adjuvant	n/a	IISE	310.545(a)(24)(i)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Alcohol, ethoxylated alkyl					
n/a	Insect bite/sting	Insect bite/sting	n/a	n/a	310.545(a)(18)(v)(A)
Aldioxa					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(ii)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIIE	Pending
Alfalpa					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Alfalpa leaves					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Alginic acid					
Antacid	Antacid	Antacid	IIIE	IIIE	[39 FR 19873]
Miscellaneous internal	Weight control	Anorectic	IIIE	IISE	310.545(a)(20)
Alkyl arylsulfonate					
Contraceptive/vaginal	Vaginal	Lowers surface tension, mucolytic effects	IIIE	Withdrawn	n/a
Alkyl dimethyl amine oxide and alkyl dimethyl glycine					
n/a	Gingivitis/plaque	Antiplaque/gingivitis	n/a	IIIE	Pending
Alkyl isoquinolinium bromide					
Antimicrobial II	Acne	Acne	IISE	IISE	310.545(a)(1)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff	IISE	IIIE	310.545(a)(7)
Allantoin					
Contraceptive/vaginal	Vaginal	Minor irritations	IIIE	Withdrawn	n/a
Dental	Oral mucosal injury	Wound healing agent	IIIE	IIIE	310.534(a)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis/psoriasis	IIIE	IIIE	310.545(a)(7)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)

(Continued)

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	Pending
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	IISE	Pending
Miscellaneous external	Hair growth/loss	Hair grower	IISE	n/a	310.527(a)
Miscellaneous external	Skin protectant	Diaper rash	Defer	I	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	I	Pending
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IISE	Pending
Miscellaneous external	Corn/callus remover	Corn/callus remover	IISE	IISE	[55 FR 33261]
Topical analgesic	Skin protectant	Skin protectant	I	I	347.10(a)
Topical analgesic	Skin protectant	Wound healing agent	IIIE	IIIE	310.545(a)(18)(i)(A)
Allantoin (with aminobenzoic acid)					
Topical analgesic	Sunscreen	Sunscreen	IIIE	IIIE	[64 FR 27682]
Allyl isothiocyanate					
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	IISE	IISE	310.545(a)(6)(ii)(A)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IISE	310.545(a)(10)(v)
Topical analgesic	External analgesic	Counterirritant	I	I	Pending
Almadrate sulfate					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIIE	n/a	310.545(a)(8)(ii)
Aloe					
n/a	Skin protectant	Diaper rash	n/a	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Minor irritations	IIIE	Withdrawn	n/a
Laxative	Laxative	Stimulant laxative	I	I/IIIS	310.545(a)(12)(iv)(C)
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Aloe extract					
n/a	Laxative	Stimulant laxative	n/a	n/a	310.545(a)(12)(iv)(C)
Aloe flower extract					
n/a	Laxative	Stimulant laxative	n/a	n/a	310.545(a)(12)(iv)(C)
Aloe vera (see Aloe)					
n/a	Gingivitis/plaque	Antiplaque/gingivitis	n/a	IIIE	Pending
Aloin					
Laxative	Laxative	Stimulant laxative	IIISE	IIISE	310.545(a)(12)(iv)(A)
Alum, ammonium					
Contraceptive/vaginal	Vaginal	Astringent	IIIE	Withdrawn	n/a
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Oral cavity	Astringent	Astringent	I	Defer	n/a
Oral cavity	Oral health care	Astringent	I	I	Pending
Alum, potassium					
Antimicrobial II	Antifungal	Antifungal	IIIE	IIIE	310.545(a)(22)(ii)
Antiperspirant	Antiperspirant	Antiperspirant	IIISE	IIISE	310.545(a)(4)
Contraceptive/vaginal	Vaginal	Astringent	IIIE	Withdrawn	n/a
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(18)(ii)
Oral cavity	Oral health care	Astringent	I	I	Pending
Aluminum acetate					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending

(Continued)

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	External analgesic	Astringent	I	I	347.12(a)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Astringent	I	I	347.10(a)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIISE	Pending
Aluminum bromohydrate					
Antiperspirant	Antiperspirant	Antiperspirant	IISE	IISE	310.545(a)(4)
Aluminum carbonate gel (basic)					
Antacid	Antacid	Antacid	I	I	331.11(a)(1)
Aluminum chlorhydroxy complex					
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Aluminum chloride (aerosol) (15% or less aqueous solution)					
Antiperspirant	Antiperspirant	Antiperspirant	IIIS	IIIS	310.545(a)(4)
Aluminum chloride (alcoholic solutions)					
Antiperspirant	Antiperspirant	Antiperspirant	IIS	IIS	310.545(a) (4)
Aluminum chloride (nonaerosol) (15% or less aqueous solution)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(a)
Aluminum chloride hexahydrate					
Miscellaneous external	External analgesic	Astringent	n/a	IIIE	Pending
Aluminum chlorohydrate (aerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIIS	I	350.10(b)
Aluminum chlorohydrate (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(b)
Aluminum chlorohydrate (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(c)
Aluminum chlorohydrate (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(c)
Aluminum chlorohydrate (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(d)
Aluminum chlorohydrate (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(d)
Aluminum chlorohydrate (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(e)
Aluminum chlorohydrate (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(e)
Aluminum chlorohydrate (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(f)
Aluminum chlorohydrate (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(f)

(Continued)

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Aluminum dichlorohydrate propylene glycol (aerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIIS	I	350.10(g)
Aluminum dichlorohydrate propylene glycol (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(g)
Aluminum hydroxide					
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Antimicrobial II	Antifungal	Acne	IIE	IIE	310.545(a)(1)
Antacid	Antacid	Antacid	I	I	331.11(a)(2)
Laxative	Antidiarrheal	Antidiarrheal	IIIE	IIIE	310.545(a)(3)(i)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIISE	310.545(a)(18)(iii)
Miscellaneous internal	Digestive aid	Digestive aid (ipquad)	IIE	n/a	310.545(a)(8)(ii)
Miscellaneous internal	Overindulgence in alcohol/food	Overindulgence remedies (hangover)	I	I	Pending
Topical analgesic	Skin protectant	Skin protectant	I	I	347.10(b)
Aluminum hydroxide gel					
n/a	Skin protectant	Poison ivy/oak/ sumac	n/a	I	347.10(b)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	I	I	346.14(1)
Hemorrhoidal	Anorectal	Protectant (external)	I	I	346.14(1)
Internal analgesic	Internal analgesic	Corrective	I	n/a	n/a
Miscellaneous internal	Overindulgence in alcohol/food	Overindulgence remedies (hangover)	I	I	Pending
Topical analgesic	Skin protectant	Skin protectant	I	I	347.10(b)
Aluminum hydroxide sucrose powder hydrated					
Antacid	Antacid	Antacid	I	I	331.11(a)(2)
Aluminum hydroxide–hexitol, stabilized polymer					
Antacid	Antacid	Antacid	I	I	331.11(a)(2)
Aluminum hydroxide–magnesium carbonate, codried gel					
Antacid	Antacid	Antacid	I	I	331.11(a)(2)
Aluminum hydroxide–magnesium trisilicate, codried gel					
Antacid	Antacid	Antacid	I	I	331.11(a)(2)
Aluminum phosphate gel					
Antacid	Antacid	Antacid	I	I	331.11(i)(1)
Miscellaneous internal	Hypophosphatemia/hyperphosphatemia	Hypophosphatemia	IIS	IIS	310.541(a)
Aluminum phosphate gel (when used as part of antacid combination)					
Antacid	Antacid	Antacid	I	I	331.11(a)(4)
Aluminum sesquichlorohydrate (aerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIIS	I	350.10(h)
Aluminum sesquichlorohydrate (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(h)
Aluminum sesquichlorohydrate propylene glycol (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(j)

(Continued)

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Aluminum sesquichlorohydrate polyethylene glycol (aerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIIS	I	350.10(i)
Aluminum sesquichlorohydrate polyethylene glycol (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(i)
Aluminum sulfate					
Antimicrobial II	Antifungal	Antifungal	IIIE	IIIE	310.545(a)(22)(ii)
Antiperspirant	Antiperspirant	Antiperspirant	IIISE	IIISE	310.545(a)(4)
Miscellaneous external	External analgesic	Astringent	IIIE	n/a	Pending
Miscellaneous external	Skin protectant	Astringent	IIIE	I	347.12(b)
Aluminum sulfate, buffered (aerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIIS	IIIS	310.545(a)(4)(ii)
Aluminum sulfate, buffered (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	310.545(a)(4)(ii)
Aluminum zirconium octachlorohydrate (aerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIS	IIS	310.502(a)(2)
Aluminum zirconium octachlorohydrate (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(k)
Aluminum zirconium octachlorohydrate glycine (aerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIS	IIS	310.502(a)(2)
Aluminum zirconium octachlorohydrate glycine (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(l)
Aluminum zirconium pentachlorohydrate (aerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIS	IIS	350.10(m)
Aluminum zirconium pentachlorohydrate (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(m)
Aluminum zirconium pentachlorohydrate glycine (aerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIS	IIS	310.502(a)(2)
Aluminum zirconium pentachlorohydrate glycine (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(m)
Aluminum zirconium tetrachlorohydrate (aerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIS	IIS	310.502(a)(2)
Aluminum zirconium tetrachlorohydrate (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(o)
Aluminum zirconium tetrachlorohydrate glycine (aerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIS	IIS	310.502(a)(2)
Aluminum zirconium tetrachlorohydrate glycine (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(p)
Aluminum zirconium trichlorohydrate (aerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIS	IIS	310.502(a)(2)
Aluminum zirconium trichlorohydrate (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(q)

(Continued)

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Aluminum zirconium trichlorohydrate glycine (aerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIS	IIS	310.502(a)(2)
Aluminum zirconium trichlorohydrate glycine (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	I	I	350.10(r)
Aluminum sesquichlorohydrate propylene glycol (aerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIIS	I	350.10(r)
Aminacrine hydrochloride					
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Amiloxate					
n/a	Time and extent applications (TEA)	Sunscreen	n/a		
Amino acids					
Miscellaneous external	Hair growth/loss	Hair grower	IISE	IIE	310.527(a)
Aminobenzoic acid					
Internal analgesic	Internal analgesic	Analgesic adjuvant	IISE	IISE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antipyretic adjuvant	IISE	IISE	310.545(a) (23)(i)
Internal analgesic	Internal analgesic	Antirheumatic adjuvant	IISE	n/a	310.545(a) (23)(i)
Miscellaneous external	Hair growth/loss	Hair grower	n/a	IIE	310.527(a)
Aminobenzoic acid (PABA)					
Topical analgesic	Sunscreen	Sunscreen	I	I	352.10(b)
Aminophylline					
Cough/cold	Cough/cold (bronchodilator)	Bronchodilator	I	IIS	310.545(a)(6)(iv)(A)
Ammonia					
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	Pending
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	Pending
Ammonia solution, strong					
Miscellaneous external	External analgesic	Insect bite/sting	IISE	IISE	310.545(a)(18)(v)(A)
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(18)(v)
Topical analgesic	External analgesic	Counterirritant	I	I	Pending
Topical analgesic	External analgesic	Fever blister (topical)	n/a	IISE	310.545(a)(10)(v)
Ammonium bromide					
Sedative	Daytime sedative	Sedative	IISE	IISE	310.519(a)
Sedative	Nighttime sleep aid	Sleep aid	IISE	IISE	[54 FR 6826]
Ammonium carbonate					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	Pending
Ammonium chloride					
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
Miscellaneous internal	Menstrual/diuretic	Diuretic	I	I	Pending
Oral cavity	Oral health care	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
Sedative	Stimulant	Stimulant	IIE	IIE	[39 FR 6104]
Ammonium hydroxide					
Miscellaneous external	External analgesic	Insect bite/sting	IIIE	IIIE	310.545(a)(18)(v)(A)

(Continued)

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Skin protectant	Insect bite/sting	IIIE	IIISE	310.545(a)(18)(v)(A)
Amylase					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(8)(ii)
Amyltri cresols, secondary					
Antimicrobial II	Antifungal	Antifungal	IIISE	IIISE	310.545(a)(22)(ii)
Oral cavity	Oral health care	Antimicrobial	IIISE	IIISE	Pending
Anion and cation exchange resins buffered					
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	IIIE	IIIE	Pending
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	IIIE	IIIE	310.545(a)(10)(vii)(A)
Anise					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	n/a	n/a	310.528(a)
Anise oil					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Anise seed					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Antimony potassium tartrate					
Cough/cold	Cough/cold (expectorant)	Expectorant	IISE	IISE	310.545(a)(6)(iii)
Antipyrine					
Internal analgesic	Internal analgesic	Analgesic	IIISE	IIISE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antipyretic	IIISE	IIISE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antirheumatic	IIISE	not OTC	310.545(a)(23)(i)
Oral cavity	Oral health care	Analgesic/anesthetic	IISE	IISE	310.545(a)(14)
Ophthalmic	Ophthalmic	Analgesic/anesthetic	IIS	IIS	310.545(a)(21)(i)
Topical analgesic	Otic	Analgesic/anesthetic	IISE	IISE	[51 FR 28660]
Arginine					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Aromatic oils					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	Pending
Aromatic powder					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Aromatics					
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Asafetida					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Asclepias tuberosa					
Miscellaneous internal	Menstrual/diuretic	Dysmenorrhea	IISE	IISE	310.545(a)(24)(i)
Ascorbic acid					
Miscellaneous external	Hair growth/loss	Hair grower	IIIE	IIIE	310.527(a)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Wart remover	Wart remover	IIIE	IIIE	[55 FR 33254]
Miscellaneous external	Corn/callus remover	Corn/callus remover	IISE	IISE	[55 FR 33261]
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Asparagus					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
<i>Aspergillus oryzae</i> enzymes (except lactase enzyme from <i>Aspergillus oryzae</i>)					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Aspirin					
n/a	External analgesic	Fever blister (topical)	n/a	IIIE	310.545(a)(10)(v)
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	IIIE	310.545(a)(10)(vii)
Internal analgesic	Internal analgesic	Analgesic	I	I	Pending
Internal analgesic	Internal analgesic	Antipyretic	I	I	Pending
Internal analgesic	Internal analgesic	Antirheumatic	I	not OTC	n/a
Miscellaneous internal	Menstrual/diuretic	Analgesic	I	I	Pending
Miscellaneous internal	Overindulgence in alcohol/food	Overindulgence remedies (hangover)	I	I	Pending
Oral cavity	Oral health care	Analgesic/anesthetic	I	IIIE	Pending
Sedative	Daytime sedative	Sedative	IIIE	IISE	310.519(a)
Sedative	Nighttime sleep aid	Sleep aid	IIIE	IIIE	[54 FR 6826]
Topical analgesic	External analgesic	Analgesic/anesthetic	IIIE	IIIE	310.545(a)(10)(i)
Aspirin, aluminum					
Internal analgesic	Internal analgesic	Analgesic	n/a	IISE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antipyretic	IIIE	IIIE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antirheumatic	IIIE	Not OTC	310.545(a)(23)(i)
Aspirin, calcium					
Internal analgesic	Internal analgesic	Analgesic	I	I	Pending
Internal analgesic	Internal analgesic	Antipyretic	I	I	Pending
Internal analgesic	Internal analgesic	Antirheumatic	I	Not OTC	n/a
Miscellaneous internal	Menstrual/diuretic	Analgesic	I	I	Pending
Atropine					
n/a	Menstrual/diuretic	Menstrual	n/a	n/a	310.545(a)(24)(ii)
n/a	Internal analgesic	Analgesic	n/a	n/a	310.545(a)(23)(ii)
Hemorrhoidal	Anorectal	Anticholinergic (external)	IISE	IISE	310.545(a)(26)(i)
Hemorrhoidal	Anorectal	Anticholinergic (intrarectal)	IISE	IISE	310.545(a)(26)(i)
Atropine sulfate					
Cough/cold	Cough/cold (anticholinergic)	Anticholinergic	IIIE	IIIE	310.533(a)
Laxative	Antidiarrheal	Antidiarrheal	IIIE	IIIE	310.545(a)(3)(i)
Attapulgite, activated					
Laxative	Antidiarrheal	Antidiarrheal	IIIE	I	310.545(a)(3)(ii)
Avobenzone					
n/a	n/a	Sunscreen	n/a	I	352.10(a)
<i>Bacillus acidophilus</i>					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Bacitracin					
Antimicrobial II	Antibiotic	First aid antibiotic	n/a	I	333.110(a)
Antimicrobial II	Antibiotic	Skin wound antibiotic	IIIE	Defer	n/a
Bacitracin zinc					
Antimicrobial II	Antibiotic	First aid antibiotic	n/a	I	333.110(b)
Barosma					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Basic aluminum carbonate gel					
Miscellaneous internal	Hypophosphatemia/ hyperphosphatemia	Hyperphosphatemia	IIS	IIS	310.541(a)
Basic fuchsin					
Antimicrobial II	Antifungal	Antifungal	IIISE	IIISE	310.545(a)(22)(ii)
Bean					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Bearberry					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Bearberry (extract of <i>Uva ursi</i>)					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Bearberry fluid extract (extract of bearberry)					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Beeswax					
n/a	Insect bite/sting	Insect bite/sting	n/a	n/a	310.545(a)(18)(v)(B)
n/a	Poison ivy/oak/sumac	Poison ivy/oak/ sumac	n/a	n/a	310.545(a)(18)(vi)(B)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	310.545(a)(18)(i)(B)
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	Pending
Belladonna alkaloids					
Cough/cold	Cough/cold (bronchodilator)	Bronchodilator (inhalation)	IISE	IISE	310.545(a)(6)(iv)(A)
Cough/cold	Cough/cold (anticholinergic)	Anticholinergic	IIIE	IIIE	310.533(a)
Miscellaneous external	Corn/callus remover	Corn/callus remover	IISE	IISE	[55 FR 33261]
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Belladonna alkaloids (inhalation) <i>Atropa belladonna</i>/<i>Datura stramonium</i>					
Cough/cold	Cough/cold (anticholinergic)	Anticholinergic	IISE	IISE	310.533(a)
Belladonna extract					
Hemorrhoidal	Anorectal	Anticholinergic (intrarectal)	IISE	IISE	310.545(a)(26)(i)
Hemorrhoidal	Anorectal	Anticholinergic (external)	IISE	IISE	310.545(a)(26)(i)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Belladonna leaves, powdered extract					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Bemotrizinol					
n/a	TEA	Sunscreen	n/a	n/a	n/a
Benzalkonium chloride					
Antimicrobial I	Antimicrobial	Antimicrobial soap	n/a	IISE	Pending
Antimicrobial I	Antimicrobial	First aid antiseptic	n/a	I	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin antiseptic	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	I	I	Pending
Antimicrobial I	Antimicrobial	Skin wound protectant	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Surgical hand scrub	IIISE	IIISE	Pending
Contraceptive/vaginal	Vaginal	Minor irritations	IIISE	Withdrawn	n/a
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	IIISE	Pending
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff	IIIE	IIIE	310.545(a)(7)
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	Pending
Miscellaneous external	External analgesic	Insect bite/sting	IISE	IISE	310.545(a)(10)(vi)
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(18)(v)(A)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Benzethonium chloride					
Antimicrobial I	Antimicrobial	First aid antiseptic	n/a	I	Pending
Antimicrobial I	Antimicrobial	Surgical hand scrub	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin antiseptic	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	I	I	Pending
Antimicrobial I	Antimicrobial	Skin wound protectant	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Antimicrobial soap	n/a	IISE	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	IISE	IISE	Pending
Antimicrobial I	Antimicrobial	Health-care personnel handwash	IIIE	IIIE	Pending
Antimicrobial II	Antifungal	Antifungal	IIISE	IIISE	310.545(a)(22)(ii)
Miscellaneous external	Antifungal	Diaper rash	Defer	IISE	310.545(a)(22)(i)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/cradle cap	IIIE	IIIE	310.545(a)(7)
Miscellaneous external	External analgesic	Astringent	IISE	n/a	310.545(a)(18)(ii)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)(A)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Benzocaine					
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Contraceptive/vaginal	Vaginal	Minor irritations	IIIE	Withdrawn	n/a
Dental	Relief of oral discomfort	Oral mucosal analgesic	I	I	Pending
Dental	Relief of oral discomfort	Toothache relief	IIIE	IIIE	Pending
Hemorrhoidal	Anorectal	Anesthetic (intrarectal)	IIIE	IIIE	[55 FR 1779]
Hemorrhoidal	Anorectal	Anesthetic (external)	I	I	346.10(a)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Boil treatment	Boil treatment	IIE	IIIE	310.531(a)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Psoriasis	IIE	IIE	[56 FR 63567]
Miscellaneous external	External analgesic	Astringent	IIE	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	IIE	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	I	Pending
Miscellaneous external	External analgesic	Insect bite/sting	n/a	IIIE	Pending
Miscellaneous external	Male genital desensitizer	Male genital desensitizer	I	I	348.10(a)(1)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	I	Pending
Miscellaneous external	External analgesic	Poison/ivy/oak/sumac	Defer	IIIE	IIE (0.5–1.25%)
Miscellaneous external	Pediculicide	Pediculicide	IIE	IIE	310.545(a)(25)(i)
Miscellaneous external	Skin protectant	Astringent	IIE	IIE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	DEF	Pending
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	n/a	310.545(a)(10)(vii)
Miscellaneous external	Wart remover	Wart remover	IIE	IIE	[55 FR 33254]
Miscellaneous internal	Weight control	Anorectic	I	IIE	Pending
Oral cavity	Oral health care	Analgesic/anesthetic	I	I	Pending
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Topical analgesic	Otic	Analgesic/anesthetic	IIE	IIE	[51 FR 28660]
Topical analgesic	External analgesic	Poison ivy/oak/ sumac	IIIE	n/a	310.545(a)(10)(vii)
Benzoic acid					
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Antimicrobial II	Antifungal	Antifungal	IIIE	IIIE	310.545(a)(22)(ii)
Miscellaneous external	External analgesic	Astringent	IIE	n/a	n/a
Miscellaneous external	Hair growth/loss	Hair grower	IIE	IIE	310.527(a)
Miscellaneous external	Skin protectant	Astringent	IIE	IIE	310.545(a)(18)(ii)
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Benzoin tincture, compound					
Cough/cold	Cough/cold (expectorant)	Expectorant (topical/ inhalant)	IIIE	IIIE	310.545(a)(6)(iii)
Dental	Relief of oral discomfort	Oral mucosal protectant	I	I	Pending
Benzoin, tincture					
Cough/cold	Cough/cold (expectorant)	Expectorant	n/a	n/a	310.545(a)(6)(iii)
Benzonatate					
Cough/cold	Cough/cold (antitussive)	Antitussive	n/a	I	310.533(a)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Benzoxiquine					
Antimicrobial II	Antifungal	Antifungal	IISE	IISE	310.545(a)(22)(ii)
Benzoyl peroxide					
Antimicrobial II	Acne	Acne	I	I	Pending
Benzyl alcohol					
Dental	Relief of oral discomfort	Toothache relief	IIISE	IIISE	Pending
Dental	Relief of oral discomfort	Oral mucosal analgesic	IIISE	I	Pending
Hemorrhoidal	Anorectal	Anesthetic (external)	IIIE	I	346.10(b)
Hemorrhoidal	Anorectal	Anesthetic (intrarectal)	IIIE	IIIE	[55 FR 1779]
Miscellaneous external	Alcohols (topical)	Antiseptic	IIE	Defer	n/a
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	I	Pending
Miscellaneous external	Male genital desensitizer	Male genital desensitizer	IISE	IISE	310.545(a)(10)(iii)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	I	Pending
Miscellaneous external	Pediculicide	Pediculicide	IISE	IISE	310.545(a)(25)(i)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)(A)
Oral cavity	Oral health care	Analgesic/anesthetic	I	I	Pending
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Benzyl benzoate					
Miscellaneous external	Pediculicide	Pediculicide	IISE	IISE	310.545(a)(25)(i)
Betaine hydrochloride					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Miscellaneous internal	Stomach acidifier	Stomach acidifier	IIE	IIE	310.540(a)
Bicarbonate					
Antacid	Antacid	Antacid	n/a	n/a	331.11(b)
Bile salts/acids					
Laxative	Laxative	Stimulant laxative	IIISE	IIISE	310.545(a)(12)(iv)(A)
Biotin					
Miscellaneous external	Hair growth/loss	Hair grower	n/a	IISE	310.527(a)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Bisacodyl					
Laxative	Laxative	Stimulant laxative	I	I/IIIS	Pending
Bismuth aluminate					
Antacid	Antacid	Antacid	I	I	331.11(c)(1)
Bismuth carbonate					
Antacid	Antacid	Antacid	I	I	331.11(c)(2)
Bismuth oxide					
Hemorrhoidal	Anorectal	Protectant (external)	IIIE	IIIE	310.545(a)(26)(viii)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	IIIE	IIIE	310.545(a)(26)(viii)
Bismuth sodium tartrate					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIISE	310.545(a)(10)(v)
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	Defer	Pending

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IISE	IISE	310.545(a)(8)(i)
Bismuth subcarbonate					
Antacid	Antacid	Antacid	I	I	331.11(c)(3)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	IIIE	IIIE	310.545(a)(26)(viii)
Hemorrhoidal	Anorectal	Protectant (external)	IIIE	IIIE	310.545(a)(26)(viii)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Bismuth subgallate					
Antacid	Antacid	Antacid	I	I	331.11(c)(4)
Hemorrhoidal	Anorectal	Protectant (external)	IIIE	IIIE	310.545(a)(26)(viii)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	IIIE	IIIE	310.545(a)(26)(viii)
Miscellaneous internal	Deodorants for internal use	Internal deodorant	IIIE	I	357.810(a)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Bismuth subnitrate					
n/a	Insect bite/sting	Insect bite/sting	n/a	n/a	310.545(a)(18)(v)(B)
n/a	Poison ivy/oak/sumac	Poison ivy/oak/sumac	n/a	n/a	310.545(a)(18)(vi)(B)
n/a	Skin protectant	Fever blister (topical)	n/a	IISE	310.545(a)(10)(iv)
n/a	Skin protectant	Poison ivy/oak/sumac	n/a	IISE	310.545(a)(10)(vii)(A)
Antacid	Antacid	Antacid	I	I	331.11(c)(5)
Hemorrhoidal	Anorectal	Protectant (external)	IIS	IIS	310.545(a)(26)(viii)
Laxative	Antidiarrheal	Antidiarrheal	IIISE	IIISE	Pending
Miscellaneous external	Anorectal	Protectant (intrarectal)	IIS	IIS	310.545(a)(26)(viii)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IISE	Pending
Topical analgesic	Skin protectant	Skin protectant	IISE	IISE	Pending
Bismuth subsalicylate					
Laxative	Antidiarrheal	Antidiarrheal	IIIE	IIIE	335.10(a)
Laxative	Antiemetic	Antiemetic	IIIE	IIIE	Defer (overindulgence)
Miscellaneous internal	Overindulgence in alcohol/food	Upset stomach	I	I	Pending
Bisoctrizole					
n/a	TEA	Sunscreen	n/a	n/a	n/a
Bithionol					
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Black radish powder					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Blessed thistle (<i>Cnicus benedictus</i>)					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous internal	Menstrual/diuretic	Menstrual	n/a	IISE	310.545(a)(24)(i)
		Bone marrow, red			
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Boric acid			
n/a	Insect bite/sting	Insect bite/sting	n/a	n/a	310.545(a)(18)(v)(B)
n/a	Poison ivy/oak/sumac	Poison ivy/oak/sumac	n/a	n/a	310.545(a)(18)(vi)(B)
n/a	Skin protectant	Fever blister (topical)	n/a	IISE	310.545(a)(18)(iv)
n/a	Skin protectant	Poison ivy/oak/sumac	n/a	IISE	310.545(a)(10)(vii)(A)
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Antimicrobial II	Antifungal	Antifungal	IIIE	IIIE	310.545(a)(22)(ii)
Contraceptive/vaginal	Vaginal	Astringent	IIISE	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Alters vaginal pH	IIISE	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Lowers surface tension, mucolytic effects	IIISE	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Minor irritations	IIISE	Withdrawn	n/a
Hemorrhoidal	Anorectal	Antiseptic (external)	IISE	IISE	310.545(a)(26)(ii)
Hemorrhoidal	Anorectal	Antiseptic (intrarectal)	IISE	IISE	310.545(a)(26)(ii)
Miscellaneous external	Antifungal	Diaper rash	Defer	IISE	310.545(a)(22)(ii)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	IISE	Pending
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis	IISE	IISE	310.545(a)(7)
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIS	Pending
Oral cavity	Oral health care	Antimicrobial	IISE	IISE	Pending
Ophthalmic	Ophthalmic	Anti-infective	IIIE	IIE	310.545(a)(21)(ii)
Topical analgesic	Skin protectant	Skin protectant	IISE	IISE	310.545(a)(18)(i)(B)
		Bornelone			
Topical analgesic	Sunscreen	Sunscreen	IIIE	IIIE	[64 FR 27682]
		Bornyl acetate			
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical)	IIIE	IIIE	310.545(a)(6)(ii)(B)
		Boroglycerin			
Contraceptive/vaginal	Vaginal	Minor irritations	IIISE	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Alters vaginal pH	IIISE	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Astringent	IIISE	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Lowers surface tension, mucolytic effects	IIISE	Withdrawn	n/a
Hemorrhoidal	Anorectal	Antiseptic (external)	IISE	IISE	310.545(a)(26)(ii)
Hemorrhoidal	Anorectal	Antiseptic (intrarectal)	IISE	IISE	310.545(a)(26)(ii)
Oral cavity	Oral health care	Antimicrobial	IISE	IISE	Pending
		Bran			
Laxative	Laxative	Bulk laxative	I	I	Pending
		Bromopheniramine maleate			
Cough/cold	Cough/cold (antihistamine)	Antihistamine	I	I	341.12(a)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Buchu					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Buchu powdered extract (extract of buchu)					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Buchu, extract					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Buckthorn					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Butacaine sulfate					
Dental	Relief of oral discomfort	Oral mucosal analgesic	I	I	Pending
Dental	Relief of oral discomfort	Toothache relief	IIISE	IIISE	Pending
Butamben picrate					
n/a	External analgesic	Fever blister (topical)	n/a	I	Pending
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	I	Pending
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Butylated hydroxyanisole					
n/a	External analgesic	Fever blister (topical)	n/a	n/a	Pending
n/a	Skin protectant	Fever blister (topical)	n/a	n/a	Pending
Caffeine					
Cough/cold	Cough/cold (miscellaneous)	Corrective	IIIE	IIIE	Pending
Internal analgesic	Internal analgesic	Analgesic adjuvant	IIIE	IIIE	Pending
Internal analgesic	Internal analgesic	Antipyretic adjuvant	IIIE	IIIE	Pending
Internal analgesic	Internal analgesic	Antirheumatic adjuvant	IIIE	n/a	Pending
Miscellaneous internal	Menstrual/diuretic	Analgesic adjuvant	IIIE	IIIE	Pending
Miscellaneous internal	Menstrual/diuretic	Diuretic	I	I	Pending
Miscellaneous internal	Overindulgence in alcohol/food	Overindulgence remedies (hangover)	I	I	Pending
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Sedative	Stimulant	Stimulant	I	I	340.10
Calamine					
Hemorrhoidal	Anorectal	Astringent (external)	I	I	346.18(a)
Hemorrhoidal	Anorectal	Astringent (intrarectal)	I	I	346.18(a)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	I	I	346.14(b)(1)
Hemorrhoidal	Anorectal	Protectant (external)	I	I	346.14(b)(1)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(ii)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Insect bite/sting	IISE	IISE	310.545(a)(10)(vi)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Skin protectant	I	I	347.10(c)
Miscellaneous external	Skin protectant	Diaper rash	Defer	I	Pending
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(10)(vi)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	I	347.10(c)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Topical analgesic	Skin protectant	Skin protectant	I	I	347.10(c)
		Calamine (in combination only)			
Hemorrhoidal	Anorectal	Protectant (intrarectal)	I	I	346.14(b)(1)
Hemorrhoidal	Anorectal	Protectant (external)	I	I	346.14(b)(1)
		Calcium			
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Calcium acetate			
n/a	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
		Calcium carbonate			
Antacid	Antacid	Antacid	I	I	331.11(d)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIIE	IIIE	310.545(a)(8)(i)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Calcium carbonate, precipitated			
Laxative	Antidiarrheal	Antidiarrheal	IIIE	IIIE	310.545(a)(3)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
		Calcium caseinate			
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Calcium gluconate			
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
		Calcium hydroxide			
Laxative	Antidiarrheal	Antidiarrheal	IIIE	IIIE	310.545(a)(3)(ii)
		Calcium iodide, anhydrous			
Cough/cold	Cough/cold (expectorant)	Expectorant	IISE	IISE	310.545(a)(6)(iii)
		Calcium lactate			
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Calcium pantothenate			
Laxative	Laxative	Stimulant laxative	IIIE	IIIE	310.545(a)(12)(iv)(A)
Miscellaneous external	Wart remover	Wart remover	IIIE	IIIE	[55 FR 33254]
Miscellaneous internal	Menstrual/diuretic	Premenstrual/ menstrual period	n/a	IISE	310.545(a)(24)(i)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Calcium phosphate			
Antacid	Antacid	Antacid	I	I	331.11(d)
		Calcium phosphate, dibasic			
Dental	Anticaries	Anticavity agent	IIE	n/a	[60 FR 52504]
Internal analgesic	Internal analgesic	Corrective	I	n/a	n/a
		Calcium phosphate, tribasic			
Antacid	Antacid	Antacid	I	I	331.11(d)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Calcium polysulfide					
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Calcium propionate					
Contraceptive/vaginal	Vaginal	Minor irritations	I	Withdrawn	n/a
Calcium salicylate					
Internal analgesic	Internal analgesic	Analgesic	n/a	IISE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antirheumatic	n/a	Not OTC	310.545(a)(23)(i)
Calcium salt (mono- or dibasic)					
Antacid	Antacid	Antacid	n/a	n/a	331.11(i)(2)
Calcium silicate					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	Pending
Calcium sucrose phosphate					
Dental	Anticaries	Anticavity agent	IIE	n/a	310.545(a)(2)(ii)
Calcium thiosulfate					
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Calcium undecylenate					
Antimicrobial II	Antifungal	Antifungal	I	I	333.210(f)
Miscellaneous external	Antifungal	Diaper rash	Defer	IISE	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	IIISE	Pending
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis/psoriasis	IIISE	IIISE	310.545(a)(7)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Calomel					
Laxative	Laxative	Stimulant laxative	IIS	IIS	310.545(a)(12)(iv)(A)
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Miscellaneous external	Mercury	Antiseptic	IISE	IISE	310.545(a)(27)(i)
Calomel (see Mercuric chloride)					
Miscellaneous external	Antimicrobial	First aid antiseptic	n/a	IIIE	310.545(a)(27)(i)
Camphor					
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Antimicrobial II	Antifungal	Antifungal	IIE	IIE	310.545(a)(22)(ii)
Cough/cold	Cold/cough (antitussive)	Antitussive (topical/inhalant)	IIIE	I	341.14(b)(1)
Cough/cold	Cough/cold (expectorant)	Expectorant (lozenge)	IIIE	IIIE	310.545(a)(6)(iii)
Cough/cold	Cough/cold (expectorant)	Expectorant (topical/inhalant)	IIIE	IIIE	310.545(a)(6)(iii)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	IIIE	IIIE	[59 FR 43408]
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (lozenge)	IIIE	IIIE	310.545(a)(6)(ii)(A)
Dental	Relief of oral discomfort	Oral mucosal analgesic	IISE	IISE	Pending
Hemorrhoidal	Anorectal	Analgesic (external)	n/a	I	346.16(a)
Miscellaneous external	Antifungal	Diaper rash	Defer	IISE	310.545(a)(22)(ii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Boil treatment	Boil treatment	IISE	IIISE	310.531(a)
Miscellaneous external	External analgesic	Diaper rash	Defer	IISE	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Insect bite/sting	IISE	I	Pending
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	I	Pending
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	Defer	Pending
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(18)(v)(A)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)(A)
Miscellaneous external	Wart remover	Wart remover	IISE	IISE	[55 FR 33254]
Miscellaneous external	External analgesic	External analgesic (less than 2.5%)	I	I	Pending
Miscellaneous external	External analgesic	External analgesic (greater than 2.5%)	IISE	IISE	Pending
Oral cavity	Oral health care	Antimicrobial	IISE	IISE	Pending
Oral cavity	Oral health care	Analgesic/anesthetic	IISE	IISE	310.545(a)(14)
Topical analgesic	External analgesic	Counterirritant	I	I	Pending
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Topical analgesic	External analgesic	External analgesic	I	I	Pending
Topical analgesic	Sunscreen	Sunscreen	IISE	IISE	[64 FR 27682]
Topical analgesic	External analgesic	Antipyretic	n/a	I	Pending
Camphor (>3%–11%)					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IISE	310.545(a)(10)(v)
Camphor (0.1%–3%)					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	I	Pending
Camphor (greater than 3%–11%)					
Hemorrhoidal	Anorectal	Counterirritant (intrarectal)	IISE	IISE	310.545(a)(26)(iv)
Hemorrhoidal	Anorectal	Counterirritant (external)	IISE	IISE	310.545(a)(26)(iv)
Camphor gum					
Miscellaneous external	External analgesic	Astringent	IISE	n/a	n/a
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Camphorated metacresol					
n/a	External analgesic	Fever blister (topical)	n/a	I	Pending
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	I	Pending
Antimicrobial II	Antifungal	Antifungal	IIISE	IIISE	310.545(a)(22)(iv)
Miscellaneous external	Male genital desensitizer	Male genital desensitizer	n/a	IISE	310.545(a)(10)(iii)
Topical analgesic	External analgesic	Analgesic/anesthetic	IIISE	I	Pending
Camphorated oil					
Miscellaneous external	Camphorated oil	Counterirritant	IIS	n/a	310.502(a)(4)
Candididin					
Antimicrobial II	Antifungal	Anticandidal	IISE	IISE	310.545(a)(22)(ii)
Cantharides					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IISE	IISE	310.528(a)
Capsaicin					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IISE	310.545(a)(10)(v)
Topical analgesic	External analgesic	Counterirritant	I	I	Pending

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Capsicum					
Dental	Relief of oral discomfort	Counterirritant (external)	IIIE	IIIE	Pending
Dental	Relief of oral discomfort	Toothache relief	IISE	IISE	Pending
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IISE	310.545(a)(10)(v)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(8)(ii)
Topical analgesic	External analgesic	Counterirritant	I	I	Pending
Capsicum oleoresin					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IISE	310.545(a)(10)(v)
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Topical analgesic	External analgesic	Counterirritant	I	I	Pending
Capsicum, fluid extract of					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Captan					
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff	IIIE	IIIE	310.545(a)(7)
Caramiphen edisylate					
Cough/cold	Cold/cough (antitussive)	Antitussive	IIIE	IIIE	[52 FR 30054]
Carbamide peroxide					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	Defer	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	Defer	Pending
Oral cavity	Oral health care	Debriding agent	III	III	Pending
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Carbamide peroxide (in anhydrous glycerin)					
Dental	Oral mucosal injury	Wound cleanser	I	I	Pending
Dental	Oral mucosal injury	Wound healing agent	IIIE	IIIE	310.534(a)
Carbamide peroxide 6.5 % (in anhydrous glycerin)					
Topical analgesic	Otic	Ear wax softening agent	I	I	344.10
Carbaspirin calcium					
Internal analgesic	Internal analgesic	Antipyretic	I	I	Pending
Internal analgesic	Internal analgesic	Analgesic	I	I	Pending
Internal analgesic	Internal analgesic	Antirheumatic	I	Not OTC	n/a
Miscellaneous internal	Menstrual/diuretic	Analgesic	I	I	Pending
Carbetapentane citrate					
Cough/cold	Cold/cough (antitussive)	Antitussive	IIIE	IIIE	[52 FR 30054]
Carbon					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Carbon dioxide, released					
Laxative	Laxative	Laxative	I	I	Pending
Carboxymethylcellulose					
Antacid	Antacid	Antacid	IIIE	IIIE	[39 FR 19874]
Carboxymethylcellulose sodium					
Laxative	Antidiarrheal	Antidiarrheal	IIIE	IIIE	310.545(a)(3)(i)
Laxative	Laxative	Bulk laxative	I	I	Pending
Miscellaneous internal	Weight control	Anorectic	IIIE	IISE	310.545(a)(20)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Ophthalmic	Ophthalmic	Demulcent	I	I	349.12(a)(1)
		Carrageenan			
Miscellaneous internal	Weight control	Anorectic	IIIE	IISE	310.545(a)(20)
		Carrageenan, degraded			
Laxative	Laxative	Bulk laxative	IIS	IIS	310.545(a)(12)(i)
		Carrageenan, native			
Laxative	Laxative	Bulk laxative	IIIE	IIIE	310.545(a)(12)(i)
		Casanthranol			
Laxative	Laxative	Stimulant laxative	I	I/IIIS	Pending
		Cascara fluid extract, aromatic			
Laxative	Laxative	Stimulant laxative	I	I/IIIS	310.545(a)(12)(iv)(C)
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
		Cascara sagrada			
Laxative	Laxative	Stimulant laxative	I	I/IIIS	310.545(a)(12)(iv)(C)
		Cascara sagrada bark (see Cascara sagrada)			
=====	=====	=====	=====	=====	=====
		Cascara sagrada extract			
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Laxative	Laxative	Stimulant laxative	I	I/IIIS	310.545(a)(12)(iv)(C)
		Cascara sagrada fluid extract			
Laxative	Laxative	Stimulant laxative	I	I/IIIS	310.545(a)(12)(iv)(C)
		Casein			
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	n/a
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	Withdrawn	n/a
		Castor oil			
Laxative	Laxative	Stimulant laxative	I	I	Pending
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Wart remover	Wart remover	IISE	IISE	[55 FR 33254]
		Catechu, tincture			
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
		Catnip			
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
		Cedar leaf oil			
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical)	IIIE	IIIE	310.545(a)(6)(ii)(B)
		Cellulase			
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIIE	IIIE	310.545(a)(8)(i)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIE	IIE	310.545(a)(8)(i)
		Cellulose			
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	n/a

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	n/a
Cellulose, microporous					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIIE	Pending
Cetalkonium chloride					
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	IIE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IIE	310.545(a)(18)(vii)(A)
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Cetyl alcohol					
n/a	Insect bite/sting	Insect bite/sting	n/a	n/a	310.545(a)(18)(v)(B)
n/a	Poison ivy/oak/sumac	Poison ivy/oak/sumac	n/a	n/a	310.545(a)(18)(vi)(B)
n/a	Skin protectant	Skin protectant	n/a	n/a	310.545(a)(18)(i)(B)
Miscellaneous external	External analgesic	Fever blister (topical)	n/a	n/a	n/a
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	Pending
Cetylpyridinium chloride					
n/a	Antigingivitis/antiplaque	Antigingivitis/antiplaque	I	====	Pending
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Chamomile flowers					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Charcoal, activated					
Antacid	Antacid	Antacid	IIE	IIE	[39 FR 19873]
Laxative	Antidiarrheal	Antidiarrheal	IIIE	IIIE	310.545(a)(3)(ii)
Miscellaneous internal	Deodorants for internal use	Internal deodorant	IIIE	IIIE	[55 FR 19864]
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIIE	IIIE	310.545(a)(8)(iii)
Miscellaneous internal	Overindulgence in alcohol/food	Minimize hangover symptoms	IIIE	IIIE	[48 FR 32873]
Miscellaneous internal	Poison treatment	Poison absorbent	n/a	I	Pending
Miscellaneous internal	Acute toxic ingestion	Poison treatment	I	I	Pending
Charcoal, wood					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIIE	IIIE	310.545(a)(18)(ii)
Chlophedianol hydrochloride					
Cough/cold	Cold/cough (antitussive)	Antitussive	n/a	I	341.14(a)(1)
Chloral hydrate					
n/a	External analgesic	Fever blister (topical)	n/a	IIE	310.545(a)(10)(v)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IIE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IIIE	310.545(a)(10)(vii)(A)
Topical analgesic	External analgesic	Analgesic/anesthetic	IIE	IIE	310.545(a)(10)(i)
Topical analgesic	External analgesic	Counterirritant	n/a	n/a	310.545(a)(10)(ii)
Chlorcyclizine hydrochloride					
Cough/cold	Cough/cold (antihistamine)	Antihistamine	n/a	I	341.12(b)

(Continued)

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Chlorobutanol					
n/a	External analgesic	Fever blister (topical)	n/a	IIIE	310.545(a)(10)(v)
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	IIIE	310.545(a)(10)(vii)
Miscellaneous external	Alcohols (topical)	Antiseptic	IIE	Defer	n/a
Miscellaneous external	Corn/callus remover	Corn/callus remover	IISE	IISE	[55 FR 33261]
Topical analgesic	External analgesic	Analgesic/anesthetic	IIIE	IIIE	310.545(a)(10)(i)
Chloroform					
Cough/cold	Cough/cold (expectorant)	Expectorant	IISE	IISE	310.545(a)(6)(iii)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Chlorophenothane					
Miscellaneous external	Pediculicide	Pediculicide	IISE	IISE	310.545(a)(25)(i)
Chlorophyllin					
Dental	Relief of oral discomfort	Oral mucosal analgesic	n/a	IIIE	Pending
Chlorophyllin copper complex					
Dental	Oral mucosal injury	Wound healing agent	IIIE	IIIE	310.534(a)
Miscellaneous internal	Deodorants for internal use	Internal deodorant	IIIE	I	357.810(b)
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Chlorothymol					
Antimicrobial II	Antifungal	Antifungal	IIIE	IIIE	310.545(a)(22)(ii)
Chloroxylonol					
Antimicrobial I	Antimicrobial	First aid antiseptic	n/a	IIIE	Pending
Antimicrobial I	Antimicrobial	Antimicrobial soap	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Skin wound protectant	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Skin antiseptic	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Surgical hand scrub	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Health-care personnel handwash	IIIE	IIIE	Pending
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Antimicrobial II	Antifungal	Antifungal	IIIE	IIIE	310.545(a)(22)(iv)
Miscellaneous external	Antifungal	Diaper rash	Defer	IISE	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	IIIE	Pending
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis	IIIE	IIIE	310.545(a)(7)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Ingrown toenail	Ingrown toenail	IISE	IISE	310.538(a)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Chlorpheniramine maleate					
Cough/cold	Cough/cold (antihistamine)	Antihistamine	I	I	341.12(c)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)(A)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Chlorprophenpyridamine maleate					
Miscellaneous internal	Menstrual/diuretic	Menstrual	n/a	IISE	310.545(a)(24)(i)
Chlortetracycline hydrochloride					
Antimicrobial II	Antibiotic	First aid antibiotic	n/a	I	333.110(c)
Antimicrobial II	Antibiotic	Skin wound antibiotic	IIE	Defer	n/a
Antimicrobial II	Antibiotic	Skin wound protectant	I	Defer	n/a
Cloxyquin					
Antimicrobial II	Acne	Acne	IISE	IISE	310.545(a)(1)
Cholecalciferol					
Hemorrhoidal	Anorectal	Wound healing agent (external)	IIIE	IIIE	310.545(a)(26)(x)
Hemorrhoidal	Anorectal	Wound healing agent (intrarectal)	IIIE	IIIE	310.545(a)(26)(x)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIISE	Pending
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Cholesterol					
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Choline					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Choline salicylate					
Internal analgesic	Internal analgesic	Analgesic	I	I	Pending
Internal analgesic	Internal analgesic	Antipyretic	I	I	Pending
Internal analgesic	Internal analgesic	Antirheumatic	I	Not OTC	n/a
Miscellaneous internal	Menstrual/diuretic	Analgesic	I	I	Pending
Chondrus					
Miscellaneous internal	Weight control	Anorectic	IIIE	IISE	310.545(a)(20)
<i>Cimicifuga racemosa</i>					
Miscellaneous internal	Menstrual/diuretic	Dysmenorrhea	IISE	IISE	310.545(a)(24)(i)
Cinnamedrine hydrochloride					
Miscellaneous internal	Menstrual/diuretic	Smooth muscle relaxant	IIIE	IIIE	Pending
Cinnamon oil					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Cinnamon tincture					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Cinoxate					
Topical analgesic	Sunscreen	Sunscreen	I	I	352.10(c)
Citric acid					
Contraceptive/vaginal	Vaginal	Alters vaginal pH	IIIE	Withdrawn	n/a
Dental	Relief of oral discomfort	Tooth desensitizer (in combination only)	IIIE	IIIE	Pending

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Internal analgesic	Internal analgesic	Corrective	I	n/a	n/a
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIIE	n/a	310.545(a)(18)(ii)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIIE	n/a	310.545(a)(18)(ii)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Citric acid/salt					
Antacid	Antacid	Antacid	I	I	331.11(e)
Citrus pectin					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Climbazole					
n/a	TEA	Dandruff	n/a	n/a	n/a
Clioquinol					
Antimicrobial II	Antifungal	Antifungal	I	I	333.210(a)
Cloflucarban					
Antimicrobial I	Antimicrobial	Skin antiseptic	n/a	IISE	Pending
Antimicrobial I	Antimicrobial	Skin wound protectant	IISE	IISE	Pending
Antimicrobial I	Antimicrobial	First aid antiseptic	IISE	IISE	Pending
Antimicrobial I	Antimicrobial	Antimicrobial soap	IIIS	IIIS	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	IISE	IISE	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	IISE	IISE	Pending
Antimicrobial I	Antimicrobial	Surgical hand scrub	IISE	IISE	Pending
Antimicrobial I	Antimicrobial	Health-care personnel handwash	IIISE	IIISE	Pending
Clotrimazole					
n/a	n/a	Antifungal	n/a	I	[67 FR 5942]
Clove					
Miscellaneous internal	Smoking deterrent	Smoking deterrent	IIIE	IIIE	310.544(d)
Clove oil					
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Cnicus benedictus					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Coal tar					
Antimicrobial II	Acne	Acne	IISE	IISE	310.545(a)(1)
Antimicrobial II	Antifungal	Antifungal	IISE	IISE	310.545(a)(22)(ii)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Psoriasis	I	I	358.710(c)(1)
Coal tar (shampoo)					
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff	I	I	358.710(a)(1)
Coal tar (nonshampoo)					
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Seborrheic dermatitis	IIIE	I	358.710(b)(1)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Cocoa butter					
n/a	Skin protectant	Diaper rash	Defer	IIISE	310.545(a)(18)(iii)
n/a	Skin protectant	Fever blister (topical)	n/a	I	Pending
Hemorrhoidal	Anorectal	Protectant (external)	I	I	346.14(2)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	I	I	346.14(2)
Topical analgesic	Skin protectant	Skin protectant	I	I	347.10(d)
Coconut oil soap, aqueous					
Miscellaneous external	Pediculicide	Pediculicide	IISE	IISE	310.545(a)(25)(i)
Cod liver oil					
n/a	Skin protectant	Skin protectant	n/a	n/a	347.10(e)
Cough/cold	Cold/cough (antitussive)	Antitussive	IIIE	IIIE	[52 FR 30054]
Hemorrhoidal	Anorectal	Wound healing agent (intrarectal)	IIISE	IIISE	310.545(a)(26)(x)
Hemorrhoidal	Anorectal	Wound healing agent (external)	IIISE	IIISE	310.545(a)(26)(x)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	I	Pending
Cod liver oil (in combination only)					
Hemorrhoidal	Anorectal	Protectant (external)	I	I	346.14(b)(2)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	I	I	346.14(b)(2)
Codeine					
n/a	Menstrual/diuretic	Menstrual	n/a	n/a	310.545(a)(24)(i)
Cough/cold	Cold/cough (antitussive)	Antitussive	I	I	341.14(a)(2)(i)
Internal analgesic	Internal analgesic	Analgesic	IISE	IISE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antipyretic	IISE	IISE	310.545(a)(23)(i)
Miscellaneous internal	Menstrual/diuretic	Analgesic	IIS	IISE	310.545(a)(24)(i)
Codeine phosphate					
Cough/cold	Cold/cough (antitussive)	Antitussive	I	I	341.14(a)(2)(ii)
Internal analgesic	Internal analgesic	Analgesic	IISE	n/a	310.545(a)(23)(i)
Codeine sulfate					
Cough/cold	Cold/cough (antitussive)	Antitussive	I	I	341.14(a)(2)(iii)
Internal analgesic	Internal analgesic	Analgesic	IISE	n/a	310.545(a)(23)(i)
Collinsonia extract					
Hemorrhoidal	Anorectal	Anorectal (external)	IISE	IISE	310.545(a)(26)(vii)
Hemorrhoidal	Anorectal	Anorectal (intrarectal)	IISE	IISE	310.545(a)(26)(vii)
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Colloidal oatmeal					
n/a	Skin protectant	Skin protectant	n/a	n/a	347.10(f)
n/a	Skin protectant	Poison ivy/oak/sumac	n/a	I	347.10(f)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff	IIIE	IIIE	310.545(a)(7)
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	Skin protectant	Astringent	IISE	IIIE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IISE	Pending
Colocynth					
Laxative	Laxative	Stimulant laxative	IIS	IIS	310.545(a)(12)(iv)(A)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Copper					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Copper gluconate					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Copper oleate					
Miscellaneous external	Pediculicide	Pediculicide	IISE	IISE	310.545(a)(25)(i)
Copper undecylenate					
Antimicrobial II	Antifungal	Antifungal	I	I	333.210(f)
Coriander					
Miscellaneous internal	Smoking deterrent	Smoking deterrent	IIE	IIE	310.544(d)
Corn oil					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Corn oil, aqueous emulsion					
Miscellaneous internal	Cholecystokinetic	Cholecystokinetic	I	I	357.210(a)
Corn silk					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Corn silk, potassium extract					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Corn syrup					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Couch grass					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Creosote					
n/a	Skin protectant	Poison ivy/oak/ sumac	n/a	IISE	310.545(a)(18)(vi)(A)
Dental	Relief of oral discomfort	Toothache relief	IIIE	IIIE	Pending
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(10)(vii)(A)
Creosote, beechwood					
n/a	Skin protectant	Poison ivy/oak/sumac	n/a	IISE	310.545(a)(18)(vi)
Cough/cold	Cold/cough (antitussive)	Antitussive	IIIE	IIIE	[52 FR 30054]
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (oral)	IIIE	IIIE	310.545(a)(6)(ii)(A)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical)	IIIE	IIIE	310.545(a)(6)(ii)(B)
Dental	Relief of oral discomfort	Toothache relief	IIIE	IIIE	Pending
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(10)(vii)
Cresol					
Antimicrobial II	Antifungal	Antifungal	IIIE	IIIE	310.545(a)(22)(iv)
Dental	Relief of oral discomfort	Toothache relief	IIIE	IIIE	Pending
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	Astringent	Antiseptic	IIE	Defer	n/a
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Oral cavity	Oral health care	Antimicrobial	IIS	IISE	Pending
Oral cavity	Oral health care	Analgesic/anesthetic	IISE	IISE	310.545(a)(14)
Oral cavity	Relief of oral discomfort	Oral mucosal analgesic	IIIE	IIIE	Pending

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Cresol saponated					
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Psoriasis	IIE	IIE	310.545(a)(7)
Cupric sulfate					
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Cyanocobalamin (vitamin B12)					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Cyclizine hydrochloride					
Laxative	Antiemetic	Antiemetic	I	I	336.10(a)
Cyclomethycaine sulfate					
n/a	External analgesic	Fever blister (topical)	n/a	IIIE	310.545(a)(10)(v)
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	IIIE	310.545(a)(10)(vii)
Internal analgesic	External analgesic	Analgesic/anesthetic	IIIE	IIIE	310.545(a)(10)(i)
Cysteine hydrochloride					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIIE	310.545(a)(18)(iii)
Cystine					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Danthron					
Laxative	Laxative	Stimulant laxative	I	IIS	310.545(a)(12)(iv)(B)
Dehydrocholic acid					
Laxative	Laxative	Stimulant laxative	I	I	Pending
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIE	IIE	310.545(a)(8)(i)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIE	IIE	310.545(a)(8)(i)
Denatonium benzoate					
Miscellaneous external	Nailbiting/thumbsucking	Nailbiting/ thumbsucking deterrent	IIIE	IIIE	310.536(a)
Dequalinium chloride					
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Dexbromopheniramine maleate					
Cough/cold	Cough/cold (antihistamine)	Antihistamine	IIIE	I	341.12(d)
Cough/cold	Cough/cold (antihistamine)	Antihistamine	n/a	I	341.12(f)
Dexchlorpheniramine maleate					
Cough/cold	Cough/cold (antihistamine)	Antihistamine	n/a	I	341.12(e)
Dexpanthenol					
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	IIIE	310.545(a)(10)(vii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Insect bite/sting	n/a	IIIE	Pending
Miscellaneous external	Hair growth/loss	Hair grower	n/a	IIE	310.527(a)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIISE	Pending
Dextran 70					
Ophthalmic	Ophthalmic	Demulcent	I	I	349.12(b)
Dextromethorphan					
Cough/cold	Cold/cough (antitussive)	Antitussive	I	I	341.14(a)(3)
Dextromethorphan hydrobromide					
Cough/cold	Cough/cold (antitussive)	Antitussive	n/a	n/a	341.14(a)(4)
Dextrose					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Diastase					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Diastase malt					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Dibenzothiophene					
Antimicrobial II	Acne	Acne	IIS	IIS	310.545(a)(1)
Dibucaine					
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	I	Pending
Hemorrhoidal	Anorectal	Anesthetic (intrarectal)	IIISE	IIISE	[55 FR 1779]
Hemorrhoidal	Anorectal	Anesthetic (external)	IIIS	I	346.10(d)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	IISE	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	I	Pending
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Oral cavity	Oral health care	Analgesic/anesthetic	IIS	IIS	310.545(a)(14)
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Dibucaine hydrochloride					
n/a	External analgesic	Fever blister (topical)	n/a	I	Pending
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	I	Pending
Hemorrhoidal	Anorectal	Anesthetic (external)	IIIS	I	346.10(c)
Hemorrhoidal	Anorectal	Anesthetic (intrarectal)	IIISE	IIISE	[55 FR 1779]
Oral cavity	Oral health care	Analgesic/anesthetic	IIS	IIS	310.545(a)(14)
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Dicalcium phosphate dihydrate (see Calcium phosphate, dibasic)					
n/a	Gingivitis/plaque	Gingivitis/antiplaque	n/a	IIIE	Pending
Dichlorophen					
Antimicrobial II	Antifungal	Antifungal	IIISE	IIISE	310.545(a)(22)(ii)
Miscellaneous external	Hair growth/loss	Hair grower	IISE	n/a	310.527(a)
Diethanolamine methoxycinnamate					
Topical analgesic	Sunscreen	Sunscreen	I	I	310.545(a)(29)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Diethylhexyl butamido triazone (Uvasorb HEB)					
n/a	Sunscreen	Sunscreen	n/a	n/a	n/a
Digalloyltrioleate					
Topical analgesic	Sunscreen	Sunscreen	I	I	310.545(a)(29)
Dihydroxyaluminum aminoacetate					
Antacid	Antacid	Antacid	I	I	331.11(a)(3)
Dihydroxyaluminum aminoacetic acid					
Antacid	Antacid	Antacid	n/a	n/a	331.11(a)(3)
Internal analgesic	Internal analgesic	Corrective	I	n/a	n/a
Dihydroxyaluminum sodium carbonate					
Antacid	Antacid	Antacid	I	I	331.11(a)(5)
Internal analgesic	Internal analgesic	Corrective	I	n/a	n/a
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIIE	IIIE	310.545(a)(8)(i)
Dimenhydrinate					
Laxative	Antiemetic	Antiemetic	I	I	336.10(b)
Dimethicone					
n/a	Skin protectant	Diaper rash	n/a	I	Pending
n/a	Skin protectant	Fever blister (topical)	n/a	I	Pending
Topical analgesic	Skin protectant	Skin protectant	I	I	347.10(g)
Dimethisoquin hydrochloride					
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	I	Pending
n/a	External analgesic	Fever blister (topical)	n/a	I	Pending
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Dioxybenzone					
Topical analgesic	Sunscreen	Sunscreen	I	I	352.10(e)
Diperodon					
Hemorrhoidal	Anorectal	Anesthetic (intrarectal)	IIISE	IIISE	310.545(a)(26)(vi)
Hemorrhoidal	Anorectal	Anesthetic (external)	IIE	IIIE	310.545(a)(26)(vi)
Diperodon hydrochloride					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(10)(vii)(A)
Miscellaneous external	Corn/callus remover	Corn/callus remover	IISE	IISE	[55 FR 33261]
Diphenhydramine citrate					
Cough/cold	Cough/cold (antitussive)	Antitussive	n/a	n/a	341.14(a)(5)
Cough/cold	Cough/cold (antihistamine)	Antihistamine	n/a	n/a	341.12(f)
Sedative	Nighttime sleep aid	Sleep aid	n/a	n/a	338.10(b)
Diphenhydramine hydrochloride					
n/a	External analgesic	Fever blister (topical)	n/a	I	Pending
Cough/cold	Cough/cold (antitussive)	Antitussive	I	IIIE	341.14(a)(6)
Cough/cold	Cough/cold (antihistamine)	Antihistamine	I	I	341.12(g)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Laxative	Antiemetic	Antiemetic	IIIE	IIIE	336.10(c)
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	I	Pending
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Sedative	Daytime sedative	Sedative	IISE	IISE	310.519(a)
Sedative	Nighttime sleep aid	Sleep aid	IIIE	IIIE	336.10(a)
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Dipropylene glycol salicylate					
Topical analgesic	Sunscreen	Sunscreen	IIIE	IIIE	[64 FR 27682]
Docusate calcium					
Laxative	Laxative	Stool softener	I	I	Pending
Docusate potassium					
Laxative	Laxative	Stool softener	I	I	Pending
Docusate sodium					
Contraceptive/vaginal	Vaginal	Lowers surface tension, mucolytic effects	I	Withdrawn	n/a
Laxative	Laxative	Stool softener	I	I	Pending
Miscellaneous external	Pediculicide	Pediculicide	IISE	IISE	310.545(a)(25)(i)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Dodecaethylene glycol monolaurate					
Contraceptive/vaginal	Contraceptive (vaginal)	Contraceptive	IIIE	Withdrawn	310.545(a)(28)
Dog grass					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Dog grass extract					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Domiphen bromide					
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Dong quai					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IISE	IISE	310.528(a)
Doxylamine succinate					
Cough/cold	Cough/cold (antihistamine)	Antihistamine	I	I	341.12(h)
Sedative	Daytime sedative	Sedative	IISE	IISE	310.519(a)
Sedative	Nighttime sleep aid	Sleep aid	IIIE	IIIE	[54 FR 6826]
Duodenal substance					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IISE	IISE	310.545(a)(8)(i)
Dyclonine hydrochloride					
n/a	External analgesic	Fever blister (topical)	n/a	I	Pending
n/a	External analgesic	Poison ivy/oak/sumac	n/a	I	Pending
Hemorrhoidal	Anorectal	Anesthetic (external)	IIIE	I	346.10(e)
Hemorrhoidal	Anorectal	Anesthetic (intrarectal)	IIIE	IIIE	[55 FR 1779]
Oral cavity	Oral health care	Analgesic/anesthetic	I	I	Pending
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
E. coli vaccines					
Hemorrhoidal	Anorectal	Anorectal (external)	IISE	IISE	310.545(a)(26)(vii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Hemorrhoidal	Anorectal	Anorectal (intrarectal)	IISE	IISE	310.545(a)(26)(vii)
		Edetate disodium			
Contraceptive/vaginal	Vaginal	Minor irritations	IIISE	Withdrawn	n/a
Dental	Relief of oral discomfort	Tooth desensitizer (in combination only)	IISE	IISE	Pending
		Edetate sodium			
Contraceptive/vaginal	Vaginal	Minor irritations	IIISE	Withdrawn	n/a
		Elaterin resin			
Laxative	Laxative	Stimulant laxative	IIS	IIS	310.545(a)(12)(iv)(A)
		Elecampane			
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
		Elm bark			
Cough/cold	Cough/cold (antitussive)	Antitussive	IIIE	IIIE	[52 FR 30054]
Oral cavity	Oral health care	Demulcent	I	I	Pending
		Ensulizole			
Topical analgesic	Sunscreen	Sunscreen	I	I	352.10(n)
		Enzacamene			
n/a	TEA	Sunscreen	n/a	n/a	n/a
		Ephedrine			
Cough/cold	Cough/cold (bronchodilator)	Bronchodilator	I	I	341.16(a)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	I	I	341.20(b)(1)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (oral)	IIIE	IIIE	310.545(a)(6)(ii)(B)
		Ephedrine (any ingredient)			
n/a	Menstrual/diuretic	Menstrual	n/a	n/a	310.545(a)(24)(ii)
n/a	Internal analgesic	Analgesic	n/a	n/a	310.545(a)(23)(ii)
		Ephedrine hydrochloride			
Cough/cold	Cough/cold (bronchodilator)	Bronchodilator	I	I	341.16(b)
Miscellaneous external	Male genital desensitizer	Male genital desensitizer	IISE	IISE	310.545(a)(10)(iii)
Ophthalmic	Ophthalmic	Vasoconstrictor	I	I	349.18(a)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (oral)	IIIE	IIIE	310.545(a)(6)(ii)(B)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	I	I	341.20(b)(3)
		Ephedrine sulfate			
Cough/cold	Cough/cold (bronchodilator)	Bronchodilator	I	I	341.16(c)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	I	I	341.20(b)(4)
Hemorrhoidal	Anorectal	Vasoconstrictor (intrarectal)	I	I	346.12(a)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Hemorrhoidal	Anorectal	Vasoconstrictor (external)	I	I	346.10(a)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (oral)	IIIE	IIIE	310.545(a)(6)(ii)(B)
Epinephrine					
Cough/cold	Cough/cold (bronchodilator)	Bronchodilator (inhalation)	I	I	341.16(d)
Hemorrhoidal	Anorectal	Vasoconstrictor (external)	IIISE	I	346.10(b)
Hemorrhoidal	Anorectal	Vasoconstrictor (intrarectal)	IIISE	IIISE	346.10(b)
Epinephrine bitartrate					
Cough/cold	Cough/cold (bronchodilator)	Bronchodilator (inhalation)	I	I	341.16(e)
Epinephrine hydrochloride					
Hemorrhoidal	Anorectal	Vasoconstrictor (external)	I	I	346.10(c)
Hemorrhoidal	Anorectal	Vasoconstrictor (intrarectal)	IIE	IIE	346.10(c)
Epinephrine undecylenate					
Hemorrhoidal	Anorectal	Vasoconstrictor (external)	IIISE	IIISE	310.545(a)(26)(ix)
Hemorrhoidal	Anorectal	Vasoconstrictor (intrarectal)	IIE	IIE	310.545(a)(26)(ix)
Ergocalciferol					
Contraceptive/vaginal	Vaginal	Minor irritations	IIIE	Withdrawn	
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Ergot fluid extract					
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Miscellaneous external	External analgesic	Insect bite/sting	IISE	IISE	310.545(a)(10)(vi)
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(18)(v)(A)
Escalol 506 (see Padimate A)					
Essential oils					
Miscellaneous external	Hair growth/loss	Hair grower	IISE	n/a	310.527(a)
Estradiol					
Miscellaneous external	Hair growth/loss	Hair grower	IIE	IIE	310.527(a)
Estrogens					
Miscellaneous external	Hormone	Hormone	IIE	IIE	310.530(a)
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IIS	IIS	310.528(a)
Estrone					
Antimicrobial II	Acne	Acne	IISE	IISE	310.545(a)(1)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Ether					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Ethohexadiol					
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff	IIIE	IIIE	310.545(a)(7)
Ethoxylated alkyl alcohol					
Miscellaneous external	External analgesic	Insect bite/sting	IISE	IISE	310.545(a)(10)(vi)
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(18)(v)
Ethyl 4-[bis(hydroxypropyl)] aminobenzoate					
Topical analgesic	Sunscreen	Sunscreen	I	I	310.545(a)(29)
Ethyl nitrate					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Ethylmorphine hydrochloride					
Cough/	Cough/cold (antitussive)	Antitussive	IIIE	IIIE	[52 FR 30054]
Eucalyptol					
Cough/cold	Cough/cold (antitussive)	Antitussive (topical/inhalant)	IIIE	IIIE	[52 FR 30055]
Cough/cold	Cough/cold (antitussive)	Antitussive (mouthwash)	IIIE	IIIE	[52 FR 30055]
Cough/cold	Cough/cold (antitussive)	Antitussive (lozenge)	IIIE	IIIE	[52 FR 30054]
Cough/cold	Cough/cold (expectorant)	Expectorant (lozenge)	IIIE	IIIE	310.545(a)(6)(iii)
Cough/cold	Cough/cold (expectorant)	Expectorant (topical/inhalant)	IIIE	IIIE	310.545(a)(6)(iii)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	IIIE	IIIE	310.545(a)(6)(ii)(A)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (mouthwash)	IIIE	IIIE	310.545(a)(6)(ii)(A)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (lozenge)	IIIE	IIIE	310.545(a)(6)(ii)(A)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (lozenge)	IIIE	IIIE	310.545(a)(6)(ii)(A)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff	IIIE	IIIE	310.545(a)(7)
Miscellaneous external	External analgesic	Diaper rash	Defer	IISE	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Oral cavity	Oral health care	Analgesic/anesthetic	IIIE	IIIE	310.545(a)(14)
Eucalyptol, menthol, methyl salicylate, and thymol					
n/a	Gingivitis/plaque	Antiplaque/gingivitis	I	n/a	pending
Eucalyptus oil					
n/a	External analgesic	Fever blister (topical)	n/a	IIIE	310.545(a)(10)(v)
Cough/cold	Cough/cold (antitussive)	Antitussive (mouthwash)	IIIE	IIIE	[52 FR 30055]
Cough/cold	Cough/cold (antitussive)	Antitussive (lozenge)	IIIE	IIIE	[52 FR 30054]

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Cough/cold	Cough/cold (antitussive)	Antitussive (topical/inhalant)	IIIE	IIIE	[52 FR 30055]
Cough/cold	Cough/cold (expectorant)	Expectorant (lozenge)	IIIE	IIIE	310.545(a)(6)(iii)
Cough/cold	Cough/cold (expectorant)	Expectorant (topical/inhalant)	IIIE	IIIE	310.545(a)(6)(iii)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (mouthwash)	IIIE	IIIE	310.545(a)(6)(ii)(A)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (inhalant room spray)	IIIE	IIIE	[59 FR 43408]
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (lozenge)	IIIE	IIIE	310.545(a)(6)(ii)(A)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Hair growth/loss	Hair grower	IISE	n/a	310.527(a)
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(18)(vi)
Miscellaneous internal	Smoking deterrent	Smoking deterrent	IIE	IIE	310.544(d)
Topical analgesic	External analgesic	Counterirritant	IIIE	IIIE	310.545(a)(10)(ii)
Eugenol					
n/a	External analgesic	Poison ivy/oak/sumac	n/a	IIIE	310.545(a)(10)(vii)
Dental	Relief of oral discomfort	Toothache relief	I	IIIE	Pending
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIIE	310.545(a)(10)(v)
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Topical analgesic	External analgesic	Analgesic/anesthetic	IIIE	IIIE	310.545(a)(10)(i)
<i>Euphorbia pilulifera</i>					
Cough/cold	Cough/cold (bronchodilator)	Bronchodilator	IIIE	IIIE	310.545(a)(6)(iv)(A)
Fatty acids					
Miscellaneous external	Hair growth/loss	Hair grower	IISE	n/a	310.527(a)
Fennel acid					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Ferric ammonium citrate					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Ferric chloride					
Miscellaneous external	External analgesic	Insect bite/sting	IISE	IISE	310.545(a)(10)(vi)
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(18)(v)(A)
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	IISE	IISE	310.545(a)(18)(vi)(A)
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Oral cavity	Oral health care	Antimicrobial	IISE	IISE	Pending
Ferric pyrophosphate					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
		Ferric subsulfate			
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
		Ferrous fumarate			
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Ferrous gluconate			
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Ferrous sulfate			
Miscellaneous internal	Menstrual/diuretic	Premenstrual/ menstrual period	n/a	IISE	310.545(a)(24)(i)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Flax seed			
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Fluorosalan			
Antimicrobial I	Antimicrobial	Antimicrobial	IIS	IIS	Pending
		Folic acid			
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Formaldehyde solution			
Dental	Relief of oral discomfort	Tooth desensitizer	IIIE	IIIE	Pending
		Formic acid			
Miscellaneous external	Pediculicide	Pediculicide	n/a	n/a	310.545(a)(25)(i)
		Frangula			
Laxative	Laxative	Stimulant laxative	IIISE	IIISE	310.545(a)(12)(iv)(A)
		Fructose			
Miscellaneous internal	Overindulgence in alcohol/food	Minimize inebriation	IIIE	IIIE	[48 FR 32873]
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Galega			
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
		Gamboge			
Laxative	Laxative	Stimulant laxative	IIS	IIS	310.545(a)(12)(iv)(A)
		Garlic, dehydrated			
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIE	IIE	310.545(a)(8)(i)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIE	IIE	310.545(a)(8)(i)
		Gastric mucin			
Antacid	Antacid	Antacid	IIIE	IIIE	[39 FR 19873]
		Gelatin			
Oral cavity	Oral health care	Demulcent	I	I	Pending
Ophthalmic	Ophthalmic	Demulcent	I	I	349.12(c)
		Gentian violet			
Miscellaneous internal	Anthelmintic	Anthelmintic	I	IIS	[51 FR 27758]
Oral cavity	Oral health care	Antimicrobial	IIIE	IIE	Pending

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
<i>Gentiana lutea</i> (gentian)					
Miscellaneous internal	Menstrual/diuretic	Premenstrual/ menstrual period	n/a	IISE	310.545(a)(24)(i)
Ginger					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Ginger, Jamaica					
Miscellaneous internal	Smoking deterrent	Smoking deterrent	IIE	IIE	310.544(d)
Ginseng					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IISE	IISE	310.528(a)
Sedative	Stimulant	Stimulant	IIE	IIE	[39 FR 6104]
Ginseng, Korean					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IISE	IISE	310.528(a)
Glutamic acid					
Miscellaneous internal	Benign prostatic hypertrophy	Benign prostatic hypertrophy	IIE	IIISE	310.532((a))
Glutamic acid hydrochloride					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIE	IIE	310.545(a)(8)(i)
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIE	IIE	310.545(a)(8)(i)
Miscellaneous internal	Stomach acidifier	Stomach acidifier	IIE	IIE	310.540(a)
Glycerin					
Hemorrhoidal	Anorectal	Antiseptic (intrarectal)	IISE	IISE	310.545(a)(26)(ii)
Hemorrhoidal	Anorectal	Antiseptic (external)	IISE	IISE	310.545(a)(26)(ii)
Hemorrhoidal	Anorectal	Protectant (external)	I	I	346.14(3)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	I	I	346.14(3)
Laxative	Laxative	Hyperosmotic laxative	I	I	Pending
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	DEF	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIISE	310.545(a)(18)(iii)
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	I	Pending
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Oral cavity	Oral health care	Demulcent	I	I	Pending
Ophthalmic	Ophthalmic	Demulcent	I	I	349.12(d)(1)
Topical analgesic	Otic	Ear wax softening agent	I	IIIE	[51 FR 28660]
Topical analgesic	Skin protectant	Skin protectant	I	I	347.10(h)
Glycerin, anhydrous					
n/a	Otic	Drying water-clogged ears	n/a	IIIE	310.545(a)(15)(ii)
n/a	Otic	Swimmer's ear prevention	n/a	IIIE	310.545(a)(15)(ii)
Glyceryl aminobenzoate					
Topical analgesic	Sunscreen	Sunscreen	I	I	310.545(a)(29)
Glycine					
Antacid	Antacid	Antacid	I	I	331.11(f)
Internal analgesic	Internal analgesic	Corrective	I	n/a	Pending

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Laxative	Antidiarrheal	Antidiarrheal	IIE	IIE	310.545(a)(3)(i)
Laxative	Antiemetic	Antiemetic	IIE	IIE	[52 FR 15891]
Miscellaneous internal	Benign prostatic hypertrophy	Benign prostatic hypertrophy	IIE	IIIE	310.532(a)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Glycol salicylate					
n/a	External analgesic	Poison ivy/oak/sumac	n/a	IIIE	310.545(a)(10)(vii)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIIE	310.545(a)(10)(v)
Topical analgesic	External analgesic	Analgesic/anesthetic	IIIE	IIIE	Pending
Glycyrrhiza					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IIE	IIIE	310.528(a)
Miscellaneous internal	Menstrual/diuretic	Premenstrual/ menstrual period	n/a	IIIE	310.545(a)(24)(i)
Golden seal (see also Hydrastis)					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IIIE	IIIE	310.528(a)
Gotu kola					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IIIE	IIIE	310.528(a)
Gramicidin					
Antimicrobial II	Antibiotic	First aid antibiotic	n/a	IIIE	[52 FR 47322]
Antimicrobial II	Antibiotic	Skin wound protectant	IIS	Defer	[52 FR 47322]
Antimicrobial II	Antibiotic	Skin wound antibiotic	IIIE	Defer	[52 FR 47322]
Guaifenesin					
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	341.18
Guar gum					
Laxative	Laxative	Bulk laxative	IIIE	IIIE	310.545(a)(12)(i)
Miscellaneous internal	Weight control	Anorectic	IIIE	IIIE	310.545(a)(20)
Haloprogin					
Antimicrobial II	Antifungal	Anticandidal	I	n/a	n/a
Antimicrobial II	Antifungal	Antifungal	I	I	333.210(b)
Hard fat					
=====	Skin protectant	Skin protectant	n/a	n/a	347.10(i)
Hemorrhoidal	Anorectal	Protectant (external)	n/a	n/a	346.14(4)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	n/a	n/a	346.14(4)
Hectorite					
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	IIIE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IIIE	310.545(a)(18)(vi)(A)
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Hemicellulase					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIIE	IIIE	310.545(a)(8)(i)
Miscellaneous internal	Exocrine pancreatic insufficiency	Exocrine pancreatic insufficiency	IIE	IIE	310.543(a)
Hexachlorophene					
Antimicrobial I	Antimicrobial	Antimicrobial	IIS	n/a	[37 FR 20163]
Contraceptive/vaginal	Vaginal	Minor irritations	IIIE	Withdrawn	n/a

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	IISE	Pending
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Hexylresorcinol					
n/a	External analgesic	Poison ivy/oak/sumac	n/a	IIIE	310.545(a)(10)(vii)
Antimicrobial I	Antimicrobial	Antimicrobial soap	n/a	IIE	Pending
Antimicrobial I	Antimicrobial	First aid antiseptic	n/a	I	Pending
Antimicrobial I	Antimicrobial	Health care personnel handwash	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Skin antiseptic	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	I	I	Pending
Antimicrobial I	Antimicrobial	Skin wound protectant	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Surgical hand scrub	IIIE	IIIE	Pending
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIIE	310.545(a)(10)(v)
Oral cavity	Oral health care	Analgesic/anesthetic	I	I	Pending
Topical analgesic	External analgesic	Analgesic/anesthetic	IIIE	IIIE	310.545(a)(10)(i)
Histamine dihydrochloride					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IISE	310.545(a)(10)(v)
Topical analgesic	External analgesic	Counterirritant	I	I	Pending
Histidine					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Homatropine methylbromide					
Laxative	Antidiarrheal	Antidiarrheal	IIISE	IIISE	310.545(a)(3)
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIIE	IIIE	310.545(a)(8)(i)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIE	IIE	310.545(a)(8)(i)
Miscellaneous internal	Menstrual/diuretic	Smooth muscle relaxant	IIE	IIIE	310.545(a)(24)(i)
Homosalate					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	Defer	Pending
Topical analgesic	n/a	Sunscreen	n/a	I	352.10(f)
Honey					
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Horehound					
Cough/cold	Cough/cold (antitussive)	Antitussive	IIIE	IIIE	[52 FR 30054]
Oral cavity	Oral health care	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
Hormone constituents					
Miscellaneous external	Hair growth/loss	Hair grower	IISE	IIE	310.527(a)
Horsetail					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Huckleberry					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Hydrangea, powdered extract (extract of hydrangea)					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Hydrastis					
Hemorrhoidal	Anorectal	Counterirritant (intrarectal)	IISE	IISE	310.545(a)(26)(iv)
Hemorrhoidal	Anorectal	Antiseptic (external)	IISE	IISE	310.545(a)(26)(iv)
Hemorrhoidal	Anorectal	Counterirritant (external)	IISE	IISE	310.545(a)(26)(iv)
Hemorrhoidal	Anorectal	Antiseptic (intrarectal)	IISE	IISE	310.545(a)(26)(ii)
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IISE	IISE	310.528(a)
Hydrastis canadensis (golden seal)					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Miscellaneous internal	Menstrual/diuretic	Menstrual	n/a	IISE	310.545(a)(24)(i)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Hydrastis fluid extract					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Hydrate magnesium aluminate activated sulfate					
Antacid	Antacid	Antacid	n/a	n/a	331.11(g)(1)
Hydriodic acid syrup					
Cough/cold	Cough/cold (expectorant)	Expectorant	IISE	IISE	310.545(a)(6)(iii)
Hydrochloric acid					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Hydrochloric acid, diluted					
Miscellaneous internal	Stomach acidifier	Stomach acidifier	IIE	IIE	310.540(a)
Hydrocodone bitartrate					
Cough/cold	Cough/cold (antitussive)	Antitussive	IIS	IIS	[52 FR 30054]
Hydrocortisone					
Antimicrobial II	Antifungal	Anti-inflammatory	I combo	n/a	n/a
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis/psoriasis	IIISE	Defer	n/a
Topical analgesic	External analgesic	Antipruritic	I	I	Pending
Hydrocortisone (0.25%–5%)					
Miscellaneous external	External analgesic	Dandruff/seborrheic dermatitis/psoriasis	n/a	I	Pending
Hydrocortisone (0.5%–1%)					
Miscellaneous external	External analgesic	Dandruff	n/a	IIISE	Pending
Hydrocortisone acetate					
====	External analgesic	Poison ivy/oak/sumac	n/a	I	Pending
Antimicrobial II	Antifungal	Anti-inflammatory (dissent)	I combo	n/a	n/a
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis/psoriasis	IIISE	Defer	n/a
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Topical analgesic	External analgesic	Antipruritic	I	I	Pending
Hydrocortisone acetate (0.25%–5.0%)					
Miscellaneous external	External analgesic	Dandruff/seborrheic dermatitis/psoriasis	n/a	I	Pending
Hydrocortisone acetate (0.25%–0.5%)					
Miscellaneous external	External analgesic	Dandruff/seborrheic dermatitis /psoriasis	n/a	I	Pending
Hydrogen fluoride					
Dental	Anticaries	Anticavity dental rinse	n/a	IIISE	310.545(a)(2)(i)
Hydrogen peroxide					
Antimicrobial I	Antimicrobial	First aid antiseptic	n/a	I	Pending
Dental	Oral mucosal injury	Wound cleanser	I	I	Pending
Dental	Oral mucosal injury	Wound healing agent	IIIE	IIIE	310.534(a)
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Oral cavity	Oral health care	Debriding agent	III	III	Pending
Hydrogen peroxide and povidone iodine					
n/a	Gingivitis/plaque	Antiplaque/gingivitis	n/a	IIISE	Pending
Hydrogen peroxide and sodium bicarbonate					
n/a	Gingivitis/plaque	Antiplaque/gingivitis	n/a	IIISE	Pending
Hydrogen peroxide, sodium citrate, sodium lauryl sulfate, and zinc chloride					
n/a	Gingivitis/plaque	Antiplaque/gingivitis	n/a	IIISE	Pending
Hydroquinone					
Miscellaneous external	Skin bleach	Skin bleaching	I	I	Pending
Hydroxyethyl cellulose					
Ophthalmic	Ophthalmic	Demulcent	I	I	349.12(a)(2)
Hyoscyamine sulfate					
Laxative	Antidiarrheal	Antidiarrheal	IIISE	IIISE	310.545(a)(3)
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Hypromellose					
Ophthalmic	Ophthalmic	Demulcent	I	I	349.12(a)(3)
Ibuprofen					
n/a	Internal analgesic	Analgesic	n/a	I	[67 FR 54139]
n/a	Internal analgesic	Antipyretic	n/a	I	[67 FR 54139]
Ichthammol					
Miscellaneous external	Boil treatment	Boil treatment	IISE	IIISE	310.531(a)
Miscellaneous external	Corn/callus remover	Corn/callus remover	IISE	IISE	[55 FR 33261]
Impatiens biflora tincture					
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(10)(vii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Inositol					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Iodine					
Miscellaneous external	Wart remover	Wart remover	IISE	IISE	[55 FR 33254]
Miscellaneous external	Corn/callus remover	Corn/callus remover	IISE	IISE	[55 FR 33261]
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Oral cavity	Oral health care	Antimicrobial	IIISE	IIISE	Pending
Iodine complex/phosphate ester of alkylaryloxy polyethylene					
Antimicrobial I	Antimicrobial	Surgical hand scrub	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin wound protectant	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Health-care personnel handwash	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Antimicrobial soap	n/a	IISE	Pending
Antimicrobial I	Antimicrobial	Skin antiseptic	IIISE	IIISE	Pending
Iodine tincture					
Antimicrobial I	Antimicrobial	First aid antiseptic	n/a	I	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	I	I	Pending
Antimicrobial I	Antimicrobial	Surgical hand scrub	IIS	IIS	Pending
Antimicrobial I	Antimicrobial	Antimicrobial soap	n/a	IISE	Pending
Antimicrobial I	Antimicrobial	Skin wound protectant	IISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	IIS	IIIS	Pending
Antimicrobial I	Antimicrobial	Skin antiseptic	IIS	IIIS	Pending
Antimicrobial I	Antimicrobial	Health-care personnel handwash	IISE	IISE	Pending
Iodine topical solution					
Antimicrobial I	Antimicrobial	First aid antiseptic	n/a	I	Pending
Iodized lime					
Cough/cold	Cough/cold (expectorant)	Expectorant	IISE	IISE	310.545(a)(6)(iii)
Iodoantipyrine					
Internal analgesic	Internal analgesic	Analgesic	IISE	IISE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antipyretic	IISE	IISE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antirheumatic	IISE	Not OTC	310.545(a)(23)(i)
Ipecac					
Cough/cold	Cough/cold (expectorant)	Expectorant	IIE	IIE	310.545(a)(6)(iii)
Ipecac fluid extract					
Cough/cold	Cough/cold (expectorant)	Expectorant	IIE	IIE	310.545(a)(6)(iii)
Miscellaneous internal	Poison treatment	Emetic	n/a	IIS	310.545(a)(16)
Ipecac syrup					
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
Miscellaneous internal	Emetic	Emetic	I	I	Pending
Miscellaneous internal	Poison treatment	Emetic	n/a	I	Pending

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Ipecac tincture					
Miscellaneous internal	Poison treatment	Emetic	n/a	IIS	310.545(a)(16)
Ipomea					
Laxative	Laxative	Stimulant laxative	IIS	IIS	310.545(a)(12)(iv)(A)
Iron ox bile					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Iron oxide					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Isobornyl thiocynoacetate					
Miscellaneous external	Pediculicide	Pediculicide	IISE	IISE	310.545(a)(25)(i)
Isobutamphen					
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Isoleucine					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Isopropyl alcohol					
Miscellaneous external	Alcohols (topical)	Antiseptic	I	I	Pending
Miscellaneous external	Mercury	First aid antiseptic	n/a	I	Pending
Miscellaneous external	Analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Isopropyl palmitate					
n/a	Insect bite/sting	Insect bite/sting	n/a	n/a	310.545(a)(18)(v)(B)
n/a	Poison ivy/oak/sumac	Poison ivy/oak/sumac	n/a	n/a	310.545(a)(18)(vi)(B)
n/a	Skin protectant	Skin protectant	n/a	n/a	310.545(a)(18)(i)(B)
Jalap					
Laxative	Laxative	Stimulant laxative	IIS	IIS	310.545(a)(12)(iv)(A)
John's wort					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Jojoba oil					
Miscellaneous external	Hair growth/loss	Hair grower	n/a	IIE	310.527(a)
Juniper					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Juniper oil (oil of juniper)					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Juniper tar					
n/a	Antifungal	Diaper rash	n/a	n/a	310.545(a)(22)(i)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
n/a	Antimicrobial	Diaper rash	n/a	n/a	Pending
n/a	External analgesic	Diaper rash	n/a	IISE	310.545(a)(10)(iv)
n/a	External analgesic	Fever blister (topical)	n/a	I	Pending
n/a	External analgesic	Poison ivy/oak/sumac	n/a	I	Pending
n/a	Skin protectant	Diaper rash	n/a	n/a	Pending
Hemorrhoidal	Anorectal	Counterirritant (external)	IIISE	n/a	n/a
Hemorrhoidal	Anorectal	Analgesic (external)	n/a	I	346.16(b)
Hemorrhoidal	Anorectal	Counterirritant (intrarectal)	IIISE	n/a	n/a
Miscellaneous external	Boil treatment	Boil treatment	IISE	IIISE	310.531(a)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis/psoriasis	IIIE	IIIE	310.545(a)(7)
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Juniper, extract					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Kaolin					
n/a	Skin protectant	Poison ivy/oak/sumac	n/a	I	347.10(j)
Antacid	Antacid	Antacid	IIIE	IIIE	[39 FR 19873]
Hemorrhoidal	Anorectal	Protectant (intrarectal)	I	I	346.14(5)
Hemorrhoidal	Anorectal	Protectant (external)	I	I	346.14(5)
Laxative	Antidiarrheal	Antidiarrheal	IIIE	IIIE	347.10(b)
Miscellaneous external	Skin protectant	Diaper rash	n/a	I	Pending
Topical analgesic	Skin protectant	Skin protectant	I	I	347.10(j)
Kaolin, colloidal					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Karaya gum					
Laxative	Laxative	Bulk laxative	I	I	Pending
Miscellaneous internal	Weight control	Anorectic	IIIE	IISE	310.545(a)(20)
Kelp					
Miscellaneous internal	Weight control	Anorectic	IIIE	IISE	310.545(a)(20)
Knotgrass					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Lactic acid					
Contraceptive/vaginal	Vaginal	Lowers surface tension, mucolytic effects	IIIE	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Alters vaginal pH	IIIE	Withdrawn	n/a
Miscellaneous external	Wart remover	Wart remover	IIIE	IIIE	[55 FR 33254]
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Lactobacillus acidophilus					
Laxative	Antidiarrheal	Antidiarrheal	IIIE	IIIE	310.545(a)(3)(i)
Miscellaneous internal	Fever blister (oral)	Fever blister/oral	IIIE	IIIE	310.537(a)
Lactobacillus bulgaricus					
Laxative	Antidiarrheal	Antidiarrheal	IIIE	IIIE	310.545(a)(3)(i)
Miscellaneous internal	Fever blister (oral)	Fever blister/oral	IIIE	IIIE	310.537(a)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Lactose					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Lanolin					
n/a	Skin protectant	Skin protectant	n/a	n/a	347.10(k)
Hemorrhoidal	Anorectal	Protectant (external)	I	I	346.14(6)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	I	I	346.14(6)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Hair growth/loss	Hair grower	IIE	IIE	310.527(a)
Miscellaneous external	Skin protectant	Diaper rash	Defer	I	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(18)(vi)
Lanolin (in combination)					
Ophthalmic	Ophthalmic	Emollient	I	I	349.14(a)(2)
Lanolin alcohols					
Hemorrhoidal	Anorectal	Protectant (external)	I	IIISE	310.545(a)(26)(viii)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	I	IIISE	310.545(a)(26)(viii)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	Pending
Lanolin nonionic derivatives					
Ophthalmic	Ophthalmic	Emollient	I	I	349.14
Lanolin, anhydrous (in combination)					
Ophthalmic	Ophthalmic	Emollient	I	I	349.14(a)(1)
Lappa extract					
Hemorrhoidal	Anorectal	Anorectal (external)	IISE	IISE	310.545(a)(26)(vii)
Hemorrhoidal	Anorectal	Anorectal (intrarectal)	IISE	IISE	310.545(a)(26)(vii)
Laureth 10					
Contraceptive/vaginal	Contraceptive (vaginal)	Contraceptive	IIIE	Withdrawn	310.545(a)(28)
Lauric diethanolamide					
Miscellaneous external	Hair growth/loss	Hair grower	IISE	n/a	310.527(a)
Lauryl isoquinolinium bromide					
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff	IIIE	IIIE	310.545(a)(7)
Lavender compound, tincture of					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Lavender oil					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Lawsonia with dihydroxyacetone					
Topical analgesic	Sunscreen	Sunscreen	I	I	310.545(a)(29)
Lead acetate					
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Lecithin					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Lemon oil (terpeneless)					
Miscellaneous internal	Smoking deterrent	Smoking deterrent	IIE	IIE	310.544(d)
Leptandra extract					
Hemorrhoidal	Anorectal	Anorectal (external)	IISE	IISE	310.545(a)(26)(vii)
Hemorrhoidal	Anorectal	Anorectal (intrarectal)	IISE	IISE	310.545(a)(26)(vii)
Leucine					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Levmetamfetamine					
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	IIIE	I	341.20(b)(1)
Licorice					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IISE	IISE	310.528(a)
Licorice root extract					
Miscellaneous internal	Smoking deterrent	Smoking deterrent	IIE	IIE	310.544(d)
Lidocaine					
Hemorrhoidal	Anorectal	Anesthetic (external)	IIIE	I	346.10(f)
Hemorrhoidal	Anorectal	Anesthetic (intrarectal)	IIIE	IIIE	[55 FR 1779]
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	I	Pending
Miscellaneous external	Male genital desensitizer	Male genital desensitizer	I	I	348.10(a)(2)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	I	Pending
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Oral cavity	Oral health care	Analgesic/anesthetic	IIS	IIS	310.545(a)(14)
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Lidocaine hydrochloride					
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	I	Pending
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	I	Pending
Oral cavity	Oral health care	Analgesic/anesthetic	IIS	IIS	310.545(a)(14)
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Linden					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Lipase					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Live yeast cell derivative					
n/a	Insect bite/sting	Insect bite/sting	n/a	n/a	310.545(a)(18)(v)(B)
n/a	Poison ivy/oak/sumac	Poison ivy/oak/ sumac	n/a	n/a	310.545(a)(18)(vi)(B)
Topical analgesic	Skin protectant	Skin protectant	IIIE	IIIE	310.545(a)(18)(i)(B)

(Continued)

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
		Liver concentrate			
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Lobeline			
Miscellaneous internal	Smoking deterrent	Smoking deterrent	IIIE	IIIE	310.544(d)
		Lysine			
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Lysine aspirin			
Internal analgesic	Internal analgesic	Analgesic	n/a	IISE	310.545(a)(23)(i)
		Lysine hydrochloride			
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Miscellaneous internal	Fever blister (oral)	Fever blister/oral	IIIE	IIIE	310.537(a)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Magaldrate			
Antacid	Antacid	Antacid	I	I	331.11(g)(2)
		Magnesium			
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Magnesium aluminum silicate			
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Antacid	Antacid	Antacid	I	I	331.11(g)(3) 331.11(k)(2)(1)
		Magnesium carbonate			
Antacid	Antacid	Antacid	I	I	331.11(g)(4)
Internal analgesic	Internal analgesic	Corrective	I	n/a	n/a
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous internal	Overindulgence in alcohol/food	Overindulgence remedies (hangover)	I	I	Pending
		Magnesium citrate			
Laxative	Laxative	Saline laxative (oral solution)	I	I	Pending
		Magnesium glycinate			
Antacid	Antacid	Antacid	I	I	331.11(g)(5)
		Magnesium hydroxide			
Antacid	Antacid	Antacid	I	I	331.11(g)(6)
Internal analgesic	Internal analgesic	Corrective	I	n/a	Pending
Laxative	Laxative	Saline laxative	I	I	Pending
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIIE	IIIE	310.545(a)(8)(i)
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIIE	IIIE	310.545(a)(8)(i)
		Magnesium oxide			
Antacid	Antacid	Antacid	I	I	331.11(g)(7)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Magnesium salicylate					
Internal analgesic	Internal analgesic	Analgesic	I	I	Pending
Internal analgesic	Internal analgesic	Antipyretic	I	I	Pending
Internal analgesic	Internal analgesic	Antirheumatic	I	Not	OTC n/a
Miscellaneous internal	Menstrual/diuretic	Analgesic	I	I	Pending
Magnesium sulfate					
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Laxative	Laxative	Saline laxative	I	I	Pending
Miscellaneous external	Boil treatment	Boil treatment	IISE	IIISE	310.531(a)
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Magnesium trisilicate					
Antacid	Antacid	Antacid	I	I	331.11(g)(8) 331 11(k)(3)(1)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIIE	IIIE	310.545(a)(8)(i)
Miscellaneous internal	Overindulgence in alcohol/food	Overindulgence remedies (hangover)	I	I	Pending
Malt					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Malt soup extract					
Laxative	Laxative	Bulk laxative	I	I	Pending
Maltodextrin					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Mandrake					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	n/a	n/a	310.528(a)
Manganese citrate					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Mannitol					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Meclizine hydrochloride					
Laxative	Antiemetic	Antiemetic	I	I	336.10(d)
Menfegol					
Contraceptive/vaginal	Contraceptive (vaginal)	Contraceptive (dissent)	I	Withdrawn	n/a
Menthol					
Antimicrobial II	Antifungal	Antifungal	IIE	IIE	310.545(a)(22)(ii)
Cough/cold	Cough/cold (antitussive)	Antitussive (mouthwash)	IIIE	IIIE	[52 FR 30055]
Cough/cold	Cough/cold (antitussive)	Antitussive (topical/inhalant)	IIIE	I	341.14(b)(2)
Cough/cold	Cough/cold (antitussive)	Antitussive (lozenge)	IIIE	I	341.14(b)(2)
Cough/cold	Cough/cold (expectorant)	Expectorant (topical/inhalant)	IIIE	IIIE	310.545(a)(6)(iii)
Cough/cold	Cough/cold (expectorant)	Expectorant (lozenge)	IIIE	IIIE	310.545(a)(6)(iii)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (lozenge)	IIIE	IIIE	[59 FR 43408]
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (mouthwash)	IIIE	IIIE	310.545(a)(6)(ii)(A)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Dental	Relief of oral discomfort	Toothache relief	IIS	IIS	Pending
Hemorrhoidal	Anorectal	Analgesic (external)	n/a	I	346.16(c)
Miscellaneous external	Antifungal	Diaper rash	Defer	IISE	310.545(a)(22)(ii)
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis/psoriasis	IIIE	IIIE	310.545(a)(7)
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	IISE	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Insect bite/sting	IISE	I	Pending
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	I	Pending
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	Defer	Pending
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(18)(v)(A)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Miscellaneous external	Wart remover	Wart remover	IISE	IISE	[55 FR 33254]
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous internal	Smoking deterrent	Smoking deterrent	IIE	IIE	310.544(d)
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Oral cavity	Oral health care	Analgesic/anesthetic	I	I	Pending
Topical analgesic	External analgesic	Counterirritant	I	I	Pending
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Menthol (0.1%–1.0%)					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	I	Pending
Menthol (1.25%–16%)					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIIE	310.545(a)(10)(v)
Hemorrhoidal	Anorectal	Counterirritant (intrarectal)	IIE	IIE	310.545(a)(26)(iv)
Hemorrhoidal	Anorectal	Counterirritant (external)	I	IIE	310.545(a)(26)(iv)
Meradimate					
Topical analgesic	Sunscreen	Sunscreen	I	I	352.10(h)
Meralein sodium					
Oral cavity	Oral health care	Antimicrobial	IISE	IISE	Pending
Merbromin					
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(18)(vi)
Miscellaneous external	Mercury	Antiseptic	IISE	IISE	310.545(a)(27)(i)
Merbromin (mercurochrome)					
Miscellaneous external	Mercury	First aid antiseptic	n/a	IIIE	310.545(a)(27)(i)
Mercufenol chloride					
Miscellaneous external	Mercury	First aid antiseptic	n/a	IIIE	310.545(a)(27)(i)
Miscellaneous external	Mercury	Antiseptic	IISE	IISE	310.545(a)(27)(i)
Miscellaneous external	Antimicrobial	First aid antiseptic	n/a	IIS	310.545(a)(27)(i)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Mercuric oxide, yellow					
Miscellaneous external	Mercury	First aid antiseptic	n/a	IISE	310.545(a)(27)(i)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Mercury	Antiseptic	IISE	IISE	310.545(a)(27)(i)
Ophthalmic	Ophthalmic	Anti-infective	IIISE	IISE	310.545(a)(21)(ii)
Mercuric salicylate					
Miscellaneous external	Mercury	First aid antiseptic	n/a	IISE	310.545(a)(27)(i)
Miscellaneous external	Mercury	Antiseptic	IISE	IISE	310.545(a)(27)(i)
Mercuric sulfide, red					
Miscellaneous external	Mercury	First aid antiseptic	n/a	IISE	310.545(a)(27)(i)
Miscellaneous external	Mercury	Antiseptic	IISE	IISE	310.545(a)(27)(i)
Mercury					
Miscellaneous external	Mercury	First aid antiseptic	n/a	IISE	310.545(a)(27)(i)
Miscellaneous external	Mercury	Antiseptic	IISE	IISE	310.545(a)(27)(i)
Mercury (any ingredient)					
n/a	Antimicrobial	Diaper rash	Defer	n/a	310.545(a)(27)(ii)
n/a	Contraceptive (vaginal)	Contraceptive	n/a	n/a	310.545(a)(28)
Mercury oleate					
Miscellaneous external	Mercury	First aid antiseptic	n/a	IISE	310.545(a)(27)(i)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Psoriasis	IIE	IIE	310.545(a)(7)
Miscellaneous external	Mercury	Antiseptic	IISE	IISE	310.545(a)(27)(i)
Mercury, ammoniated					
Miscellaneous external	Antimicrobial	First aid antiseptic	n/a	IISE	310.545(a)(27)(i)
Miscellaneous external	Skin bleach	Skin bleaching	IISE	IISE	310.545(a)(17)
Miscellaneous external	Mercury	Antiseptic	IISE	IISE	310.545(a)(27)(i)
Metaproterenol sulfate					
Cough/cold	Cough/cold (bronchodilator)	Bronchodilator	n/a	III	310.545(a)(6)(iv)(A)
Methapyrilene					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Methapyrilene fumarate					
Cough/cold	Cough/cold (antihistamine)	Antihistamine	I	IIS	310.545(a)(6)(i)(A)&(B)
Internal analgesic	Internal analgesic	Analgesic adjuvant	IIIE	IIS	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antihistamine	IIE	n/a	310.545(a)(6)(A)
Internal analgesic	Internal analgesic	Antipyretic adjuvant	IIIE	IIS	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antirheumatic adjuvant	IIIE	IIS	310.545(a)(23)(i)
Sedative	Daytime sedative	Sedative	IIISE	IISE	310.519(a)
Sedative	Nighttime sleep aid	Sleep aid	IIISE	IIS	[54 FR 6826]
Methapyrilene hydrochloride					
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	IISE	310.545(a)(10)(vii)
Cough/cold	Cough/cold (antihistamine)	Antihistamine	I	IIS	310.545(a)(6)(i)(A)&(B)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIE	310.545(a)(10)(v)
Miscellaneous internal	Menstrual/diuretic	Menstrual	n/a	IISE	310.545(a)(24)(i)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Sedative	Nighttime sleep aid	Sleep aid	IISE	IIS	[54 FR 6826]
Sedative	Daytime sedative	Sedative	IISE	IIS	310.519(a)
Topical analgesic	External analgesic	Analgesic/anesthetic	I	IIS	310.545(a)(10)(i)
Methenamine					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Methionine					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Methoxyphenamine hydrochloride					
Cough/cold	Cough/cold (bronchodilator)	Bronchodilator	I	IIIE	310.545(a)(6)(iv)(A)
Methoxypolyoxyethylene glycol 550 laurate					
Contraceptive/vaginal	Contraceptive (vaginal)	Contraceptive	IIIE	IIIE	310.545(a)(28)
Methyl nicotinate					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIIE	310.545(a)(10)(v)
Topical analgesic	External analgesic	Counterirritant	I	I	Pending
Methyl salicylate					
Dental	Relief of oral discomfort	Toothache relief	IISE	IISE	Pending
Dental	Relief of oral discomfort	Oral mucosal analgesic	IISE	IISE	Pending
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff	IIIE	IIIE	310.545(a)(7)
Miscellaneous external	External analgesic	Astringent	n/a	n/a	Pending
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIIE	310.545(a)(10)(v)
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Corn/callus remover	Corn/callus remover	IISE	IISE	[55 FR 33261]
Miscellaneous internal	Smoking deterrent	Smoking deterrent	IIIE	IIIE	310.544(d)
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Oral cavity	Oral health care	Analgesic/anesthetic	IIIE	IIIE	310.545(a)(14)
Topical analgesic	External analgesic	Counterirritant	I	I	Pending
Methylbenzethonium chloride					
Antimicrobial I	Antimicrobial	First aid antiseptic	n/a	I	Pending
Antimicrobial I	Antimicrobial	Antimicrobial soap	n/a	IISE	Pending
Antimicrobial I	Antimicrobial	Skin antiseptic	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Skin protectant	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	I	I	Pending
Antimicrobial I	Antimicrobial	Surgical hand scrub	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Health-care personnel handwash	IIIE	IIIE	Pending
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	IIIE	Pending

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Cradle cap	IIIE	IIIE	310.545(a)(7)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Corn/callus remover	Corn/callus remover	IISE	IISE	[55 FR 33261]
Methylcellulose					
Antacid	Antacid	Antacid	IIIE	IIIE	[39 FR 19873]
Laxative	Laxative	Bulk laxative	I	I	Pending
Miscellaneous internal	Weight control	Anorectic	IIIE	IISE	310.545(a)(20)
Ophthalmic	Ophthalmic	Demulcent	I	I	349.12(a)(4)
Methylene blue					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Methylparaben					
Antimicrobial II	Antifungal	Antifungal	IIISE	IIISE	310.545(a)(22)(ii)
Methyltestosterone					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IIS	IIS	310.528(a)
Miconazole nitrate					
Antimicrobial II	Antifungal	Anticandidal	I	n/a	n/a
Antimicrobial II	Antifungal	Antifungal	I	I	333.210(c)
Milk solids, dried					
Antacid	Antacid	Antacid	I	I	331.11(h)
Mineral oil					
Hemorrhoidal	Anorectal	Protectant (external)	I	I	346.14(7)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	I	I	346.14(7)
Laxative	Laxative	Lubricant laxative	I	I	Pending
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Diaper rash	Defer	I	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	Pending
Ophthalmic	Ophthalmic	Emollient	I	I	349.14(b)(2)
Mineral oil, light					
Ophthalmic	Ophthalmic	Emollient	I	I	349.14(b)(1)
Minerals					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	n/a	IISE	310.528(a)
Mono- and diglycerides					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Mullein					
Hemorrhoidal	Anorectal	Anorectal (external)	IISE	IISE	310.545(a)(26)(vii)
Hemorrhoidal	Anorectal	Anorectal (intrarectal)	IISE	IISE	310.545(a)(26)(vii)
Mycozyme					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
		Myrrh			
Dental	Relief of oral discomfort	Oral mucosal protectant	IIISE	IIISE	Pending
		Myrrh tincture			
Oral cavity	Oral health care	Antimicrobial	IISE	IISE	310.545(a)(14)
Oral cavity	Oral health care	Astringent	IISE	IISE	Pending
		Myrrh, fluid extract of			
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
		Naphazoline hydrochloride			
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	I	I	341.20(b)(6)
Ophthalmic	Ophthalmic	Vasoconstrictor	I	I	349.18(b)
		Natural estrogenic hormone			
Miscellaneous internal	Menstrual/diuretic	Menstrual	n/a	IISE	310.545(a)(24)(i)
		Neomycin sulfate			
Antimicrobial II	Antibiotic	Skin wound protectant	IIIS	Defer	n/a
		Neomycin sulfate (cream)			
Antimicrobial II	Antibiotic	First aid antibiotic	n/a	I	333.110(e)
		Neomycin sulfate (ointment)			
Antimicrobial II	Antibiotic	First aid antibiotic	n/a	I	333.110(d)
		Nettle			
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
		Niacinamide			
Miscellaneous internal	Menstrual/diuretic	Menstrual	n/a	IISE	310.545(a)(24)(i)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Sedative	Daytime sedative	Sedative	IIE	IISE	310.519(a)
		Nickel-pectin			
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
		Nitromersol			
Miscellaneous external	Mercury	First aid antiseptic	n/a	IISE	310.545(a)(27)(i)
Miscellaneous external	Mercury	Antiseptic	IISE	IISE	310.545(a)(27)(i)
Oral cavity	Oral health care	Antimicrobial	IISE	IISE	Pending
		Nonoxynol 9			
Contraceptive/vaginal	Vaginal	Lowers surface tension, mucolytic effects	I	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Minor irritations	IIIE	Withdrawn	n/a
Contraceptive/vaginal	Contraceptive (vaginal)	Contraceptive	I	Withdrawn	n/a
		Nonylphenoxypoly (ethyleneoxy) ethanol iodine			
Antimicrobial I	Antimicrobial	Surgical hand scrub	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Antimicrobial soap	n/a	IISE	Pending
Antimicrobial I	Antimicrobial	Health-care personnel handwash	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	IIISE	IIISE	Pending

(Continued)

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Antimicrobial I	Antimicrobial	Preoperative skin preparation	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin antiseptic	IIISE	IIISE	Pending
Noscapine					
Cough/cold	Cough/cold (antitussive)	Antitussive	IIIE	IIIE	[52 FR 30054]
Noscapine hydrochloride					
Cough/cold	Cough/cold (antitussive)	Antitussive	IIIE	IIIE	[52 FR 30054]
Nucleic acids					
Miscellaneous external	Hair growth/loss	Hair grower	n/a	n/a	310.527(a)
Nutmeg oil (oil of nutmeg)					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Nux vomica					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IISE	IISE	310.528(a)
Nux vomica extract					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Nystatin					
Antimicrobial II	Antifungal	Anticandida	I	IIISE	310.545(a)(22)(iv)
Obtundia surgical dressing					
Miscellaneous external	External analgesic	Insect bite/sting	IISE	IISE	Pending
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	Pending
Octinoxate					
Topical analgesic	Sunscreen	Sunscreen	I	I	352.10(j)
Octisalate					
Topical analgesic	Sunscreen	Sunscreen	I	I	352.10(k)
Octocrylene					
Topical analgesic	Sunscreen	Sunscreen	I	I	352.10(i)
Octoxynol 9					
Contraceptive/vaginal	Vaginal	Minor irritations	IIIE	Withdrawn	310.545(a)(28)(ii)
Contraceptive/vaginal	Vaginal	Lowers surface tension, mucolytic effects	I	Withdrawn	310.545(a)(28)(ii)
Contraceptive/vaginal	Contraceptive (vaginal)	Contraceptive	I	Withdrawn	310.545(a)(28)(ii)
Octyldodecanol					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	Pending
Octyl triazone					
n/a	TEA	Sunscreen	n/a		
Oil of erigeron					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Olive oil					
Miscellaneous external	Hair growth/loss	Hair grower	IISE	n/a	310.527(a)
Opium, powdered					
Laxative	Antidiarrheal	Antidiarrheal	I	IIISE	310.545(a)(3)(i)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Laxative	Antidiarrheal	Opium tincture Antidiarrheal	I	IIISE	310.545(a)(3)(i)
Miscellaneous internal	Weight control	Organic vegetables Anorectic	IISE	IISE	310.545(a)(20)
Miscellaneous internal	Digestive aid	Orthophosphoric acid Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Laxative	Laxative	Ox bile Stimulant laxative	IIISE	IIISE	310.545(a)(12)(iv)(A)
Miscellaneous internal	Digestive aid	Ox bile extract Digestive aid (intestinal distress)	IIE	IIE	310.545(a)(8)(i))
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIE	IIE	310.545(a)(8)(i)
Topical analgesic	Sunscreen	Oxybenzone Sunscreen	I	I	352.10(1)
Cough/cold	Cough/cold (nasal decongestant)	Oxymetazoline hydrochloride Nasal decongestant (topical/inhalant)	I	I	341.20(b)(7)
Antimicrobial II	Antifungal	Oxyquinoline Antifungal	IIISE	IIISE	310.545(a)(22)(ii)
Miscellaneous external	Antifungal	Diaper rash	Defer	IISE	310.545(a)(22)(ii)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	IIISE	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Oral cavity	Oral health care	Antimicrobial	IIISE	IIISE	Pending
Contraceptive/vaginal	Vaginal	Oxyquinoline citrate Minor irritations	IIISE	Withdrawn	n/a
Antimicrobial II	Antifungal	Oxyquinoline sulfate Antifungal	IIISE	IIISE	310.545(a)(22)(ii)
Contraceptive/vaginal	Vaginal	Minor irritations	IIISE	Withdrawn	n/a
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Miscellaneous external	External analgesic	Astringent	IISE	n/a	n/a
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Antimicrobial II	Antibiotic	Oxytetracycline hydrochloride First aid antibiotic	n/a	I	333.120 [combos]
Antimicrobial II	Antibiotic	Skin wound antibiotic	IIIE	Defer	n/a
Antimicrobial II	Antibiotic	Skin wound protectant	I	Defer	n/a
Miscellaneous external	External analgesic	Ozokerite Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	External analgesic	Padimate A Fever blister (topical)	Defer	Defer	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	Defer	Pending
Topical analgesic	Sunscreen	Sunscreen (≥5%)	I	IISE	Pending
Topical analgesic	Sunscreen	Sunscreen (<5%)	I	IIISE	Pending

(Continued)

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Padimate O					
Topical analgesic	Sunscreen	Sunscreen	I	I	352.10(m)
Pamabrom					
Miscellaneous internal	Menstrual/diuretic	Diuretic	I	I	Pending
Pancreatin					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIE	IIE	310.545(a)(8)(i)
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIIE	IIIE	310.545(a)(8)(i)
Miscellaneous internal	Exocrine pancreatic insufficiency	Exocrine pancreatic insufficiency	I	I	310.543(a)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Pancrelipase					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIIE	IIIE	310.545(a)(8)(i)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIE	IIE	310.545(a)(8)(i)
Miscellaneous internal	Exocrine pancreatic insufficiency	Exocrine pancreatic insufficiency	I	I	310.543(a)
Panthenol					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Insect bite/sting	n/a	IIIE	310.545(a)(10)(vi)
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	IIIE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(18)(vi)
Miscellaneous external	Corn/callus remover	Corn/callus remover	IISE	IISE	[55 FR 33261]
Pantothenic acid					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Papain					
Contraceptive/vaginal	Vaginal	Lowers surface tension, mucolytic effects	IIIE	n/a	Withdrawn
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIE	IIE	310.545(a)(8)(i)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Papaya enzymes					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Papaya, natural					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Para-chloromercuriphenol					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	IISE	310.545(a)(27)(ii)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Mercury	First aid antiseptic	IISE	n/a	310.545(a)(27)(i)
Miscellaneous external	Mercury	Antiseptic	IISE	IISE	310.545(a)(27)(i)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	310.545(a)(27)(ii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Para-<i>t</i>-butyl-<i>m</i>-cresol					
Miscellaneous external	External analgesic	Astringent	IISE	n/a	n/a
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Paraffin					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	n/a
Ophthalmic	Ophthalmic	Emollient	I	I	349.14(b)(3)
Paregoric					
Laxative	Antidiarrheal	Antidiarrheal	I	IIISE	310.545(a)(3)(i)
Parethoxycaine hydrochloride					
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Parsley					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Passion flower extract					
Sedative	Nighttime sleep aid	Sleep aid	IIE	IIE	[54 FR 6826]
Pectin					
Laxative	Antidiarrheal	Antidiarrheal	IIIE	IIIE	310.545(a)(3)(ii)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIISE	310.545(a)(10)(v)
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	Defer	Pending
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Oral cavity	Oral health care	Demulcent	I	I	Pending
Pega palo					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IISE	IISE	310.528(a)
Peppermint					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Peppermint oil					
Cough/cold	Cough/cold (antitussive)	Antitussive (topical/inhalant)	IIIE	IIIE	[52 FR 30054]
Cough/cold	Cough/cold (expectorant)	Expectorant (lozenge)	IIIE	IIIE	310.545(a)(6)(iii)
Cough/cold	Cough/cold (expectorant)	Expectorant (topical/inhalant)	IIIE	IIIE	310.545(a)(6)(iii)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (inhalant room spray)	IIIE	IIIE	[59 FR 43408]
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (lozenge)	IIIE	IIIE	[59 FR 43408]
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (mouthwash)	IIIE	IIIE	310.545(a)(6)(ii)(A)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	IIIE	IIIE	[59 FR 43408]
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Astringent	IISE	n/a	n/a
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	External analgesic	Insect bite/sting	IISE	IISE	310.545(a)(10)(vi)
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(18)(v)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIIE	IIIE	310.545(a)(8)(i)
Peppermint oil and sage oil					
=====	Gingivitis/plaque	Antiplaque/gingivitis	n/a	IIIE	Pending
Peppermint spirit					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Miscellaneous internal	Menstrual/diuretic	Premenstrual/ menstrual period	n/a	IISE	310.545(a)(24)(i)
Pepsin					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIE	IIE	310.545(a)(8)(i)
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIE	IIE	310.545(a)(8)(i)
Miscellaneous internal	Stomach acidifier	Stomach acidifier	IIE	IIE	310.540(a)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Pepsin, essence					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Peruvian balsam					
Hemorrhoidal	Anorectal	Wound healing agent (intrarectal)	IIIE	IIIE	310.545(a)(26)(x)
Hemorrhoidal	Anorectal	Wound healing (external)	IIIE	IIIE	310.545(a)(26)(x)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIIE	Pending
Peruvian balsam oil					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIIE	Pending
Petrolatum					
Hemorrhoidal	Anorectal	Protectant (external)	n/a	I	346.14(8)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	n/a	I	346.14(8)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Diaper rash	Defer	I	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	I	Pending
Ophthalmic	Ophthalmic	Emollient	n/a	I	349.14(b)(4)
Topical analgesic	Skin protectant	Skin protectant	I	I	347.10(m)
Petrolatum, red					
Topical analgesic	Sunscreen	Sunscreen	I	I	310.545(a)(29)
Petrolatum, white					
Hemorrhoidal	Anorectal	Protectant (intrarectal)	I	I	346.14(10)
Hemorrhoidal	Anorectal	Protectant (external)	I	I	346.14(10)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Diaper rash	Defer	I	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	I	Pending
Ophthalmic	Ophthalmic	Emollient	I	I	349.14(b)(6)
Topical analgesic	Skin protectant	Skin protectant	I	I	347.10(r)
Phenacaine hydrochloride					
Hemorrhoidal	Anorectal	Anesthetic (external)	IIS	IIS	310.545(a)(26)(vi)
Hemorrhoidal	Anorectal	Anesthetic (intrarectal)	IIS	IIS	310.545(a)(26)(vi)
Phenacetin					
Internal analgesic	Internal analgesic	Analgesic	IIS	IIS	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antipyretic	IIS	IIS	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antirheumatic	IISE	Not OTC	310.545(a)(23)(i)
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Miscellaneous internal	Menstrual/diuretic	Analgesic	IIS	IISE	310.545(a)(24)(i)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Phenindamine tartrate					
Cough/cold	Cough/cold (antihistamine)	Antihistamine	I	I	341.12(i)
Miscellaneous internal	Menstrual/diuretic	Menstrual	n/a	IISE	310.545(a)(24)(i)
Pheniramine maleate					
Cough/cold	Cough/cold (antihistamine)	Antihistamine	I	I	341.12(j)
Internal analgesic	Internal analgesic	Analgesic adjuvant	IIIE	IIIE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antipyretic adjuvant	IIIE	IIIE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antirheumatic adjuvant	IIIE	n/a	310.545(a)(23)(i)
Phenobarbital					
Cough/cold	Cough/cold (miscellaneous)	Corrective	IIIE	IIS	Pending
Phenol					
Antimicrobial I	Antimicrobial	First aid antiseptic	n/a	n/a	Pending
Antimicrobial I	Antimicrobial	Surgical hand scrub	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Surgical hand scrub	IIS	IIS	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Skin antiseptic	IIS	IIS	Pending
Antimicrobial I	Antimicrobial	Skin wound protectant	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Antimicrobial soap	IIS	IIS	Pending
Antimicrobial I	Antimicrobial	Antimicrobial soap	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Skin wound protectant	n/a	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin wound protectant	IIS	IIS	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	IIS	IIS	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	IIS	IIS	Pending
Antimicrobial I	Antimicrobial	First aid antiseptic	n/a	I	Pending

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Antimicrobial I	Antimicrobial	Skin antiseptic	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Health-care personnel handwash	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Health-care personnel handwash	IIS	IIS	Pending
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Antimicrobial II	Antifungal	Antifungal	IISE	IIISE	310.545(a)(22)(ii)
Contraceptive/vaginal	Vaginal	Minor irritations	IIISE	Withdrawn	n/a
Dental	Relief of oral discomfort	Toothache relief	IIISE	IIISE	Pending
Dental	Relief of oral discomfort	Oral mucosal analgesic	I	I	Pending
Hemorrhoidal	Anorectal	Antiseptic (intrarectal)	IISE	IISE	310.545(a)(26)(ii)
Hemorrhoidal	Anorectal	Antiseptic (external)	IISE	IISE	310.545(a)(26)(ii)
Miscellaneous external	Antifungal	Diaper rash	Defer	IISE	310.545(a)(22)(ii)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	IISE	310.545(a)(27)(ii)
Miscellaneous external	Boil treatment	Boil treatment	IISE	IIISE	310.531(a)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis/psoriasis	IIIE	IIIE	310.545(a)(7)
Miscellaneous external	External analgesic	Astringent	IISE	n/a	n/a
Miscellaneous external	External analgesic	Diaper rash	Defer	IISE	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	I	Pending
Miscellaneous external	External analgesic	Insect bite/sting	IISE	I	Pending
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	I	Pending
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	310.545(a)(27)(ii)
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(18)(v)(A)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Oral cavity	Oral health care	Analgesic/anesthetic	I	I	Pending
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Phenol sulfonate					
Laxative	Antiemetic	Antiemetic	IIIE	IIE	[52 FR 15891]
Topical analgesic	Sunscreen	Sunscreen	n/a	n/a	[64 FR 27682]
Phenolate sodium					
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	I	Pending
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Antimicrobial II	Antifungal	Antifungal	IISE	IIISE	310.545(a)(22)(ii)
Contraceptive/vaginal	Vaginal	Minor irritations	IISE	Withdrawn	n/a
Dental	Relief of oral discomfort	Toothache relief	IIISE	IIISE	Pending
Dental	Relief of oral discomfort	Oral mucosal analgesic	I	I	Pending
Hemorrhoidal	Anorectal	Antiseptic (external)	IISE	IISE	310.545(a)(26)(ii)
Hemorrhoidal	Anorectal	Antiseptic (intrarectal)	IISE	IISE	310.545(a)(26)(ii)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis/psoriasis	IIIE	IIIE	310.545(a)(7)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	I	Pending
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Phenolphthalein, yellow					
Laxative	Laxative	Stimulant laxative	I	I/IIS	310.545(a)(12)(iv)(B)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Phenolphthalein, white					
Laxative	Laxative	Stimulant laxative	I	I/IIS	310.545(a)(12)(iv)(B)
Phenoxyacetic acid					
Miscellaneous external	Corn/callus remover	Corn/callus remover	IIIE	IIIE	[55 FR 33261]
Phenyl salicylate					
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Antimicrobial II	Antifungal	Antifungal	IIISE	IIISE	310.545(a)(22)(ii)
Laxative	Antidiarrheal	Antidiarrheal	IIIE	IIIE	310.545(a)(3)(i)
Laxative	Antiemetic	Antiemetic	IIIE	IIE	[52 FR 15891]
Miscellaneous external	Corn/callus remover	Corn/callus remover	IISE	IISE	[55 FR 33261]
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Phenylalanine					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Phenylephrine bitartrate (in an effervescent dosage form)					
n/a	n/a	Nasal decongestant (oral)	n/a	n/a	341.20(a)(4)
Phenylephrine hydrochloride					
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (oral)	I	I	341.20(a)(1)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	I	I	341.20(b)(8)
Hemorrhoidal	Anorectal	Vasoconstrictor (intrarectal)	I	I	346.10(d)
Hemorrhoidal	Anorectal	Vasoconstrictor (external)	I	I	346.10(d)
Oral cavity	Oral health care	Oral mucosal decongestant	IIIE	IIIE	Pending
Phenylephrine hydrochloride (0.08%–0.2%)					
Ophthalmic	Ophthalmic	Vasoconstrictor	I	I	349.18(c)
Phenylephrine hydrochloride (less than 0.08%)					
Ophthalmic	Ophthalmic	Vasoconstrictor	IIIE	IIIE	310.545(a)(21)(v)
Phenylmercuric acetate					
Contraceptive/vaginal	Contraceptive (vaginal)	Contraceptive	IIS	Withdrawn	310.545(a)(28)
Phenylmercuric nitrate					
Contraceptive/vaginal	Contraceptive (vaginal)	Contraceptive	IIS	Withdrawn	310.545(a)(28)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Mercury	First aid antiseptic	n/a	IIIE	310.545(a)(27)(i)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Mercury	Antiseptic	IISE	IISE	310.545(a)(27)(i)
Phenylpropanolamine bitartrate					
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (oral)	I	II	Pending
Phenylpropanolamine hydrochloride					
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (oral)	I	II	Pending

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	IIIE	II	Pending
Miscellaneous internal	Weight control	Anorectic	I	I/IIS	Pending
Oral cavity	Oral health care	Oral mucosal decongestant	IIIE	IIIE	Pending
Phenylpropanolamine maleate					
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (oral)	I	II	Pending
Phenyltoloxamine citrate					
Internal analgesic	Internal analgesic	Antipyretic adjuvant	IIIE	IIIE	Pending
Internal analgesic	Internal analgesic	Antirheumatic adjuvant	IIIE	n/a	n/a
Phenyltoloxamine dihydrogen citrate					
Cough/cold	Cough/cold (antihistamine)	Antihistamine	IIIE	IIIE	310.545(a)(6)(i)(B)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(18)(vi)
Sedative	Nighttime sleep aid	Sleep aid	IIISE	IIISE	[54 FR 6826]
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)
Phosphorated carbohydrate					
Laxative	Antiemetic	Antiemetic	IIIE	IIIE	[52 FR 15891]
Phosphoric acid					
Dental	Anticaries	Anticavity agent	IIE	n/a	310.545(a)(2)(ii)
Phosphorus					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Phytolacca					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Picrotoxin					
Miscellaneous external	Pediculicide	Pediculicide	IISE	IISE	310.545(a)(25)(i)
Pine tar					
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis/psoriasis	IIIE	IIIE	310.545(a)(7)
Pine tar syrup					
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
Pineapple enzymes					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Piperazine citrate					
Miscellaneous internal	Anthelmintic	Anthelmintic	IIS	IIS	[51 FR 27758]
Piperocaine hydrochloride					
Ophthalmic	Ophthalmic	Analgesic/anesthetic	IIS	IIS	310.545(a)(21)(i)
Pipsissewa					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Piroctone olamine					
n/a	TEA	Dandruff	n/a		

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
<i>Piscidia erythrina</i>					
Miscellaneous internal	Menstrual/diuretic	Dysmenorrhea	IIE	IIE	310.545(a)(24)(i)
Plantago seed					
Laxative	Laxative	Bulk laxative	I	IISE	Pending
Miscellaneous internal	Weight control	Anorectic	IIIE	IISE	310.545(a)(20)
Podophyllum resin					
Laxative	Laxative	Stimulant laxative	IIS	IIS	310.545(a)(12)(iv)(A)
Poloxamer 188					
Antimicrobial I	Antimicrobial	Skin wound cleanser	n/a	I	Pending
Laxative	Laxative	Stool softener	IIIE	IIIE	310.545(a)(12)(iii)
Poloxamer 407					
Dental	Relief of oral discomfort	Tooth desensitizer (in combination only)	IIIE	IIIE	Pending
Poloxamer–iodine complex					
Antimicrobial I	Antimicrobial	Surgical hand scrub	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Antimicrobial soap	n/a	IISE	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Skin antiseptic	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Skin protectant	IIIE	IIIE	Pending
Antimicrobial I	Antimicrobial	Health-care personnel handwash	IIIE	IIIE	Pending
Polycarbophil					
Laxative	Antidiarrheal	Antidiarrheal	I	I	310.545(a)(3)(ii)
Laxative	Laxative	Bulk laxative	I	I	Pending
Polycarbophil, calcium					
Laxative	Antidiarrheal	Antidiarrheal	n/a	I	310.545(a)(3)(ii)
Laxative	Laxative	Bulk laxative	n/a	n/a	n/a
Polydimethylsiloxane and poloxamer					
n/a	Gingivitis/plaque	Antiplaque/gingivitis	n/a	IIIE	Pending
Polyethylene glycol 300					
Ophthalmic	Ophthalmic	Demulcent	I	I	349.12(d)(2)
Polyethylene glycol 400					
Ophthalmic	Ophthalmic	Demulcent	I	I	349.12(d)(3)
Polyethylene glycol 6000					
Ophthalmic	Ophthalmic	Demulcent	n/a	IIIE	310.545(a)(21)(iv)
Polymyxin B sulfate					
Antimicrobial II	Antibiotic	Skin wound protectant	I	Defer	n/a
Antimicrobial II	Antibiotic	First aid antibiotic	IIIE	I	333.120 [combos]
Antimicrobial II	Antibiotic	Skin wound antibiotic	I	Defer	n/a
Polyoxyethylene laurate					
Miscellaneous external	External analgesic	Astringent	IISE	n/a	n/a
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Polysorbate 20					
Miscellaneous external	Hair growth/loss	Hair grower	n/a	IIE	310.527(a)
Polysorbate 60					
Miscellaneous external	Hair growth/loss	Hair grower	n/a	IIE	310.527(a)
Polysorbate 80					
Ophthalmic	Ophthalmic	Demulcent	I	I	349.12(d)(4)
Polyvinyl alcohol					
Ophthalmic	Ophthalmic	Demulcent	I	I	349.12(e)
Potassium acetate					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IIE	310.545(a)(24)(i)
Potassium bicarbonate					
Antacid	Antacid	Antacid	n/a	n/a	331.11(j)(1)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Potassium bromide					
Sedative	Nighttime sleep aid	Sleep aid	IIE	IIE	[54 FR 6826]
Sedative	Daytime sedative	Sedative	IIS	IIE	310.519(a)
Potassium carbonate					
Antacid	Antacid	Antacid	n/a	n/a	331.11(j)(1)
Laxative	Antidiarrheal	Antidiarrheal	IIE	IIE	310.545(a)(3)(ii)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Potassium chlorate					
Oral cavity	Oral health care	Antimicrobial	IIE	IIE	Pending
Potassium citrate					
Miscellaneous internal	Weight control	Anorectic	IIE	IIE	310.545(a)(20)
Potassium extract					
Miscellaneous internal	Weight control	Anorectic	IIE	IIE	310.545(a)(20)
Potassium ferrocyanide					
Miscellaneous external	External analgesic	Astringent	IIE	n/a	Pending
Miscellaneous external	Skin protectant	Astringent	IIE	IIE	310.545(a)(18)(ii)
Potassium guaiacolsulfonate					
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
Potassium iodide					
Cough/cold	Cough/cold (expectorant)	Expectorant	IIS	IIE	310.545(a)(6)(iii)
Oral cavity	Oral health care	Expectorant	IIS	IIS	310.545(a)(6)(iii)
Potassium nitrate					
Dental	Relief of oral discomfort	Tooth desensitizer	IIIE	I	Pending
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IIE	310.545(a)(24)(i)
Potassium sorbate					
Contraceptive/vaginal	Vaginal	Minor irritations	I	Withdrawn	n/a
Povidone					
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IIE	310.545(a)(18)(vi)(A)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IIE	310.545(a)(18)(vi)(A)
Ophthalmic	Ophthalmic	Demulcent	I	I	349.12(f)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Povidone silver nitrate					
Miscellaneous internal	Smoking deterrent	Smoking deterrent	n/a	n/a	310.544(d)
Povidone vinylacetate copolymers					
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	n/a	n/a	310.545(a)(18)(vi)(A)
Povidone-iodine					
Antimicrobial I	Antimicrobial	Antiseptic	n/a	I	Pending
Antimicrobial I	Antimicrobial	Surgical hand scrub	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Antimicrobial soap	n/a	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin protectant	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin antiseptic	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Health-care personnel handwash	IIISE	IIISE	Pending
Antimicrobial II	Acne	Acne	IIIE	IIIE	310.545(a)(1)
Antimicrobial II	Antifungal	Antifungal	IIIE	I	333.210(d)
Contraceptive/vaginal	Vaginal	Minor irritations	I	Withdrawn	n/a
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis/psoriasis	IIIE	IIIE	310.545(a)(7)
Oral cavity	Oral health care	Antimicrobial	IIISE	IIISE	Pending
Pramoxine hydrochloride					
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	I	Pending
Hemorrhoidal	Anorectal	Anesthetic (external)	I	I	346.10(g)
Hemorrhoidal	Anorectal	Anesthetic (intrarectal)	IIIE	IIIE	[55 FR 1779]
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	IISE	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	I	Pending
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Pregnenolone					
Miscellaneous external	Hormone	Hormone	IISE	IIIE	310.530(a)
Pregnenolone acetate					
Miscellaneous external	Hormone	Hormone	IISE	IIIE	310.530(a)
Progesterone					
Miscellaneous external	Hormone	Hormone	IIIE	IIIE	310.530(a)
Prolase					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Promethazine hydrochloride					
Cough/cold	Cough/cold (antihistamine)	Antihistamine	I	IIIS	[57 FR 58373]
Propionic acid					
Antimicrobial II	Antifungal	Antifungal	IIIE	IIIE	310.545(a)(22)(ii)
Propyl benzoate					
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	n/a

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Propyl p-benzoate					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Propylene glycol					
Miscellaneous external	Pediculicide	Pediculicide	IISE	IISE	310.545(a)(25)(i)
Ophthalmic	Ophthalmic	Demulcent	I	I	349.12(d)(5)
Miscellaneous external	Hair growth/loss	Hair grower	IISE	n/a	310.527(a)
Propylhexedrine					
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	I	I	341.20(b)(9)
Propylparaben					
Antimicrobial II	Antifungal	Antifungal	IIISE	IIISE	310.545(a)(22)(ii)
Protease					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Protein					
Miscellaneous external	Hair growth/loss	Hair grower	IISE	n/a	310.527(a)
Protein hydrolysate					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIISE	310.545(a)(18)(iii)
Prune concentrate dehydrate					
Laxative	Laxative	Stimulant laxative	IIIE	IIIE	310.545(a)(12)(iv)(A)
Prune powder					
Laxative	Laxative	Stimulant laxative	IIIE	IIIE	310.545(a)(12)(iv)(A)
Pseudoephedrine hydrochloride					
Cough/cold	Cough/cold (bronchodilator)	Bronchodilator nasal	IIE	IIE	310.545(a)(6)(iv)(A)
Cough/cold	Cough/cold (nasal decongestant)	Decongestant (oral)	I	I	341.20(a)(2)
Pseudoephedrine sulfate					
Cough/cold	Cough/cold (bronchodilator)	Bronchodilator	IIE	IIE	310.545(a)(6)(iv)(A)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (oral)	I	I	341.20(a)(3)
Psyllium hydrophilic mucilloid					
Laxative	Laxative	Bulk laxative	I	IISE	Pending
Psyllium seed					
Laxative	Laxative	Bulk laxative	I	IISE	Pending
Psyllium seed (blond)					
Laxative	Laxative	Bulk laxative	I	IISE	Pending
Psyllium seed husks					
Laxative	Laxative	Bulk laxative	I	IISE	Pending

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Pyrantel pamoate					
Miscellaneous internal	Anthelmintic	Anthelmintic	I	I	357.110
Pyrethrum extract (aerosol) with piperonyl butoxide					
n/a	Pediculicide	Pediculicide	n/a	n/a	310.545(a)(25)(ii)
Pyrethrum extract (nonaerosol) with piperonyl butoxide					
Miscellaneous external	Pediculicide	Pediculicide	I	I	358.610
Pyridoxine hydrochloride					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	DEF	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	IISE	310.545(a)(18)(iv)
Miscellaneous internal	Menstrual/diuretic	Premenstrual/ menstrual period	IIIE	IIIE	Pending
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Pyrilamine maleate					
Antimicrobial II	Acne	Acne	IIIE	IIIE	310.545(a)(1)
Cough/cold	Cough/cold (antihistamine)	Antihistamine	I	I	341.12(k)
Internal analgesic	Internal analgesic	Analgesic adjuvant	IIIE	IIIE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antipyretic adjuvant	IIIE	IIIE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antirheumatic adjuvant	IIIE	n/a	310.545(a)(23)(i)
Miscellaneous external	External analgesic	Insect bite/sting	IISE	IISE	310.545(a)(10)(vi)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(18)(v)(A)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	n/a	IISE	Pending
Miscellaneous internal	Menstrual/diuretic	Antihistamine	I	IIIE	Pending
Oral cavity	Oral health care	Analgesic/anesthetic	IIIE	IIIE	310.545(a)(14)
Sedative	Nighttime sleep aid	Sleep aid	IIIE	IIIE	[54 FR 6826]
Sedative	Daytime sedative	Sedative	IIIE	IIIE	310.519(a)
Pyrithione zinc					
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff	I	I	358.710(a)(2)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff	I	I	358.710(a)(3)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Seborrheic dermatitis	I	I	358.710(b)(3)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Seborrheic dermatitis	I	I	358.710(b)(2)
Quinine					
Internal analgesic	Internal analgesic	Analgesic	IIS	IIS	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antipyretic	IIS	IIS	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antirheumatic	IISE	Not OTC	310.545(a)(23)(i)
Quinine ascorbate					
Miscellaneous internal	Smoking deterrent	Smoking deterrent	IIIE	IIIE	310.544(d)
Quinine sulfate					
Miscellaneous internal	Leg muscle cramp	Nocturnal leg muscle cramps	IIIE	IIIE	310.546
Racemethionine					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIISE	310.545(a)(18)(iii)
Racephedrine hydrochloride					
Cough/cold	Cough/cold (bronchodilator)	Bronchodilator	I	I	341.16(f)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	I	I	310.545(a)(6)(ii)(B)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (oral)	IIIE	IIIE	310.545(a)(6)(ii)(B)
Racpinephrine hydrochloride					
Cough/cold	Cough/cold (bronchodilator)	Bronchodilator	n/a	n/a	341.16(g)
Resorcinol					
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	I	Pending
n/a		Dandruff/seborrheic dermatitis/ psoriasis	n/a	n/a	310.545(a)(7)
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Antimicrobial II	Antifungal	Antifungal	IISE	IISE	310.545(a)(22)(ii)
Hemorrhoidal	Anorectal	Antiseptic (intrarectal)	IISE	IISE	310.545(a)(26)(ii)
Hemorrhoidal	Anorectal	Keratolytic (external)	I	I	346.20(a)
Hemorrhoidal	Anorectal	Keratolytic (intrarectal)	IISE	IISE	346.20(a)
Hemorrhoidal	Anorectal	Antiseptic (external)	IISE	IISE	310.545(a)(26)(ii)
Miscellaneous external	Antifungal	Diaper rash	Defer	IISE	310.545(a)(22)(ii)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	IISE	Pending
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Psoriasis	IIE	IIE	[56 FR 63567]
Miscellaneous external	External analgesic	Diaper rash	Defer	IISE	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	I	Pending
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Resorcinol monoacetate					
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Rhubarb fluid extract					
Laxative	Antidiarrheal	Antidiarrheal	IISE	IISE	310.545(a)(3)(ii)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Rhubarb, Chinese					
Laxative	Laxative	Stimulant laxative	IIISE	IIISE	310.545(a)(12)(iv)(A)
Riboflavin					
Miscellaneous internal	Menstrual/diuretic	Premenstrual/ menstrual period	n/a	IISE	310.545(a)(24)(i)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Rice polishings					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Rose petals, infusion of					
Ophthalmic	Ophthalmic	Astringent	IIIE	IIIE	310.545(a)(21)(iii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Rosin					
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Rosin cerate					
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Sabadilla alkaloids					
Miscellaneous external	Pediculicide	Pediculicide	IISE	IISE	310.545(a)(25)(i)
Sabel, liposterolic extract of					
Miscellaneous internal	Benign prostatic hypertrophy	Benign prostatic hypertrophy	n/a	n/a	310.532(a)
Saccharin					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Sage oil					
Miscellaneous external	Skin protectant	Astringent	n/a	IISE	310.545(a)(18)(ii)
Salicyl alcohol					
Oral cavity	Oral health care	Analgesic/anesthetic	I	I	Pending
Salicylamide					
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	IIIE	310.545(a)(10)(vii)
Internal analgesic	Internal analgesic	Analgesic adjuvant	IIISE	IIISE	Pending
Internal analgesic	Internal analgesic	Analgesic	IIISE	IIISE	Pending
Internal analgesic	Internal analgesic	Antipyretic adjuvant	IIISE	IIISE	Pending
Internal analgesic	Internal analgesic	Antipyretic	IIISE	IIISE	Pending
Internal analgesic	Internal analgesic	Antirheumatic adjuvant	IIISE	n/a	n/a
Internal analgesic	Internal analgesic	Antirheumatic	IISE	Not OTC	n/a
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIIE	310.545(a)(10)(v)
Miscellaneous internal	Menstrual/diuretic	Analgesic	IIISE	IIISE	Pending
Sedative	Nighttime sleep aid	Sleep aid	IIE	IIE	[54 FR 6826]
Sedative	Daytime sedative	Sedative	IIE	IISE	310.519(a)
Topical analgesic	External analgesic	Analgesic/anesthetic	IIIE	IIIE	310.545(a)(10)(i)
Salicylic acid					
Antimicrobial II	Acne	Acne	IIIE	I	333.310(c)
Antimicrobial II	Antifungal	Antifungal	IIIE	IIIE	310.545(a)(22)(ii)
Antimicrobial II	Acne	Acne	IISE	IISE	310.545(a)(1)
Miscellaneous external	Antifungal	Diaper rash	Defer	IISE	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff	I	I	358.710(a)(4)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Miscellaneous external	Corn/callus remover	Corn/callus remover	I	I	358.510(a)
Miscellaneous external	Wart remover	Wart remover	I	IISE	358.110(a)
Miscellaneous external	Wart remover	Wart remover	I	I	358.110(b)
Miscellaneous external	Wart remover	Wart remover	I	I	358.110(c)
Miscellaneous external	Corn/callus remover	Corn/callus remover	I	I	358.510 (b)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Seborrheic dermatitis	I	I	358.710(b)(4)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Psoriasis	I	I	358.710(c)(2)
Salsalate					
Internal analgesic	Internal analgesic	Analgesic	IIISE	IIISE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antipyretic	IIISE	IIISE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antirheumatic	IIISE	Not OTC	310.545(a)(23)(i)
Sanguinaria extract					
n/a	Gingivitis/plaque	Gingivitis/antiplaque	n/a	IIIE	Pending
Sarsaparilla					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IISE	IISE	310.528(a)
Sassafras oil					
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Saw palmetto					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Scopolamine aminoxide hydrobromide					
Sedative	Nighttime sleep aid	Sleep aid	IISE	IIS	[54 FR 6826]
Sedative	Daytime sedative	Sedative	IISE	IISE	310.519(a)
Scopolamine hydrobromide					
Laxative	Antidiarrheal	Antidiarrheal	IIE	IIE	310.545(a)(3)(i)
Laxative	Antiemetic	Antiemetic	n/a	IIIE	[52 FR 15891]
Sedative	Nighttime sleep aid	Sleep aid	IISE	IIS	[54 FR 6826]
Sedative	Daytime sedative	Sedative	IISE	IISE	310.519(a)
Sea minerals					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Selenium sulfide					
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff	I	I	358.710(a)(5)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Seborrheic dermatitis	I	I	358.710(b)(5)
Selenium sulfide, micronized					
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff	n/a	I	358.710(a)(6)
Senecio aureus					
Miscellaneous internal	Menstrual/diuretic	Dysmenorrhea	IISE	IISE	310.545(a)(24)(i)
Senna					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(8)(ii)
Senna fluid extract					
Laxative	Laxative	Stimulant laxative	I	I/IIIS	Pending
Senna pod concentrate					
Laxative	Laxative	Stimulant laxative	I	I/IIIS	Pending
Senna syrup					
Laxative	Laxative	Stimulant laxative	I	I/IIIS	Pending

(Continued)

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Sennosides					
Laxative	Laxative	Stimulant laxative	I	I/IIIS	Pending
Sesame oil					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	Pending
Sesame seed					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Shark liver oil					
n/a	Insect bite/sting	Insect bite/sting	n/a	n/a	310.545(a)(18)(v)(B)
n/a	Poison ivy/oak/sumac	Poison ivy/oak/ sumac	n/a	n/a	310.545(a)(18)(vi)(B)
n/a	Skin protectant	Fever blister (topical)	n/a	I	Pending
Hemorrhoidal	Anorectal	Wound healing agent (intrarectal)	IIIE	IIIE	310.545(a)(26)(x)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	I	I	346.14(b)(3)
Hemorrhoidal	Anorectal	Wound healing agent (external)	IIIE	IIIE`	310.545(a)(26)(x)
Hemorrhoidal	Anorectal	Protectant (external)	I	I	346.14(b)(3)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Protectant	I	I	Pending
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIISE	Pending
Topical analgesic	Skin protectant	Skin protectant	I	I	310.545(a)(18)(i)(B)
Silicone					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Silver acetate					
Miscellaneous internal	Smoking deterrent	Smoking deterrent	IIIE	IIIE	310.544(d)
Silver nitrate					
Miscellaneous external	External analgesic	Astringent	IISE	n/a	n/a
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous internal	Smoking deterrent	Smoking deterrent	IISE	IISE	310.544(d)
Silver protein, mild					
Ophthalmic	Ophthalmic	Anti-infective	IIIE	IIIE	310.545(a)(21)(ii)
Simethicone					
Antacid	Antacid	Antacid	IIIE	IIIE	[39 FR 19873]
Antacid	Antiflatulent	Antiflatulent	IIIE	I	332.10
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIIE	IIIE	[58 FR 54454]
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIIE	IIIE	[58 FR 54454]
Sodium					
Miscellaneous internal	Weight control	Anorectic	IIISE	IISE	310.545(a)(20)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Sodium 3, 4-dimethylphenyl-glyoxylate					
Topical analgesic	Sunscreen	Sunscreen	IISE	IISE	[64 FR 27682]
Sodium acetylsalicylate					
Miscellaneous internal	Overindulgence in alcohol/food	Overindulgence remedies (hangover)	I	I	Pending
Sodium aluminum chlorohydroxy lactate (aerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIISE	IIISE	310.545(a)(4)
Sodium aluminum chlorohydroxy lactate (nonaerosol)					
Antiperspirant	Antiperspirant	Antiperspirant	IIIE	IIIE	310.545(a)(4)
Sodium aminobenzoate					
Internal analgesic	Internal analgesic	Analgesic adjuvant	IISE	IISE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antipyretic adjuvant	IISE	IISE	310.545(a)(23)(i)
Internal analgesic	Internal analgesic	Antirheumatic adjuvant	IISE	n/a	310.545(a)(23)(i)
Sodium benzoate					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Sodium bicarbonate					
n/a	Gingivitis/plaque	Gingivitis/antiplaque	n/a	IIIE	Pending
Antacid	Antacid	Antacid	I	I	331.11(k)(1)
Contraceptive/vaginal	Vaginal	Alters vaginal pH	IIIE	Withdrawn	n/a
Dental	Anticaries	Anticavity agent	IIE	IIE	[60 FR 52504]
Internal analgesic	Internal analgesic	Corrective	I	n/a	n/a
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Insect bite/sting	IISE	n/a	n/a
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIISE	Pending
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	Pending
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	I	Pending
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIIE	IIIE	310.545(a)(8)(i)
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIIE	IIISE	310.545(a)(8)(i)
Miscellaneous internal	Weight control	Anorectic	IIIE	IISE	310.545(a)(20)
Oral cavity	Oral health care	Debriding agent	I	I	Pending
Topical analgesic	Skin protectant	Skin protectant	I	I	347.10(O)
Sodium borate					
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Antimicrobial II	Antifungal	Antifungal	IIISE	IIIE	310.545(a)(22)(ii)
Contraceptive/vaginal	Vaginal	Lowers surface tension, mucolytic effects	IIISE	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Minor irritations	IIISE	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Alters vaginal pH	IIISE	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Astringent	IIE	IIE	n/a
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis/psoriasis	n/a	n/a	310.545(a)(7)
Miscellaneous external	External analgesic	Astringent	n/a	n/a	n/a
Miscellaneous external	External analgesic	Insect bite/sting	IISE	IISE	310.545(a)(10)(vi)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(18)(v)(A)
Oral cavity	Oral health care	Debriding agent	IISE	IISE	Pending
Sodium borate monohydrate					
Dental	Oral mucosal injury	Skin wound cleanser			Pending
Sodium bromide					
Sedative	Nighttime sleep aid	Sleep aid	IISE	IISE	[54 FR 6826]
Sedative	Daytime sedative	Sedative	IIS	IISE	310.519(a)
Sodium caprylate					
Antimicrobial II	Antifungal	Antifungal	IIIE	IIIE	310.545(a)(22)(ii)
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Sodium carbonate					
Antacid	Antacid	Antacid	I	I	331.11(k)(1)
Contraceptive/vaginal	Vaginal	Alters vaginal pH	IIISE	Withdrawn	n/a
Internal analgesic	Internal analgesic	Corrective	I	n/a	n/a
Sodium caseinate					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Sodium chloride					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Ophthalmic	Ophthalmic	Hypertonic agent	I	I	349.16
Sodium citrate					
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
Dental	Relief of oral discomfort	Tooth desensitizer (in combination only)	IIIE	IIIE	Pending
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIIE	IIIE	310.545(a)(8)(i)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIIE	IIIE	310.545(a)(8)(i)
Sodium citrate in solution					
Miscellaneous internal	Overindulgence in alcohol/food	Overindulgence remedies (hangover)	I	I	Pending
Miscellaneous internal	Overindulgence in alcohol/food	Overindulgence remedies (hangover)	I	I	Pending
Sodium diacetate					
Miscellaneous external	External analgesic	Astringent	IISE	n/a	n/a
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Sodium dichromate					
Oral cavity	Oral health care	Antimicrobial	IIS	IISE	Pending
Sodium fluoride					
Dental	Anticaries	Anticavity dentifrice	I	I	355.10(a)(2)
Dental	Anticaries	Anticavity dental rinse	I	I	355.10(a)(3)(iv)
Dental	Anticaries	Anticavity dental rinse	I	I	355.10(a)(3)(v)
Dental	Anticaries	Anticavity dentifrice	I	I	355.10(a)(1)
Dental	Anticaries	Anticavity dental rinse	IISE	I	355.10(a)(3)(iii)
Dental	Relief of oral discomfort	Tooth desensitizer (in combination only)	IIIE	IISE	Pending

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Dental	Relief of oral discomfort	Tooth desensitizer	IIIE	IIIE	Pending
Contraceptive/vaginal	Vaginal	Sodium lactate Alters vaginal pH	IIIE	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Sodium lauryl sulfate Lowers surface tension, mucolytic effects	I	Withdrawn	n/a
Dental	Anticaries	Sodium monofluorophosphate Anticavity dentrifice	I	I	355.10(b)(1)
Dental	Anticaries	Anticavity dental rinse	IIS	IIS	310.545(a)(2)(i)
Dental	Relief of oral discomfort	Tooth desensitizer	IIIE	IIIE	Pending
Dental	Anticaries	Anticavity dentrifice	I	I	355.10(b)(2)
Miscellaneous internal	Menstrual/diuretic	Sodium nitrate Diuretic	n/a	IISE	310.545(a)(24)(i)
Laxative	Laxative	Sodium oleate Stimulant laxative	IIIE	IIIE	310.545(a)(12)(iv)(A)
Contraceptive/vaginal	Vaginal	Sodium perborate Alters vaginal pH	IIISE	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Astringent	IIISE	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Lowers surface tension, mucolytic effects	IIISE	Withdrawn	n/a
Contraceptive/vaginal	Vaginal	Minor irritations	IIISE	Withdrawn	n/a
Oral cavity	Oral health care	Debriding agent	IIISE	IIISE	Pending
Dental	Oral health care	Sodium perborate monohydrate Wound cleanser	IISE	I	Pending
Dental	Anticaries	Sodium phosphate, dibasic Anticavity agent	IIE	IIE	310.545(a)(2)(ii)
Laxative	Laxative	Saline laxative	I	I	Pending
Dental	Anticaries	Sodium phosphate, monobasic Anticavity agent	IIE	IIE	310.545(a)(2)(ii)
Laxative	Laxative	Saline laxative	I	I	Pending
n/a	TEA	Sodium picosulfate Laxative	n/a		
Antacid	Antacid	Sodium potassium tartrate Antacid	I	I	331.11(j)(2) 331.11(k)(2)
Antimicrobial II	Antifungal	Sodium propionate Antifungal	IIIE	IIIE	310.545(a)(22)(ii)
Contraceptive/vaginal	Vaginal	Minor irritations	I	Withdrawn	n/a
Miscellaneous external	Antifungal	Diaper rash	Defer	IISE	310.545(a)(22)(ii)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	IIISE	Pending
Contraceptive/vaginal	Vaginal	Sodium salicylate Minor irritations	IISE	Withdrawn	n/a
Internal analgesic	Internal analgesic	Analgesic	I	I	Pending
Internal analgesic	Internal analgesic	Antipyretic	I	I	Pending
Internal analgesic	Internal analgesic	Antirheumatic	I	Not OTC	n/a

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis/ psoriasis	IIIE	IIIE	310.545(a)(7)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Miscellaneous internal	Menstrual/diuretic	Analgesic	I	I	Pending
Miscellaneous internal	Menstrual/diuretic	Diuretic	IIIE	IIIE	310.545(a)(24)(i)
Miscellaneous internal	Overindulgence in alcohol/food	Overindulgence remedies (hangover)	I	I	Pending
Sodium salicylate acid phenolate					
Hemorrhoidal	Anorectal	Antiseptic (intrarectal)	IISE	IISE	310.545(a)(26)(ii)
Hemorrhoidal	Anorectal	Antiseptic (external)	IISE	IISE	310.545(a)(26)(ii)
Contraceptive/vaginal	Vaginal	Minor irritations	IISE	Withdrawn	n/a
Sodium sulfide					
Miscellaneous external	Ingrown toenail	Ingrown toenail	n/a	I	538.310
Miscellaneous external	Ingrown toenail	Ingrown toenail	IIIE	IIIE	310.538(a) [removed 68 FR 24348]
Sodium thiosulfate					
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Sorbitan monostearate					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Sorbitan sesquioleate					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	n/a
Sorbitol					
Laxative	Laxative	Hyperosmotic laxative	I	I	Pending
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	IIIE	IIIE	310.545(a)(8)(i)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	IIE	IIE	310.545(a)(8)(i)
Oral cavity	Oral health care	Oral health care nonantimicrobial	n/a	n/a	310.545(a)(14)
Soyasterol					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	n/a
Soybean oil, hydrogenated					
Miscellaneous internal	Cholecystokinetic	Cholecystokinetic	n/a	n/a	357.210(b)
Soybean protein					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Soymeal					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Spermaceti					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	n/a
Squill					
Cough/cold	Cough/cold (expectorant)	Expectorant	IISE	IISE	310.545(a)(6)(iii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Squill extract					
Cough/cold	Cough/cold (expectorant)	Expectorant	IISE	IISE	310.545(a)(6)(iii)
Stannous fluoride					
n/a	Antigingivitis	Antigingivitis	I	n/a	Pending
Dental	Anticaries	Anticavity dental gel	I	I	355.10(c)(2)
Dental	Anticaries	Anticavity dentrifice	I	I	355.10(c)(1)
Dental	Anticaries	Anticavity dental rinse	I	I	355.10(c)(3)
Dental	Relief of oral discomfort	Tooth desensitizer	IIIE	IIIE	Pending
Stannous pyrophosphate and zinc citrate					
n/a	Gingivitis/plaque	Antiplaque/gingivitis	n/a	IIIE	Pending
Stearyl alcohol					
n/a	Insect bite/sting	Insect bite/sting	n/a	n/a	310.545(a)(18)(v)(B)
n/a	Poison ivy/oak/sumac	Poison ivy/oak/ sumac	n/a	n/a	310.545(a)(18)(vi)(B)
n/a	Skin protectant	Skin protectant	n/a	n/a	310.545(a)(18)(i)(B)
Stem bromelain					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
Strawberry					
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Strontium chloride					
Dental	Relief of oral discomfort	Tooth desensitizer (in combination only)	IISE	IISE	Pending
Dental	Relief of oral discomfort	Tooth desensitizer	IIIE	IIIE	Pending
Strychnine					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IISE	IISE	310.528(a)
Miscellaneous internal	Digestive aid	Digestive aid (ippuad)	n/a	n/a	310.545(a)(18)(ii)
Sucrose					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Sucrose octaacetate					
Miscellaneous external	Nailbiting/thumbsucking	Nailbiting/ thumbsucking deterrent	IIIE	IIIE	310.536(a)
Sugars					
Oral cavity	Oral health care	Oral health care nonantimicrobial	n/a	n/a	310.545(a)(14)
Sulfacetamide sodium					
Miscellaneous external	Hair growth/loss	Hair grower	n/a	n/a	310.527(a)
Ophthalmic	Ophthalmic	Anti-infective	IIS	IIS	310.545(a)(21)(ii)
Sulfur					
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	IIE	310.545(a)(10)(vii)
n/a	Skin protectant	Wound healing agent	n/a	n/a	310.545(a)(18)(i)(A)
Antimicrobial II	Acne	Acne	I	I	333.310(d)
Antimicrobial II	Acne	Acne	I	I	333.310(e)
Miscellaneous external	Boil treatment	Boil treatment	n/a	IIIE	310.531(a)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff	I	I	358.710(a)(7)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IISE	310.545(a)(18)(iii)
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	IISE	310.545(a)(18)(iv)
Topical analgesic	Skin protectant	Skin protectant	IISE	IISE	310.545(a)(18)(i)(A)
Sulfur (paraffinic hydrocarbons)					
Miscellaneous external	Hair growth/loss	Hair grower	n/a	IIE	310.527(a)
Sulfur, precipitated					
Hemorrhoidal	Anorectal	Keratolytic (external)	IIIE	IIIE	310.545(a)(26)(v)
Hemorrhoidal	Anorectal	Keratolytic (intrarectal)	IIE	IIE	310.545(a)(26)(v)
Sulfur, sublimed					
Hemorrhoidal	Anorectal	Keratolytic (intrarectal)	IIE	IIE	310.545(a)(26)(v)
Hemorrhoidal	Anorectal	Keratolytic (external)	IIIE	IIIE	310.545(a)(26)(v)
Miscellaneous external	Pediculicide	Pediculicide	IISE	IISE	310.545(a)(25)(i)
Sulfurated oils of turpentine					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Sulisobenzone					
Topical analgesic	Sunscreen	Sunscreen	I	I	352.10(o)
Sweet spirits of nitre					
Miscellaneous external	Sweet spirits of nitre	All indications	IISE	n/a	310.502(a)(12)
Talc					
n/a	Antimicrobial	Diaper rash	n/a	n/a	Pending
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	External analgesic	Astringent	IISE	n/a	n/a
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	I	Pending
Talcum powder					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	n/a
Tannic acid					
n/a	Skin protectant	Diaper rash	n/a	IISE	310.545(a)(18)(iii)
n/a	Skin protectant	Wound healing agent	n/a	n/a	310.545(a)(18)(i)
Antimicrobial II	Antifungal	Antifungal	IIE	IIE	310.545(a)(22)(ii)
Hemorrhoidal	Anorectal	Astringent (external)	IISE	IISE	310.545(a)(26)(iii)
Hemorrhoidal	Anorectal	Anorectal (intrarectal)	IISE	IISE	310.545(a)(26)(iii)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIISE	310.545(a)(10)(v)
Miscellaneous external	External analgesic	Insect bite/sting	n/a	IIIE	Pending
Miscellaneous external	External analgesic	Poison ivy/oak/sumac	Defer	IIIE	310.545(a)(10)(vii)
Miscellaneous external	Ingrown toenail	Ingrown toenail	IIIE	IIIE	310.538(a)
Miscellaneous external	Ingrown toenail	Astringent (external)	IIIE	IIIE	310.538(a)
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	IIISE	310.545(a)(18)(iv)
Miscellaneous external	Skin protectant	Poison ivy/oak/sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(8)(ii)
Topical analgesic	Skin protectant	Skin protectant	IISE	IISE	310.545(a)(18)(i)(A)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Tannic acid glycerite					
Miscellaneous external	External analgesic	Astringent	IISE	n/a	n/a
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Tar oil					
Miscellaneous external	Hair growth/loss	Hair grower	IISE	n/a	310.527(a)
<i>Taraxacum officinale</i>					
Miscellaneous external	Menstrual/diuretic	Dysmenorrhea	IIE	IIE	310.545(a)(24)(i)
Tartaric acid					
Antacid	Antacid	Antacid	I	I	331.11(m)
Contraceptive/vaginal	Vaginal	Alters vaginal pH	IIIE	Withdrawn	n/a
Laxative	Laxative	Saline laxative	IIISE	IIISE	310.545(a)(12)(ii)
Terpin hydrate					
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
Terpin hydrate elixir					
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
Testosterone					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IIS	IIS	310.528(a)
Tetracaine					
n/a	External analgesic	Poison ivy/oak/sumac	n/a	I	Pending
Hemorrhoidal	Anorectal	Anesthetic (external)	IIIE	I	346.10(h)
Hemorrhoidal	Anorectal	Anesthetic (intrarectal)	IIIE	IIIE	[55 FR 1779]
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	IISE	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	I	Pending
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Oral cavity	Oral health care	Analgesic/anesthetic	IIS	IIS	310.545(a)(14)
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Tetracaine hydrochloride					
n/a	External analgesic	Poison ivy/oak/sumac	n/a	I	Pending
Antimicrobial II	Acne	Acne	IISE	IISE	310.545(a)(1)
Hemorrhoidal	Anorectal	Anesthetic (external)	IIIE	I	346.10(i)
Hemorrhoidal	Anorectal	Anesthetic (intrarectal)	IIIE	IIIE	[55 FR 1779]
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	I	Pending
Miscellaneous external	Hair growth/loss	Hair grower	IIE	IIE	310.527(a)
Oral cavity	Oral health care	Analgesic/anesthetic	IIS	IIS	310.545(a)(14)
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Tetracycline hydrochloride					
Antimicrobial II	Antibiotic	First aid antibiotic	n/a	I	333.110(f)
Antimicrobial II	Antibiotic	Skin wound antibiotic	IIIE	Defer	n/a
Antimicrobial II	Antibiotic	Skin wound protectant	I	Defer	n/a
Tetrahydrozoline hydrochloride					
Ophthalmic	Ophthalmic	Vasoconstrictor	I	I	349.18(d)
Thenylidamine hydrochloride					
Cough/cold	Cough/cold (antihistamine)	Antihistamine	IIIE	IIIE	310.545(a)(6)(i)(A)&(B)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	IIIE	IIIE	[59 FR 43408]
Miscellaneous internal	Menstrual/diuretic	Theobromine sodium salicylate Diuretic	IIIE	IIIE	310.545(a)(24)(i)
Miscellaneous internal	Menstrual/diuretic	Theophylline Diuretic	IIIE	IIIE	310.545(a)(24)(i)
Cough/cold	Cough/cold (bronchodilator)	Theophylline (all combinations) Bronchodilator	n/a	n/a	310.545(a)(6)(iv)(B)
Cough/cold	Cough/cold (bronchodilator)	Theophylline, anhydrous (see Theophylline) Bronchodilator	I	IIS	310.545(a)(6)(iv)(A)
Cough/cold	Cough/cold (bronchodilator)	Theophylline calcium salicylate Bronchodilator	I	IIS	310.545(a)(6)(iv)(A)
Cough/cold	Cough/cold (bronchodilator)	Theophylline sodium glycinate Bronchodilator	I	IIS	310.545(a)(6)(iv)(A)
Miscellaneous internal	Oral insect repellent	Thiamine Insect repellent	IIE	IIE	310.529(a)
Miscellaneous external	Hair growth/loss	Thiamine hydrochloride Hair grower	n/a	n/a	310.527(a)
Miscellaneous internal	Menstrual/diuretic	Menstrual	n/a	IISE	310.545(a)(24)(i)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Sedative	Nighttime sleep aid	Sleep aid	IIE	IIE	[54 FR 6826]
Sedative	Daytime sedative	Sedative	IIE	IISE	310.519(a)
Miscellaneous internal	Weight control	Thiamine mononitrate Anorectic	IISE	IISE	310.545(a)(20)
Miscellaneous external	Mercury	Thimerosal Antiseptic	IISE	IISE	310.545(a)(27)(i)
Miscellaneous external	Mercury	First aid antiseptic	n/a	IISE	310.545(a)(27)(i)
n/a	Pediculicide	Thiocyanoacetate Pediculicide	n/a	n/a	310.545(a)(25)(i)
Cough/cold	Cough/cold (antihistamine)	Thonzylamine hydrochloride Antihistamine	I	I	341.12(l)
Miscellaneous internal	Weight control	Threonine Anorectic	IISE	IISE	310.545(a)(20)
Miscellaneous external	Antifungal	Thyme oil, white Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
n/a	External analgesic	Thymol Poison ivy/oak/ sumac	n/a	IIIE	310.545(a)(10)(vii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Antimicrobial II	Acne	Acne	IIE	IIIE	310.545(a)(1)
Antimicrobial II	Antifungal	Antifungal	IIISE	IIISE	310.545(a)(22)(ii)
Cough/cold	Cough/cold (antihistamine)	Antitussive (topical/inhalant)	IIIE	IIIE	[52 FR 30055]
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (inhalant room spray)	IIIE	IIIE	310.545(a)(6)(ii)(A)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	IIIE	IIIE	310.545(a)(6)(ii)(A)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (lozenge)	IIIE	IIIE	310.545(a)(6)(ii)(A)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (mouthwash)	IIIE	IIIE	310.545(a)(6)(ii)(A)
Dental	Relief of oral discomfort	Toothache relief	IIIE	IIIE	Pending
Dental	Relief of oral discomfort	Oral mucosal analgesic	IIIE	IIIE	Pending
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis/psoriasis	IIIE	IIIE	310.545(a)(7)
Miscellaneous external	External analgesic	Astringent	IISE	n/a	n/a
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIISE	310.545(a)(10)(v)
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous internal	Smoking deterrent	Smoking deterrent	IIE	IIE	310.544(d)
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Oral cavity	Oral health care	Analgesic/anesthetic	IIIE	IIIE	310.545(a)(14)
Topical analgesic	External analgesic	Analgesic/anesthetic	IIIE	IIIE	310.545(a)(10)(i)
Thymol iodide					
Dental	Relief of oral discomfort	Oral mucosal analgesic	IIIE	IIIE	Pending
Dental	Relief of oral discomfort	Toothache relief	IIIE	IIIE	Pending
Oral cavity	Oral health care	Antimicrobial	IIISE	IIISE	Pending
Titanium dioxide					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	v	n/a
Topical analgesic	Sunscreen		I	I	352.10(p)
Tolindate					
Antimicrobial II	Antifungal	Antifungal	IISE	IISE	310.545(a)(22)(ii)
Tolnaftate					
Antimicrobial II	Antifungal	Antifungal	I	I	333.210(e)
Tolu					
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
Tolu balsam					
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
Oral cavity	Oral health care	Antimicrobial	IIIE	IIIE	Pending
Oral cavity	Oral health care	Expectorant	IIIE	n/a	310.545(a)(6)(iii)
Tolu balsam tincture					
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Topical starch					
n/a	Skin protectant	Poison ivy/oak/ sumac	n/a	IIIE	310.545(a)(18)(vi)(A)
Hemorrhoidal	Anorectal	Protectant (external)	I	I	346.14(9)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	I	I	346.14(9)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Astringent	IISE	IISE	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	I	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	IIISE	310.545(a)(18)(iv)
Topical analgesic	Skin protectant	Skin protectant	I	Defer	347.10(q)
Triacetin					
Antimicrobial II	Antifungal	Antifungal	IIIE	IIIE	310.545(a)(22)(ii)
Tribromsalan					
Antimicrobial I	Antimicrobial	Antimicrobial	IIS	n/a	310.502(a)(5)
Tricalcium phosphate					
Antacid	Antacid	Antacid	n/a	n/a	331.11(i)(3)
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Triclocarban					
Antimicrobial I	Antimicrobial	Skin antiseptic	n/a	IIIE	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	IISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Antimicrobial soap	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	IISE	IISE	Pending
Antimicrobial I	Antimicrobial	Surgical hand scrub	IISE	IISE	Pending
Antimicrobial I	Antimicrobial	Skin antiseptic	IISE	IISE	Pending
Antimicrobial I	Antimicrobial	Skin protectant	IISE	IISE	Pending
Antimicrobial I	Antimicrobial	Health-care personnel handwash	IIISE	IIISE	Pending
Triclosan					
Antimicrobial I	Antimicrobial	Skin antiseptic	n/a	IIIE	Pending
Antimicrobial I	Antimicrobial	Antimicrobial soap	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	IISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Surgical hand scrub	IISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin antiseptic	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin protectant	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Health-care personnel handwash	IISE	IIISE	Pending
Miscellaneous external	Antimicrobial	Diaper rash	Defer	IIISE	Pending
Miscellaneous external	Boil treatment	Boil treatment	n/a	n/a	310.531(a)
n/a	TEA	Acne	n/a		
n/a	TEA	Antigingivitis	n/a		
Trillium					
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Tripelennamine hydrochloride					
n/a	External analgesic	Poison ivy/oak/ sumac	n/a	I	Pending
Cough/cold	Cough/cold (antihistamine)	Antihistamine	n/a	n/a	[57 FR 58373]
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIIE	310.545(a)(10)(v)
Topical analgesic	External analgesic	Analgesic/anesthetic	I	I	Pending
Triple dye					
Antimicrobial I	Antimicrobial	Skin antiseptic	n/a	IIISE	Pending
Antimicrobial I	Antimicrobial	Antimicrobial soap	n/a	IISE	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	n/a	IISE	Pending
Antimicrobial I	Antimicrobial	Surgical hand scrub	n/a	IISE	Pending
Antimicrobial I	Antimicrobial	Skin antiseptic	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin protectant	n/a	IISE	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	n/a	IISE	Pending
Antimicrobial I	Antimicrobial	Health-care personnel handwash	n/a	IIISE	Pending
Tripolidine hydrochloride					
Cough/cold	Cough/cold (antihistamine)	Antihistamine	n/a	I	341.12(m)
Triticum					
Miscellaneous internal	Menstrual/diuretic	Menstrual	n/a	IISE	310.545(a)(24)(i)
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Trolamine					
Miscellaneous external	External analgesic	Insect bite/sting	IIIE	IISE	Pending
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	n/a	Pending
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	IIIE	310.545(a)(18)(iv)(A)
Miscellaneous external	Skin protectant	Insect bite/sting	IIIE	IIIE	310.545(a)(18)(v)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IIIE	310.545(a)(18)(vi)(A)
Trolamine salicylate					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIIE	310.545(a)(10)(v)
Miscellaneous external	External analgesic	Insect bite/sting	n/a	IIIE	310.545(a)(10)(vi)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	n/a	IIIE	310.545(a)(10)(vii)
Topical analgesic	External analgesic	Analgesic/anesthetic	IIIE	IIIE	Pending
Topical analgesic	Sunscreen	Sunscreen	I	I	352.10(q)
Tryptophan					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Turpentine oil					
Cough/cold	Cough/cold (antitussive)	Antitussive (oral)	IISE	IISE	Pending
Cough/cold	Cough/cold (antitussive)	Antitussive (topical/inhalant)	IIIE	IIIE	[52 FR 30055]
Cough/cold	Cough/cold (expectorant)	Expectorant (topical/inhalant)	IIIE	IIIE	310.545(a)(6)(iii)
Cough/cold	Cough/cold (expectorant)	Expectorant (oral)	IISE	IISE	310.545(a)(6)(iii)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (oral)	IISE	IISE	310.545(a)(6)(ii)(A)
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant (topical/inhalant)	IIIE	IIIE	310.545(a)(6)(ii)(A)
Topical analgesic	External analgesic	Counterirritant	I	I	Pending

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIIE	310.545(a)(10)(v)
Miscellaneous external	External analgesic	Insect bite/sting	IISE	IISE	310.545(a)(10)(vi)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(18)(v)(A)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Turpentine oil, rectified					
Hemorrhoidal	Anorectal	Counterirritant (intrarectal)	IISE	IISE	310.545(a)(26)(iv)
Hemorrhoidal	Anorectal	Counterirritant (external)	IISE	IISE	310.545(a)(26)(iv)
Turpentine, Venice					
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Tyrosine					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Undecoylium chloride iodine complex					
Antimicrobial I	Antimicrobial	Antimicrobial soap	n/a	IISE	Pending
Antimicrobial I	Antimicrobial	Skin wound cleanser	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Surgical hand scrub	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin protectant	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Skin antiseptic	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Preoperative skin preparation	IIISE	IIISE	Pending
Antimicrobial I	Antimicrobial	Health-care personnel handwash	IIIE	IIIE	Pending
Undecylenic acid					
Antimicrobial II	Antifungal	Antifungal	I	I	333.210(f)
Miscellaneous external	Antifungal	Diaper rash	Defer	IISE	310.545(a)(22)(i)
Undecylenic acid monoethanolamine sulfosuccinate sodium					
Miscellaneous external	Dandruff/seborrheic dermatitis/psoriasis	Dandruff/seborrheic dermatitis/psoriasis	IIIE	IIIE	310.545(a)(7)
Urea					
Miscellaneous external	Hair growth/loss	Hair grower	n/a	IIE	310.527(a)
Miscellaneous external	Ingrown toenail	Ingrown toenail	IISE	IISE	310.538(a)
Miscellaneous internal	Menstrual/diuretic	Diuretic	n/a	IISE	310.545(a)(24)(i)
Uva ursi, extract					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Valine					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Vegetable					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Vegetable oil					
Miscellaneous external	Hair growth/loss	Hair grower	IISE	n/a	310.527(a)
Vitamin A					
Contraceptive/vaginal	Vaginal	Minor irritations	IIIE	Withdrawn	n/a
Hemorrhoidal	Anorectal	Wound healing agent (external)	IIIE	IIIE	310.545(a)(26)(x)

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Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Hemorrhoidal	Anorectal	Wound healing agent (intrarectal)	IIIE	IIIE	310.545(a)(26)(x)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIISE	Pending
Miscellaneous external	Corn/callus remover	Corn/callus remover	IISE	IISE	[55 FR 33261]
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Vitamin A acetate					
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Vitamin A palmitate					
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Vitamin B					
Miscellaneous external	Hair growth/loss	Hair grower	n/a	IIE	310.527(a)
Vitamin E					
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Hair growth/loss	Hair grower	IIE	n/a	310.527(a)
Miscellaneous external	Skin protectant	Diaper rash	Defer	Withdrawn	n/a
Miscellaneous internal	Leg muscle cramp	Nocturnal leg muscle cramps	n/a	IIISE	310.546
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
Sedative	Stimulant	Stimulant	IIE	IIE	[39 FR 6104]
Vitamins					
Miscellaneous external	Hair growth/loss	Hair grower	IISE	n/a	310.527(a)
Miscellaneous internal	Aphrodisiac	Aphrodisiac	n/a	IISE	310.528(a)
Vitromersal					
Miscellaneous external	Mercury	First aid antiseptic	n/a	IISE	310.545(a)(27)(i)
Miscellaneous external	Mercury	Antiseptic	IISE	IISE	310.545(a)(27)(i)
Water and additives					
n/a	Ophthalmic	Emergency first aid eyewash	n/a	I	Pending
Water, purified					
n/a	Ophthalmic	Eyewash	n/a	n/a	349.20
Wax, candelilla					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	n/a
Wax, carnauba					
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	n/a

(Continued)

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
		Wax, white			
Ophthalmic	Ophthalmic	Emollient	I	I	349.14(b)(6)
		Wax, yellow			
Ophthalmic	Ophthalmic	Emollient	n/a	I	349.14(b)(7)
		Wheat germ			
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Wheat germ glycerides			
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	n/a	n/a
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	n/a	n/a
		Wheat germ oil			
Miscellaneous external	Hair growth/loss	Hair grower	IIIE	IIIE	310.527(a)
		White ointment			
Ophthalmic	Ophthalmic	Emollient	I	I	349.14(b)(8)
		White petrolatum			
n/a	Skin protectant	Skin protectant	n/a	n/a	347.10(r)
		White pine			
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
		White pine extract, compound			
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
		White pine syrup, compound			
Cough/cold	Cough/cold (expectorant)	Expectorant	IIIE	IIIE	310.545(a)(6)(iii)
		Witch hazel			
Hemorrhoidal	Anorectal	Astringent (external)	I	I	346.18 (b)
Hemorrhoidal	Anorectal	Astringent (intrarectal)	I	I	346.18 (b)
Miscellaneous external	External analgesic	Astringent	I	n/a	n/a
Miscellaneous external	Skin protectant	Astringent	I	I	347.12(c)
		Woodruff			
Miscellaneous internal	Digestive aid	Digestive aid (intestinal distress)	n/a	n/a	310.545(a)(18)(ii)
		Xanthan gum			
Miscellaneous internal	Weight control	Anorectic	IIIE	IISE	310.545(a)(20)
		Xylometazoline hydrochloride			
Cough/cold	Cough/cold (nasal decongestant)	Nasal decongestant	I	I	341.20(b)(10)
		Yeast			
Miscellaneous internal	Weight control	Anorectic	IISE	IISE	310.545(a)(20)
		Yeast cell derivative, live			
Hemorrhoidal	Anorectal	Wound healing agent (external)	IIIE	IIIE	310.545(a)(26)(vii)
Hemorrhoidal	Anorectal	Wound healing agent (intrarectal)	IIIE	IIIE	310.545(a)(26)(vii)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending

(Continued)

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Diaper rash	Defer	IIISE	Pending
Topical analgesic	Skin protectant	Wound healing agent	IIIE	IIIE	Pending
Yohimbine					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IISE	IISE	310.528(a)
Yohimbine hydrochloride					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	IISE	IISE	310.528(a)
Yohimbinum					
Miscellaneous internal	Aphrodisiac	Aphrodisiac	n/a	n/a	310.528(a)
Zinc acetate					
n/a	Skin protectant	Diaper rash	n/a	n/a	310.545(a)(18)(iii)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	I	347.10(s)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	Pending
Topical analgesic	Skin protectant	Wound healing agent	IIIE	IIIE	310.545(a)(18)(i)(A)
Topical analgesic	Skin protectant	Skin protectant	I	I	347.10(s)
Zinc caprylate					
Antimicrobial II	Antifungal	Antifungal	IIIE	IIIE	310.545(a)(22)(ii)
Zinc carbonate					
n/a	Skin protectant	Diaper rash	Defer	IIISE	310.545(a)(18)(iii)
n/a	Skin protectant	Poison ivy/oak/ sumac	n/a	I	347.10(t)
Topical analgesic	Skin protectant	Skin protectant	I	I	347.10(t)
Zinc chloride					
Miscellaneous external	Corn/callus remover	Corn/callus remover	IIIE	IIIE	[55 FR 33261]
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Oral cavity	Oral health care	Astringent	I	I	Pending
Zinc citrate					
n/a	Gingivitis/plaque	Antiplateque/gingivitis	n/a	IIIE	Pending
Zinc oxide					
n/a	n/a	Sunscreen	n/a	I	352.10(r)
n/a	Skin protectant	Poison ivy/oak/ sumac	n/a	I	347.10(u)
Antimicrobial II	Acne	Acne	IIIE	IIIE	310.545(a)(1)
Hemorrhoidal	Anorectal	Astringent (external)	I	I	346.18 (c)
Hemorrhoidal	Anorectal	Astringent (intrarectal)	I	I	346.18 (c)
Hemorrhoidal	Anorectal	Protectant (external)	I	I	346.14(b)(4)
Hemorrhoidal	Anorectal	Protectant (intrarectal)	I	I	346.14(b)(4)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Boil treatment	Boil treatment	IISE	IISE	310.531(a)
Miscellaneous external	External analgesic	Astringent	IISE	IISE	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	External analgesic	Insect bite/sting	IISE	IISE	310.545(a)(10)(vi)
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	I	Pending
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(18)(v)(A)
Miscellaneous external	Skin protectant	Protectant	I	I	Pending
Topical analgesic	Skin protectant	Skin protectant	I	I	Pending

(Continued)

Review Panel	Report	Drug Category	Advance Notice Proposed Rulemaking (ANPR)	Proposed Rule (PR)	Federal Register (FR) Listing
Zinc phenolsulfonate					
Laxative	Antidiarrheal	Antidiarrheal	IIE	IIE	310.545(a)(3)(i)
Laxative	Antiemetic	Antiemetic	IIIE	IIE	[52 FR 15891]
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Zinc propionate					
Antimicrobial II	Antifungal	Antifungal	IIIE	IIIE	310.545(a)(22)(ii)
Zinc stearate					
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Miscellaneous external	Antifungal	Diaper rash	Defer	n/a	310.545(a)(22)(i)
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	External analgesic	Diaper rash	Defer	n/a	310.545(a)(10)(iv)
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Diaper rash	Defer	n/a	Pending
Miscellaneous external	Antimicrobial	Diaper rash	Defer	n/a	Pending
Zinc sulfate					
Contraceptive/vaginal	Vaginal	Astringent	IIIE	Withdrawn	n/a
Miscellaneous external	External analgesic	Astringent	IISE	n/a	Pending
Miscellaneous external	External analgesic	Fever blister (topical)	Defer	IIIE	310.545(a)(10)(v)
Miscellaneous external	Skin protectant	Astringent	IISE	IISE	310.545(a)(18)(ii)
Miscellaneous external	Skin protectant	Fever blister (topical)	Defer	IIIE	310.545(a)(18)(iv)
Miscellaneous internal	Poison treatment	Emetic	n/a	IISE	310.545(a)(16)
Ophthalmic	Ophthalmic	Astringent	I	I	349.10
Zinc sulfide					
Antimicrobial II	Acne	Acne	IIE	IIE	310.545(a)(1)
Zinc undecylenate					
Antimicrobial II	Antifungal	Antifungal	I	I	333.210(f)
Zirconium oxide					
Miscellaneous external	External analgesic	Insect bite/sting	IISE	IISE	310.545(a)(10)(vi)
Miscellaneous external	Skin protectant	Insect bite/sting	IISE	IISE	310.545(a)(10)(vi)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(18)(vi)(A)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	n/a	IISE	310.545(a)(10)(vii)
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)
Zyloxin					
Miscellaneous external	External analgesic	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(10)(vii)
Miscellaneous external	Mercury	First aid antiseptic	IISE	n/a	310.545(a)(27)(i)
Miscellaneous external	Skin protectant	Poison ivy/oak/ sumac	Defer	IISE	310.545(a)(18)(vi)(A)

APPENDIX II UNPROVEN SAFETY OF OTC INGREDIENTS

- (1) Topical acne drug products.
 - Alcloxa
 - Alkyl isoquinolinium bromide
 - Aluminum chlorohydrate
 - Aluminum hydroxide
 - Benzocaine
 - Benzoic acid
 - Boric acid
 - Calcium polysulfide
 - Calcium thiosulfate
 - Camphor
 - Chloroxylenol
 - Cloxyquin
 - Coal tar
 - Dibenzothiophene
 - Estrone
 - Magnesium aluminum silicate
 - Magnesium sulfate
 - Phenol
 - Phenolate sodium
 - Phenyl salicylate
 - Povidone-iodine
 - Pyrimidine maleate
 - Resorcinol (as single ingredient)
 - Resorcinol monoacetate (as single ingredient)
 - Salicylic acid (over 2% up to 5%)
 - Sodium borate
 - Sodium thiosulfate
 - Tetracaine hydrochloride
 - Thymol
 - Vitamin E
 - Zinc oxide
 - Zinc stearate
 - Zinc sulfide
- (2) Anticaries drug products
 - (i) Approved as of May 7, 1991.
 - Hydrogen fluoride
 - Sodium carbonate
 - Sodium monofluorophosphate (6% rinse)
 - Sodium phosphate
 - (ii) Approved as of October 7, 1996.
 - Calcium sucrose phosphate
 - Dicalcium phosphate dihydrate
 - Disodium hydrogen phosphate¹
 - Phosphoric acid
 - Sodium dihydrogen phosphate
 - Sodium dihydrogen phosphate monohydrate
 - Sodium phosphate, dibasic anhydrous reagent
- (3) Antidiarrheal drug products
 - (i) Approved as of May 7, 1991.
 - Aluminum hydroxide
 - Atropine sulfate
 - Calcium carbonate
 - Carboxymethylcellulose sodium
 - Glycine
 - Homatropine methylbromide
 - Hyoscyamine sulfate
 - Lactobacillus acidophilus*
 - Lactobacillus bulgaricus*
 - Opium, powdered
 - Opium tincture
 - Paregoric
 - Phenyl salicylate
 - Scopolamine hydrobromide
 - Zinc phenolsulfonate
 - (ii) Approved as of April 19, 2004; April 18, 2005, for products with annual sales less than \$25,000.
 - Attapulgate, activated
 - Bismuth subnitrate
 - Calcium hydroxide
 - Calcium polycarbophil
 - Charcoal (activated)
 - Pectin
 - Polycarbophil
 - Potassium carbonate
 - Rhubarb fluid extract
- (4) Antiperspirant drug products
 - (i) Ingredients
 - Approved as of May 7, 1991.
 - Alum, potassium
 - Aluminum bromohydrate
 - Aluminum chloride (alcoholic solutions)
 - Aluminum chloride (aqueous solution) (aerosol only)
 - Aluminum sulfate
 - Aluminum sulfate, buffered (aerosol only)
 - Sodium aluminum chlorohydroxy lactate
 - (ii) Approved as of December 9, 2004; June 9, 2005, for products with annual sales less than \$25,000.
 - Aluminum sulfate buffered with sodium aluminum lactate
- (5) [Reserved]
- (6) Cold, cough, allergy, bronchodilator, and antiasthmatic drug products
 - (i) Antihistamine drug products
 - (A) Ingredients.
 - Methapyrilene hydrochloride
 - Methapyrilene fumarate
 - Thenyldiamine hydrochloride
 - (B) Ingredients.
 - Phenyltoloxamine dihydrogen citrate
 - Methapyrilene hydrochloride
 - Methapyrilene fumarate
 - Thenyldiamine hydrochloride
 - (ii) Nasal decongestant drug products
 - (A) Approved as of May 7, 1991.
 - Allyl isothiocyanate
 - Camphor (lozenge)
 - Creosote, beechwood (oral)
 - Eucalyptol (lozenge)
 - Eucalyptol (mouthwash)

- Eucalyptus oil (lozenge)
- Eucalyptus oil (mouthwash)
- Menthol (mouthwash)
- Peppermint oil (mouthwash)
- Thenyldiamine hydrochloride
- Thymol
- Thymol (lozenge)
- Thymol (mouthwash)
- Turpentine oil
- (B) Approved as of August 23, 1995.
 - Bornyl acetate (topical)
 - Cedar leaf oil (topical)
 - Creosote, beechwood (topical)
 - Ephedrine (oral)
 - Ephedrine hydrochloride (oral)
 - Ephedrine sulfate (oral)
 - Racephedrine hydrochloride (oral/topical)
- (C) Approved as of April 11, 2007; October 11, 2007, for products with annual sales less than \$25,000. Any ingredient(s) labeled with claims or directions for use for sinusitis or for relief of nasal congestion associated with sinusitis.
- (iii) Expectorant drug products.
 - Ammonium chloride
 - Antimony potassium tartrate
 - Beechwood creosote
 - Benzoin preparations (compound tincture of benzoin, tincture of benzoin)
 - Camphor
 - Chloroform
 - Eucalyptol/eucalyptus oil
 - Horehound
 - Iodides (calcium iodide anhydrous, hydriodic acid syrup, iodized lime, potassium iodide)
 - Ipecac
 - Ipecac fluid extract
 - Ipecac syrup
 - Menthol/peppermint oil
 - Pine tar preparations (extract white pine compound, pine tar, syrup of pine tar, compound white pine syrup, white pine)
 - Potassium guaiacolsulfonate
 - Sodium citrate
 - Squill preparations (squill, squill extract)
 - Terpin hydrate preparations (terpin hydrate, terpin hydrate elixir)
 - Tolu preparations (tolu, tolu balsam, tolu balsam tincture)
 - Turpentine oil (spirits of turpentine)
- (iv) Bronchodilator drug products
 - (A) Approved as of October 2, 1987.
 - Aminophylline
 - Belladonna alkaloids
 - Euphorbia pilulifera*
 - Metaproterenol sulfate
 - Methoxyphenamine hydrochloride
 - Pseudoephedrine hydrochloride
 - Pseudoephedrine sulfate
 - Theophylline, anhydrous
 - Theophylline calcium salicylate
 - Theophylline sodium glycinate
 - (B) Approved as of January 29, 1996. Any combination drug product containing theophylline (e.g., theophylline and ephedrine, or theophylline and ephedrine and phenobarbital).
 - (C) Approved as of June 19, 1996. Any ingredient(s) in a pressurized metered-dose inhaler container.
 - (D) Approved as of October 29, 2001. Any oral bronchodilator active ingredient (e.g., ephedrine, ephedrine hydrochloride, ephedrine sulfate, racephedrine hydrochloride, or any other ephedrine salt) in combination with any analgesic(s) or analgesic-antipyretic(s), anticholinergic, antihistamine, oral antitussive, or stimulant active ingredient.
- (7) Dandruff/seborrheic dermatitis/psoriasis drug products.
 - Alkyl isoquinolinium bromide
 - Allantoin
 - Benzalkonium chloride
 - Benzethonium chloride
 - Boric acid
 - Calcium undecylenate
 - Captan
 - Chloroxylenol
 - Colloidal oatmeal
 - Cresol, saponated
 - Ethohexadiol
 - Eucalyptol
 - Juniper tar
 - Lauryl isoquinolinium bromide
 - Menthol
 - Mercury oleate
 - Methylbenzethonium chloride
 - Methyl salicylate
 - Phenol
 - Phenolate sodium
 - Pine tar
 - Povidone–iodine
 - Resorcinol
 - Sodium borate
 - Sodium salicylate
 - Thymol
 - Undecylenic acid
- (8) Digestive aid drug products
 - (i) Approved as of May 7, 1991.
 - Bismuth sodium tartrate
 - Calcium carbonate
 - Cellulase
 - Dehydrocholic acid

- Dihydroxyaluminum sodium carbonate
- Duodenal substance
- Garlic, dehydrated
- Glutamic acid hydrochloride
- Hemicellulase
- Homatropine methylbromide
- Magnesium hydroxide
- Magnesium trisilicate
- Ox bile extract
- Pancreatin
- Pancrelipase
- Papain
- Peppermint oil
- Pepsin
- Sodium bicarbonate
- Sodium citrate
- Sorbitol
- (ii) Approved as of November 10, 1993.
 - Alcohol
 - Aluminum hydroxide
 - Amylase
 - Anise seed
 - Aromatic powder
 - Asafetida
 - Aspergillus oryzae* enzymes (except lactase enzyme derived from *Aspergillus oryzae*)
 - Bacillus acidophilus*
 - Bean
 - Belladonna alkaloids
 - Belladonna leaves, powdered extract
 - Betaine hydrochloride
 - Bismuth subcarbonate
 - Bismuth subgallate
 - Black radish powder
 - Blessed thistle (*Cnicus benedictus*)
 - Buckthorn
 - Calcium gluconate
 - Capsicum
 - Capsicum, fluid extract of
 - Carbon
 - Cascara sagrada extract
 - Catechu, tincture
 - Catnip
 - Chamomile flowers
 - Charcoal, wood
 - Chloroform
 - Cinnamon oil
 - Cinnamon tincture
 - Citrus pectin
 - Diastase
 - Diastase malt
 - Dog grass
 - Elecampane
 - Ether
 - Fennel acid
 - Galega
 - Ginger
 - Glycine
 - Hydrastis canadensis* (golden seal)
 - Hectorite
 - Horsetail
 - Huckleberry
 - Hydrastis fluid extract
 - Hydrochloric acid
 - Iodine
 - Iron ox bile
 - Johnswort
 - Juniper
 - Kaolin, colloidal
 - Knotgrass
 - Lactic acid
 - Lactose
 - Lavender compound, tincture of
 - Linden
 - Lipase
 - Lysine hydrochloride
 - Mannitol
 - Mycozyme
 - Myrrh, fluid extract of
 - Nettle
 - Nickel-pectin
 - Nux vomica* extract
 - Orthophosphoric acid
 - Papaya, natural
 - Pectin
 - Peppermint
 - Peppermint spirit
 - Phenacetin
 - Potassium bicarbonate
 - Potassium carbonate
 - Protease
 - Prolase
 - Rhubarb fluid extract
 - Senna
 - Sodium chloride
 - Sodium salicylate
 - Stem bromelain
 - Strawberry
 - Strychnine
 - Tannic acid
 - Trillium
 - Woodruff
- (iii) Charcoal, activated
- (9) [Reserved]
- (10) External analgesic drug products
 - (i) Analgesic and anesthetic drug products.
 - Aspirin
 - Chloral hydrate
 - Chlorobutanol
 - Cyclomethycaine sulfate
 - Eugenol
 - Hexylresorcinol
 - Methapyrilene hydrochloride
 - Salicylamide

- Thymol
- (ii) Counterirritant drug products.
 - Chloral hydrate
 - Eucalyptus oil
- (iii) Male genital desensitizer drug products.
 - Benzyl alcohol
 - Camphorated metacresol
 - Ephedrine hydrochloride
- (iv) Diaper rash drug products. Any ingredient(s) labeled with claims or directions for use in the treatment and/or prevention of diaper rash.
- (v) Fever blister and cold sore treatment drug products.
 - Allyl isothiocyanate
 - Aspirin
 - Bismuth sodium tartrate
 - Camphor (exceeding 3%)
 - Capsaicin
 - Capsicum
 - Capsicum oleoresin
 - Chloral hydrate
 - Chlorobutanol
 - Cyclomethycaine sulfate
 - Eucalyptus oil
 - Eugenol
 - Glycol salicylate
 - Hexylresorcinol
 - Histamine dihydrochloride
 - Menthol (exceeding 1%)
 - Methapyrilene hydrochloride
 - Methyl nicotinate
 - Methyl salicylate
 - Pectin
 - Salicylamide
 - Strong ammonia solution
 - Tannic acid
 - Thymol
 - Tripelennamine hydrochloride
 - Trolamine salicylate
 - Turpentine oil
 - Zinc sulfate
- (vi) Insect bite and sting drug products.
 - Alcohol
 - Alcohol, ethoxylated alkyl
 - Benzalkonium chloride
 - Calamine
 - Ergot fluid extract
 - Ferric chloride
 - Panthenol
 - Peppermint oil
 - Pyrilamine maleate
 - Sodium borate
 - Trolamine salicylate
 - Turpentine oil
 - Zinc oxide
 - Zirconium oxide
- (vii) Poison ivy, poison oak, and poison sumac drug products.
 - Alcohol
 - Aspirin
 - Benzethonium chloride
 - Benzocaine (0.5%–1.25%)
 - Bithionol
 - Calamine
 - Cetalkonium chloride
 - Chloral hydrate
 - Chlorobutanol
 - Chlorpheniramine maleate
 - Creosote, beechwood
 - Cyclomethycaine sulfate
 - Dexpantenol
 - Diperodon hydrochloride
 - Eucalyptus oil
 - Eugenol
 - Glycerin
 - Glycol salicylate
 - Hectorite
 - Hexylresorcinol
 - Hydrogen peroxide
 - Impatiens biflora* tincture
 - Iron oxide
 - Isopropyl alcohol
 - Lanolin
 - Lead acetate
 - Merbromin
 - Mercuric chloride
 - Methapyrilene hydrochloride
 - Panthenol
 - Parethoxycaine hydrochloride
 - Phenyltoloxamine dihydrogen citrate
 - Povidone–vinylacetate copolymers
 - Pyrilamine maleate
 - Salicylamide
 - Salicylic acid
 - Simethicone
 - Sulfur
 - Tannic acid
 - Thymol
 - Trolamine salicylate
 - Turpentine oil
 - Zirconium oxide
 - Zyloxin
- (11) [Reserved]
- (12) Laxative drug products
 - (i) (A) Bulk laxatives.
 - Agar
 - Carrageenan (degraded)
 - Carrageenan (native)
 - Guar gum
 - (i) (B) Bulk laxatives—Approved as of March 29, 2007. Granular dosage forms containing psyllium (hemicellulose), psyllium hydrophilic mucilloid, psyllium seed,

psyllium seed (blond), psyllium seed husks, plantago husks, or plantago seed including, but not limited to, any granules that are

- (1) swallowed dry prior to drinking liquid
- (2) dispersed, suspended, or partially dissolved in liquid prior to swallowing;
- (3) chewed, partially chewed, or unchewed, and then washed down (or swallowed) with liquid
- (4) sprinkled over food

(ii) Saline laxative.

Tartaric acid

(iii) Stool softener.

Poloxamer 188

(iv) (A) Stimulant laxatives—Approved as of May 7, 1991.

Aloin

Bile salts/acids

Calcium pantothenate

Calomel

Colocynth

Elaterin resin

Frangula

Gamboge

Ipomea

Jalap

Ox bile

Podophyllum resin

Prune concentrate dehydrate

Prune powder

Rhubarb, Chinese

Sodium oleate

(B) Stimulant laxatives—Approved as of January 29, 1999.

Danthron

Phenolphthalein

(C) Stimulant laxatives—Approved as of November 5, 2002.

Aloe ingredients (aloe, aloe extract, aloe flower extract)

Cascara sagrada ingredients (casanthranol, cascara fluid extract aromatic, cascara sagrada bark, cascara sagrada extract, cascara sagrada fluid extract).

(13) [Reserved]

(14) Oral health-care drug products (nonantimicrobial).

Antipyrine

Camphor

Cresol

Dibucaine

Dibucaine hydrochloride

Eucalyptol

Lidocaine

Lidocaine hydrochloride

Methyl salicylate

Myrrh tincture

Pyrilamine maleate

Sorbitol

Sugars

Tetracaine

Tetracaine hydrochloride

Thymol

(15) Topical otic drug products

(i) For the prevention of swimmer's ear and for the drying of water-clogged ears, approved as of May 7, 1991.

Acetic acid

(ii) For the prevention of swimmer's ear, approved as of August 15, 1995.

Glycerin and anhydrous glycerin

Isopropyl alcohol

(16) Poison treatment drug products.

Ipecac fluid extract

Ipecac tincture

Zinc sulfate

(17) Skin bleaching drug products.

Mercury, ammoniated

(18) Skin protectant drug products

(i) (A) Ingredients—Approved as of May 7, 1991.

Allantoin (wound healing claims only)

Sulfur

Tannic acid

Zinc acetate (wound healing claims only)

(B) Ingredients—Approved as of June 4, 2004; June 6, 2005, for products with annual sales less than \$25,000.

Beeswax

Bismuth subnitrate

Boric acid

Cetyl alcohol

Glyceryl stearate

Isopropyl palmitate

Live yeast cell derivative

Shark liver oil

Stearyl alcohol

(ii) Astringent drug products.

Acetone

Alcohol

Alum, ammonium

Alum, potassium

Aluminum chlorhydroxy complex

Aromatics

Benzalkonium chloride

Benzethonium chloride

Benzocaine

Benzoic acid

Boric acid

Calcium acetate

Camphor gum

Clove oil

Colloidal oatmeal

Cresol

Cupric sulfate

- Eucalyptus oil
- Eugenol
- Ferric subsulfate (Monsel's Solution)
- Honey
- Isopropyl alcohol
- Menthol
- Methyl salicylate
- Oxyquinoline sulfate
- p-t*-Butyl-*m*-cresol
- Peppermint oil
- Phenol
- Polyoxyethylene laurate
- Potassium ferrocyanide
- Sage oil
- Silver nitrate
- Sodium borate
- Sodium diacetate
- Talc
- Tannic acid glycerite
- Thymol
- Topical starch
- Zinc chloride
- Zinc oxide
- Zinc phenolsulfonate
- Zinc stearate
- Zinc sulfate
- (iii) Diaper rash drug products.
 - Aluminum hydroxide
 - Cocoa butter
 - Cysteine hydrochloride
 - Glycerin
 - Protein hydrolysate
 - Racemethionine
 - Sulfur
 - Tannic acid
 - Zinc acetate
 - Zinc carbonate
- (iv) Fever blister and cold sore treatment drug products.
 - Bismuth subnitrate
 - Boric acid
 - Pyridoxine hydrochloride
 - Sulfur
 - Tannic acid
 - Topical starch
 - Trolamine
 - Zinc sulfate
- (v) Insect bite and sting drug products
 - (A) Ingredients—Approved as of November 10, 1993.
 - Alcohol
 - Alcohol, ethoxylated alkyl
 - Ammonia solution, strong
 - Ammonium hydroxide
 - Benzalkonium chloride
 - Camphor
 - Ergot fluid extract
 - Ferric chloride
 - Menthol
 - Peppermint oil
 - Phenol
 - Pyrilamine maleate
 - Sodium borate
 - Trolamine
 - Turpentine oil
 - Zirconium oxide
 - (B) Ingredients—Approved as of June 4, 2004; June 6, 2005, for products with annual sales less than \$25,000.
 - Beeswax
 - Bismuth subnitrate
 - Boric acid
 - Cetyl alcohol
 - Glyceryl stearate
 - Isopropyl palmitate
 - Live yeast cell derivative
 - Shark liver oil
 - Stearyl alcohol
- (vi) Poison ivy, poison oak, and poison sumac drug products
 - (A) Ingredients—Approved as of November 10, 1993.
 - Alcohol
 - Anion and cation exchange resins buffered
 - Benzethonium chloride
 - Benzocaine
 - Benzyl alcohol
 - Bismuth subnitrate
 - Bithionol
 - Boric acid
 - Camphor
 - Cetalkonium chloride
 - Chloral hydrate
 - Chlorpheniramine maleate
 - Creosote
 - Diperodon hydrochloride
 - Diphenhydramine hydrochloride
 - Eucalyptus oil
 - Ferric chloride
 - Glycerin
 - Hectorite
 - Hydrogen peroxide
 - Impatiens biflora* tincture
 - Iron oxide
 - Isopropyl alcohol
 - Lanolin
 - Lead acetate
 - Lidocaine
 - Menthol
 - Merbromin
 - Mercuric chloride
 - Panthenol
 - Parethoxycaine hydrochloride
 - Phenol

Phenyltoloxamine dihydrogen citrate
 Povidone–vinylacetate copolymers
 Salicylic acid
 Simethicone
 Tannic acid
 Topical starch
 Trolamine
 Turpentine oil
 Zirconium oxide
 Zyloxin

(B) Ingredients—Approved as of June 4, 2004;
 June 6, 2005, for products with annual
 sales less than \$25,000.

Beeswax
 Bismuth subnitrate
 Boric acid
 Cetyl alcohol
 Glyceryl stearate
 Isopropyl palmitate
 Live yeast cell derivative
 Shark liver oil
 Stearyl alcohol

(19) [Reserved]

(20) Weight control drug products.

Alcohol
 Alfalfa
 Alginic acid
 Anise oil
 Arginine
 Ascorbic acid
 Bearberry
 Biotin
 Bone marrow, red
 Buchu
 Buchu, potassium extract
 Caffeine
 Caffeine citrate
 Calcium
 Calcium carbonate
 Calcium caseinate
 Calcium lactate
 Calcium pantothenate
 Carboxymethylcellulose sodium
 Carrageenan
 Cholecalciferol
 Choline
 Chondrus
 Citric acid
Cnicus benedictus
 Copper
 Copper gluconate
 Corn oil
 Corn syrup
 Corn silk, potassium extract
 Cupric sulfate
 Cyanocobalamin (vitamin B12)
 Cystine

Dextrose
 Docusate sodium
 Ergocalciferol
 Ferric ammonium citrate
 Ferric pyrophosphate
 Ferrous fumarate
 Ferrous gluconate
 Ferrous sulfate (iron)
 Flax seed
 Folic acid
 Fructose
 Guar gum
 Histidine
Hydrastis canadensis
 Inositol
 Iodine
 Isoleucine
 Juniper, potassium extract
 Karaya gum
 Kelp
 Lactose
 Lecithin
 Leucine
 Liver concentrate
 Lysine
 Lysine hydrochloride
 Magnesium
 Magnesium oxide
 Malt
 Maltodextrin
 Manganese citrate
 Mannitol
 Methionine
 Methylcellulose
 Mono- and diglycerides
 Niacinamide
 Organic vegetables
 Pancreatin
 Pantothenic acid
 Papain
 Papaya enzymes
 Pepsin
 Phenacetin
 Phenylalanine
 Phosphorus
 Phytolacca
 Pineapple enzymes
 Plantago seed
 Potassium citrate
 Pyridoxine hydrochloride (vitamin B6)
 Riboflavin
 Rice polishings
 Saccharin
 Sea minerals
 Sesame seed
 Sodium
 Sodium bicarbonate

- Sodium caseinate
- Sodium chloride (salt)
- Soybean protein
- Soy meal
- Sucrose
- Thiamine hydrochloride (vitamin B1)
- Thiamine mononitrate (vitamin B1 mononitrate)
- Threonine
- Tricalcium phosphate
- Tryptophan
- Tyrosine
- Uva ursi*, potassium extract
- Valine
- Vegetable
- Vitamin A
- Vitamin A acetate
- Vitamin A palmitate
- Vitamin E
- Wheat germ
- Xanthan gum
- Yeast
- (21) Ophthalmic drug products.
 - (i) Ophthalmic anesthetic drug products.
 - Antipyrine
 - Piperocaine hydrochloride
 - (ii) Ophthalmic anti-infective drug products.
 - Boric acid
 - Mild silver protein
 - Yellow mercuric oxide
 - (iii) Ophthalmic astringent drug products.
 - Infusion of rose petals
 - (iv) Ophthalmic demulcent drug products.
 - Polyethylene glycol 6000
 - (v) Ophthalmic vasoconstrictor drug products.
 - Phenylephrine hydrochloride (less than 0.08%)
- (22) Topical antifungal drug products.
 - (i) Diaper rash drug products. Any ingredient(s) labeled with claims or directions for use in the treatment and/or prevention of diaper rash.
 - (ii) Ingredients.
 - Alcloxa
 - Alum, potassium
 - Aluminum sulfate
 - Amyltricresols, secondary
 - Basic fuchsin
 - Benzethonium chloride
 - Benzoic acid
 - Benzoxiquine
 - Boric acid
 - Camphor
 - Candididin
 - Chlorothymol
 - Coal tar
 - Dichlorophen
 - Menthol
 - Methylparaben
 - Oxyquinoline
 - Oxyquinoline sulfate
 - Phenol
 - Phenolate sodium
 - Phenyl salicylate
 - Propionic acid
 - Propylparaben
 - Resorcinol
 - Salicylic acid
 - Sodium borate
 - Sodium caprylate
 - Sodium propionate
 - Sulfur
 - Tannic acid
 - Thymol
 - Tolindate
 - Triacetin
 - Zinc caprylate
 - Zinc propionate
- (iii) Any ingredient(s) labeled with claims or directions for use on the scalp or on the nails.
- (iv) Ingredients.
 - Camphorated metacresol
 - Chloroxylenol
 - m-Cresol
 - Nystatin
- (23) Internal analgesic drug products
 - (i) Approved as of November 10, 1993.
 - Aminobenzoic acid
 - Antipyrine
 - Aspirin, aluminum
 - Calcium salicylate
 - Codeine
 - Codeine phosphate
 - Codeine sulfate
 - Iodoantipyrine
 - Lysine aspirin
 - Methapyrilene fumarate
 - Phenacetin
 - Pheniramine maleate
 - Pyrilamine maleate
 - Quinine
 - Salsalate
 - Sodium aminobenzoate
 - (ii) Approved as of February 22, 1999.
 - Any atropine ingredient
 - Any ephedrine ingredient
- (24) Orally administered menstrual drug products
 - (i) Approved as of November 10, 1993.
 - Alcohol
 - Alfalfa leaves
 - Aloes
 - Asclepias tuberosa*
 - Asparagus
 - Barosma
 - Bearberry (extract of *Uva ursi*)
 - Bearberry fluid extract (extract of bearberry)
 - Blessed thistle (*Cnicus benedictus*)

- Buchu powdered extract (extract of buchu)
 Calcium lactate
 Calcium pantothenate
 Capsicum oleoresin
 Cascara fluid extract, aromatic (extract of cascara)
 Chlorprophenpyridamine maleate
Cimicifuga racemosa
 Codeine
 Collinsonia (extract stone root)
 Corn silk
 Couch grass
 Dog grass extract
 Ethyl nitrite
 Ferric chloride
 Ferrous sulfate
Gentiana lutea (gentian)
 Glycyrrhiza (licorice)
 Homatropine methylbromide
 Hydrangea, powdered extract (extract of hydrangea)
Hydrastis canadensis (golden seal)
 Hyoscyamine sulfate
 Juniper oil (oil of juniper)
 Magnesium sulfate
 Methapyrilene hydrochloride
 Methenamine
 Methylene blue
 Natural estrogenic hormone
 Niacinamide
 Nutmeg oil (oil of nutmeg)
 Oil of erigeron
 Parsley
 Peppermint spirit
 Pepsin, essence
 Phenacetin
 Phenindamine tartrate
 Phenyl salicylate
Piscidia erythrina
 Pipsissewa
 Potassium acetate
 Potassium nitrate
 Riboflavin
 Saw palmetto
Senecio aureus
 Sodium benzoate
 Sodium nitrate
 Sucrose
 Sulfurated oils of turpentine
Taraxacum officinale
 Theobromine sodium salicylate
 Theophylline
 Thiamine hydrochloride
 Triticum
 Turpentine, Venice (Venice turpentine)
 Urea
- (ii) Approved as of February 22, 1999.
- Any atropine ingredient
 Any ephedrine ingredient
- (25) Pediculicide drug products
- (i) Approved as of November 10, 1993.
- Benzocaine
 Benzyl alcohol
 Benzyl benzoate
 Chlorophenothane (dichlorodiphenyl trichloroethane)
 Coconut oil soap, aqueous
 Copper oleate
 Docusate sodium
 Formic acid
 Isobornyl thiocynoacetate
 PicROTOXIN
 Propylene glycol
 Sabadilla alkaloids
 Sulfur, sublimed
 Thiocynoacetate
- (ii) Approved as of June 14, 1994. The combination of pyrethrum extract (formerly named pyrethrins) and piperonyl butoxide in an aerosol dosage formulation.
- (26) Anorectal drug products
- (i) Anticholinergic drug products.
- Atropine
 Belladonna extract
- (ii) Antiseptic drug products.
- Boric acid
 Boroglycerin
 Hydrastis
 Phenol
 Resorcinol
 Sodium salicylic acid phenolate
- (iii) Astringent drug products.
- Tannic acid
- (iv) Counterirritant drug products.
- Camphor (greater than 3%–11%)
 Hydrastis
 Menthol (1.25%–16%)
 Turpentine oil (rectified) (6%–50%)
- (v) Keratolytic drug products.
- Precipitated sulfur
 Sublimed sulfur
- (vi) Local anesthetic drug products.
- Dipreron
 Phenacaine hydrochloride
- (vii) Other drug products.
- Collinsonia extract
Escherichia coli vaccines
 Lappa extract
 Leptandra extract
 Live yeast cell derivative
 Mullein
- (viii) Protectant drug products.
- Bismuth oxide
 Bismuth subcarbonate

- Bismuth subgallate
- Bismuth subnitrate
- Lanolin alcohols
- (ix) Vasoconstrictor drug products.
 - Epinephrine undecylenate
- (x) Wound-healing drug products.
 - Cholecalciferol
 - Cod liver oil
 - Live yeast cell derivative
 - Peruvian balsam
 - Shark liver oil
 - Vitamin A
- (xi) Combination drug products. Any combination drug product containing hydrocortisone and pramoxine hydrochloride.
- (27) Topical antimicrobial drug products
 - (i) First aid antiseptic drug products.
 - Ammoniated mercury
 - Calomel (mercurous chloride)
 - Merbromin (mercurochrome)
 - Mercufenol chloride (ortho-chloromercuriphenol, ortho-hydroxyphenylmercuric chloride)
 - Mercuric chloride (bichloride of mercury, mercury chloride)
 - Mercuric oxide, yellow
 - Mercuric salicylate
 - Mercuric sulfide, red
 - Mercury
 - Mercury oleate
 - Mercury sulfide
 - Nitromersol
 - Para-chloromercuriphenol
 - Phenylmercuric nitrate
 - Thimerosal
 - Vitromersol
 - Zyloxin
 - (ii) Diaper rash drug products.
 - Para-chloromercuriphenol
 - Any other ingredient containing mercury
- (28) Vaginal contraceptive drug products
 - (i) Approved as of October 22, 1998.
 - Dodecaethylene glycol monolaurate (polyethylene glycol 600 monolaurate)
 - Laureth 10S
 - Methoxypolyoxyethyleneglycol 550 laurate
 - Phenylmercuric acetate
 - Phenylmercuric nitrate
 - Any other ingredient containing mercury
 - (ii) Approved as of November 5, 2002.
 - Octoxynol 9
- (29) Sunscreen drug products.
 - Diethanolamine methoxycinnamate
 - Digalloyl trioleate
 - Ethyl 4-[bis(hydroxypropyl)] aminobenzoate
 - Glyceryl aminobenzoate
 - Lawsone with dihydroxyacetone
 - Red petrolatum



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4 Bioequivalence of Complementary and Alternative Medicines

BACKGROUND

The history of legislation described previously in the United States demonstrates that the U.S. agencies have been proactive in creating pathways that will lead to affordable medicines. Whereas the United States remains the largest market of pharmaceutical products, with over \$700 billion of market, it has not ignored the emerging need to recognize other systems of medicines, such as herbal therapies and other non-conventional methods; in summary, any modality that is not clearly connected with a chemical structure and activity can be labeled as nontraditional in the modern understanding of pharmacology. In the United States, the Food and Drug Administration (FDA) chose a designation of Complementary and Alternative Medicine to encompass all herbal and nontraditional medicinal systems. This was a giant step for the U.S. FDA, which had long been a promoter of a clean connection between chemistry and pharmacology. Such is not the case in the use of the broad range of drugs that fall into this category of treatment modalities.

The term “complementary and alternative medicine” (CAM) encompasses a wide array of health-care practices, products, and therapies that are distinct from practices, products, and therapies used in “conventional” or “allopathic” medicine. Some forms of CAM, such as traditional Chinese medicine and the Indian Ayurvedic medicine, have been practiced for centuries, whereas others, such as electrotherapy, are more recent in origin. In the United States, the practice of CAM has risen dramatically in recent years. In 1992, Congress established the Office of Unconventional Therapies, which later became the Office of Alternative Medicine (OAM), to explore “unconventional medical practices.” In 1998, OAM became the National Center for Complementary and Alternative Medicine (NCCAM). NCCAM is a center within the National Institutes of Health. The Institute of Medicine, in its book entitled *Complementary and Alternative Medicine in the United States*, stated that more than one-third of American adults reported using some form of CAM and that visits to CAM providers each year exceed those to primary care physicians. As the practice of CAM has increased in the United States, FDA observed increased confusion as to whether certain products used in CAM products are subject to regulation under the Federal Food, Drug, and Cosmetic Act (FD&C Act) or Public Health Service Act (PHS Act); this is further compounded by the importation of a large number of CAM products, since these are widely used not just in the developing countries but also in many developed markets,

such as Germany and Japan. The FDA guidance regarding CAM products makes two fundamental points:

- First, depending on the CAM therapy or practice, a product used in a CAM therapy or practice *may* be subject to regulation as a biological product, cosmetic, drug, device, or food (including food additives and dietary supplements) under the Act or the PHS Act. For example, the PHS Act defines “biological product,” and the Act defines (among other things) Cosmetic, Device, Dietary supplement, and Drug, as well as “new drug” and “new animal drug,” “Food,” and Food additive.
- Second, neither the Act nor the PHS Act exempts CAM products from regulation. This means, for example, that if a person decides to produce and sell raw vegetable juice for use in juice therapy to promote optimal health, that product is a food subject to the requirements for foods in the Act and FDA regulations, including the hazard analysis and critical control point (HACCP) system requirements for juices in 21 CFR Part 120. If the juice therapy *is* intended for use as part of a disease treatment regimen instead of for general wellness, the vegetable juice would also be subject to regulation as a drug under the Act.

The NCCAM defines CAM as “a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine.” It interprets “complementary” medicine as being used together with conventional medicine, whereas “alternative” medicine is used in place of conventional medicine. NCCAM classifies CAM therapies into four categories or “domains.” These are biologically based practices; energy therapies; manipulative and body-based methods; and mind-body medicine.

NCCAM once had a fifth domain, “Alternative medical systems,” but now considers “alternative medical systems” (now known as “whole medical systems”) to be a separate category rather than another domain, because alternative medical systems use practices from the four domains listed earlier. For purposes of this guidance, FDA adopts the same domains and “whole medical systems” category that NCCAM uses.

According to NCCAM, the domain called “biologically based practices” includes, but is not limited to, botanicals, animal-derived extracts, vitamins, minerals, fatty acids, amino acids, proteins, prebiotics and probiotics, whole diets,

and “functional foods.” Many biologically based products within this domain are subject to statutory and regulatory requirements under the Act or the PHS Act. The intended use of a product plays a central role in how it is regulated. For example:

- Botanical products, depending on the circumstances, may be regulated as drugs, cosmetics, dietary supplements, or foods. All four types of products are subject to the Act. For example, a botanical product intended for use in treating a disease would generally be regulated as a drug; a botanical product taken by mouth, labeled as a dietary supplement, and intended for use to affect the structure or function of the body would generally be regulated as a dietary supplement; a raw or dried botanical intended for use as an ingredient to flavor food would generally be regulated as a food or as a food additive, depending on whether the botanical was generally recognized as safe for its intended use in food; and a lotion containing botanical ingredients and intended for use in moisturizing the skin would generally be regulated as a cosmetic.
- Probiotics may be regulated as dietary supplements, foods, or drugs under the Act, depending on the product’s intended use. Other factors may also affect the classification of the product: for example, whether the product contains a “dietary ingredient” as defined in section 201(ff)(1) of the Act (21 U.S.C. 321(ff)(1)), whether it is represented as a conventional food or as a meal replacement (see section 201(ff)(2)(B) of the Act), and for probiotics used as ingredients in a conventional food, whether the ingredient is generally recognized as safe for its intended use (see section 201(s) of the Act (21 U.S.C. 321(s))). In addition to any requirements that apply based on the product’s classification under the Act, probiotics may also be subject to the PHS Act’s provisions concerning the prevention of communicable disease, due to potential disease-causing microorganisms that might be contained in such products. Finally, if a probiotic is a drug under the Act, it may be subject to regulation as a biological product under the PHS Act as well.
- Products that NCCAM would consider to be “functional foods” may be subject to FDA regulation as foods, dietary supplements, or drugs under the Act. As with botanicals and probiotics, the classification of a “functional food” under the Act is based primarily on the product’s intended use and may also involve other factors depending on the elements of the statutory definition of a particular product category.

NCCAM considers energy medicine to involve energy fields of two types:

- Veritable energy fields, which can be measured and use either mechanical vibrations (such as sound) or electromagnetic forces, including visible light,

magnetism, monochromatic radiation (such as laser light), and other light rays.

- Putative energy fields (or biofields) that have defied measurement to date by reproducible methods. According to NCCAM, therapies involving putative energy fields “are based on the concept that human beings are infused with a subtle form of energy,” and therapists “claim that they work with this subtle energy, see it with their own eyes, and use it to effect changes in the physical body and influence health.”

In a sense, “conventional” medicine already uses various forms of “energy” medicine. For example, a magnetic resonance imaging (MRI) device uses electromagnetic waves to create images of internal body organs and tissues. As another example, an ultrasound machine uses sound waves to create images of body organs, tissues, and fetuses. Given their intended uses, we regulate these products as medical devices under the Act. The CAM products that use veritable energy fields in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease in man or animals or to affect the structure or any function of the body of man or animals may be medical devices under the Act. Additionally, if the product is electronic and emits radiation, it may be subject to additional requirements to ensure that there is no unnecessary exposure of people to radiation. CAM products that use putative energy fields in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease in man or animals may be medical devices under the Act. For example, FDA regulates acupuncture needles as “class II” medical devices.

Under the umbrella of manipulative and body-based practices is a heterogeneous group of CAM interventions and therapies. These include chiropractic and osteopathic manipulation, massage therapy, Tui Na, reflexology, rolfing, Brown technique, Trager bodywork, Alexander technique, Feldenkrais method, and a host of others. Manipulative and body-based practices focus primarily on the structures and systems of the body, including the bones and joints, the soft tissues, and the circulatory and lymphatic systems. To the extent that manipulative and body-based practices involve practitioners physically manipulating a patient’s body without using tools or machines, FDA does not consider that such practices are subject to regulation under the Act or the PHS Act. If, however, the manipulative and body-based practices involve the use of equipment (such as massage devices) or the application of a product (such as a lotion, cream, or oil) to the skin or other parts of the body, those products may be subject to regulation under the Act, depending on the nature of the product and its intended use.

NCCAM describes mind-body medicine as focusing on “the interactions among the brain, mind, body, and behavior, and the powerful ways in which emotional, mental, social, spiritual, and behavioral factors can directly affect health.” It states that mind-body medicine “typically focuses on intervention strategies that are thought to promote health, such as relaxation, hypnosis, visual imagery, meditation, yoga,

biofeedback, tai chi, qi gong, cognitive-behavioral therapies, group support, autogenic training, and spirituality.” In general, CAM practices in this domain would *not* be subject to FDA jurisdiction under the Act or the PHS Act. As with the manipulative and body-based practices domain, however, any equipment or other products used as part of the practice of mind-body medicine may be subject to FDA regulation, depending on the nature of the product and its intended use. For example, biofeedback machines intended to help a patient learn to affect body functions, such as muscle activity, are regulated as class II devices.

NCCAM describes “whole medical systems” as involving “complete systems of theory and practice that have evolved independently from or parallel to allopathic (conventional) medicine.” These may reflect individual cultural systems, such as traditional Chinese medicine and Ayurvedic medicine. Some elements common to whole medical systems are a belief that the body has the power to heal itself and that healing may involve techniques that use the mind, body, and spirit. Although it is unlikely that a whole medical system itself would be subject to regulation under the Act or the PHS Act, products used as *components* of whole medical systems may be subject to FDA regulation for the reasons described earlier.

To understand how the Act or the PHS Act might apply to CAM products, it is important to understand the Act’s statutory definitions or, in the case of the PHS Act, our authority regarding biological products.

To illustrate how the definitions of drug or new drug might apply, consider an herbal product that is intended to treat arthritis in humans. The herbal product, which would be a “biologically based practice” insofar as CAM domains are concerned, would be a “drug” under section 201(g)(1)(B) of the Act, because it is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease (arthritis) in man. The same herbal product would also be a “new drug” under section 201(p)(1) of the Act unless it is generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling. “New drug” status triggers the Act’s requirements for premarket review and approval by FDA.

To illustrate how a CAM product might be a “device” under the Act, acupuncture is a CAM therapy that seeks to stimulate energy pathways (“meridians”) by puncturing, pressing, heating, using electrical current, or using herbal medicines. Fine needles are often used, and these acupuncture needles are “devices” under section 201(h) of the Act, because they are intended for use in the cure, mitigation, treatment, or prevention of disease in man or are intended to affect the structure or function of the body of man. We regulate acupuncture needles (see 21 CFR 880.5580) but not the practice of acupuncture itself. A detailed discussion of the Act’s device provisions is beyond the scope of this guidance document. Note, however, that the Act establishes classifications for devices (class I, II, or III) that affect how they are regulated. The Act

also imposes certain requirements on those who manufacture devices (including requirements pertaining to establishment registration and product listing, premarket review, labeling, postmarket reporting, and good manufacturing practices). Certain requirements also apply to device distributors.

To illustrate how a CAM practice might involve “foods,” juice therapy uses juice made from vegetables and fruits. Absent any claims that would make the juice subject to the drug definition, the juice would be a “food” under section 201(f) of the Act, because it is an article used for food or drink for man. A detailed discussion of the Act’s food provisions is beyond the scope of this guidance document. However, anyone who intends to market CAM products that might be subject to regulation under these provisions should familiarize himself/herself with the Act’s requirements for foods, particularly with respect to safety and labeling. The Act and our food regulations can be found at www.fda.gov/opacom/laws.

To illustrate how a CAM product might involve “food additives” under section 201(s) of the Act, some CAM practices involve dietary modifications whereby substances such as botanicals or enzymes are added to foods in the diet. If a manufacturer adds such a substance to a food, the substance may fall within the “food additive” definition at section 201(s) of the Act. A food additive is subject to premarket approval by FDA under section 409 of the Act (21 U.S.C. 348). Food additives that we have not approved or that do not comply with applicable FDA regulations prescribing safe conditions of use are deemed to be unsafe under section 409(a) of the Act, and foods that contain such additives are adulterated under section 402(a)(2)(C) of the Act (21 U.S.C. 342(a)(2)(C)). The Act provides that a substance is exempt from the definition of a food additive and thus, from premarket approval if, among other reasons, it is generally recognized as safe (GRAS) by qualified experts under the conditions of intended use. Whether a substance added to a food is considered to be a food additive or is GRAS, any claims associating the substance with the reduction of a disease risk are “health claims” (defined in 21 CFR 101.14(a)(1)) that require premarket review by FDA. A detailed discussion of the Act’s food additive provisions is beyond the scope of this guidance document. However, anyone intending to market CAM products that are or contain substances that might be subject to regulation as food additives should consult with the Act’s food additive requirements.

Except for purposes of section 201(g) [of the Act], a dietary supplement shall be deemed to be a food within the meaning of this Act. To illustrate how a CAM product might be a “dietary supplement” under section 201(ff) of the Act, consider botanical products used in naturopathy.

Naturopathy is a CAM whole medical system that views disease as a manifestation of alterations in the processes by which the body heals itself. For example, naturopathic cranberry tablets might be labeled for use to maintain the health of the urinary tract. In this example, the cranberry tablets generally would be regulated as “dietary supplements” under section 201(ff)(1) of the Act if they were labeled for use to “maintain the health of the urinary tract” rather than “prevent urinary tract infections.” The cranberry tablets would be

regulated as “drugs” under section 201(g) of the Act if they were labeled for use to “treat urinary tract infections” even if they were labeled as dietary supplements. A detailed discussion of the Act’s dietary supplement provisions is beyond the scope of this guidance document.

It is possible that certain products used in conjunction with CAM practices may be “cosmetics” under the Act. For example, if a CAM practice involves massage with a moisturizer, the moisturizer could be a “cosmetic” to the extent that it is “rubbed, poured, sprinkled, or sprayed on” the body for beautification or appearance-altering purposes. However, if the moisturizer’s intended use is also for the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body, then it may also be subject to regulation as a drug. Other examples of drug/cosmetic combinations are deodorants that are also antiperspirants, moisturizers and makeup marketed with sun-protection claims, and shampoos that also treat dandruff. The Act does not require premarket approval for cosmetics, but it does prohibit the marketing of adulterated or misbranded cosmetics in interstate commerce. Anyone intending to market CAM products that might be subject to regulation as cosmetics should familiarize himself/herself with the safety and labeling requirements for these products in the Act and our regulations.

If a CAM product manufacturer attempted to use a live, disease-causing virus as a component of a CAM product, FDA could exercise its authority under section 361 of the PHS Act and 21 CFR 1240.30 to take action against the product, in addition to considering the applicability of section 351 of the PHS Act.

As the practice of CAM has increased in the United States, FDA saw increased confusion as to whether certain products used in CAM (which, for convenience, we will refer to as “CAM products”) are subject to regulation under the Act or the PHS Act. FDA also saw an increase in the number of CAM products imported into the United States.

Therefore, the draft guidance discusses when a CAM product is subject to the Act or the PHS Act. (When the draft guidance mentions a particular CAM therapy, practice, or product, it does so in order to provide background information or to serve as an example or illustration; any mention of a particular CAM therapy, practice, or product should not be construed as expressing FDA’s support for or endorsement of that particular CAM therapy, practice, or product or, unless specified otherwise, as an agency determination that a particular product is safe and effective for its intended uses or

is safe for use.) The draft guidance makes the following two fundamental points:

First, depending on the CAM therapy or practice, a product used in a CAM therapy or practice may be subject to regulation as a biological product, cosmetic, drug, device, or food (including food additives and dietary supplements) under the Act or the PHS Act.

Second, neither the Act nor the PHS Act exempts CAM products from regulation.

As the practice of CAM has increased in the United States, the Food and Drug Administration (“FDA,” “we”) has seen increased confusion as to whether certain products used in CAM (which, for convenience, we will refer to as “CAM products”) are subject to regulation under the Federal Food, Drug, and Cosmetic Act (“the Act”) or the Public Health Service Act (“PHS Act”). There is also an increase in the number of CAM products imported into the United States.

The FDA Guidance makes two fundamental points:

- First, depending on the CAM therapy or practice, a product used in a CAM therapy or practice *may* be subject to regulation as a biological product, cosmetic, drug, device, or food (including food additives and dietary supplements) under the Act or the PHS Act. For example, the PHS Act defines “biological product,” and the Act defines (among other things)
 - Cosmetic
 - Device
 - Dietary supplement
 - Drug, as well as “new drug” and “new animal drug”
 - Food
 - Food additive
- Second, neither the Act nor the PHS Act exempts CAM products from regulation. This means, for example, that if a person decides to produce and sell raw vegetable juice for use in juice therapy to promote optimal health, that product is a food subject to the requirements for foods in the Act and FDA regulations, including the hazard analysis and critical control point (HACCP) system requirements for juices in 21 CFR part 120. If the juice therapy is intended for use as part of a disease treatment regimen instead of for general wellness, the vegetable juice would also be subject to regulation as a drug under the Act.

Appendix A: GMP Audit Template

The Guidelines for cGMP Compliance:

- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/vol4-chap1_2013-01_en.pdf
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/2014-03_chapter_2.pdf
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/chapter4_01-2011_en.pdf
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/2014-11_vol4_chapter_6.pdf
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/2014-08_gmp_chap8.pdf
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/pdfs-en/cap9_en.pdf
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/2014-08_gmp_part1.pdf
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/2011_site_master_file_en.pdf
- http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002873.pdf
- http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002871.pdf
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/mra_batch-certificate_05-2011.pdf
- https://ec.europa.eu/health/sites/health/files/files/gmp/2013_01_28_template.pdf
- http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/11/WC500177735.pdf
- [http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52015XC0321\(02\)&from=EN](http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52015XC0321(02)&from=EN)
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/template_imp_batch_certification.docx
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/2008_11_25_gmp-an1_en.pdf
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/pdfs-en/2018_annex2_en.pdf
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/annex11_01-2011_en.pdf
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/2015-10_annex15.pdf
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/v4_an16_201510_en.pdf
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/pdfs-en/2018_annex17_en.pdf
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/pdfs-en/2005_12_14_annex19_en.pdf
- https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/pdfs-en/2018_annex17_en.pdf

		Compliance 1 2 3 ^a	Remarks	EU-Guide
1	PERSONNEL			
1.1	Qualified personnel available?	☐ ☐ ☐		2.1
1.2	Organization charts available?	☐ ☐ ☐		2.2
1.3	Job descriptions available?	☐ ☐ ☐		2.2
1.4	Responsibilities clearly defined?	☐ ☐ ☐		2.2
	Key Personnel			
	Responsible persons designated for			
1.5	• Production?	☐ ☐ ☐		2.5
1.6	• Quality control?	☐ ☐ ☐		2.6
1.7	Are they independent of each other?	☐ ☐ ☐		2.3
1.8	Are joint functions clearly defined?	☐ ☐ ☐		2.7
1.9	Are the responsible persons working full time?	☐ ☐ ☐		2.3
1.10	Do the responsible persons have the appropriate formulation, knowledge, and experience?	☐ ☐ ☐		2.1/2.2
1.11	Do the relevant departments have enough personnel?	☐ ☐ ☐		2.1
	Training			
1.12	Continuous training programs for the production and QC staff?	☐ ☐ ☐		2.8
1.13	Initial job training for all employees?	☐ ☐ ☐		2.9
1.14	Teaching aids (videos, slides, and brochures) available?	☐ ☐ ☐		2.9
1.15	External training courses for the staff?	☐ ☐ ☐		2.9
1.16	Training records?	☐ ☐ ☐		2.9
1.17	Special training in sensitive areas (sterile production and toxic substances)?	☐ ☐ ☐		2.10
1.18	Information for visitors to the manufacturing area?	☐ ☐ ☐		2.11
2	HYGIENE			
	Personnel Hygiene			
	Detailed written hygiene programs for			
2.1	• Clothing?	☐ ☐ ☐		2.13
2.2	• Use of washrooms?	☐ ☐ ☐		2.13
2.3	• Behavior in production areas?	☐ ☐ ☐		2.13
2.4	Precautions against sick personnel or personnel with open wounds in production?	☐ ☐ ☐		2.14
	Medical examination:			
2.5	• On recruitment?	☐ ☐ ☐		2.15
2.6	• Regular reexaminations?	☐ ☐ ☐		2.15
	Duty of notification after			
2.7	• Trips to tropical countries?	☐ ☐ ☐		2.15
2.8	• Cases of contagious illness in the family?	☐ ☐ ☐		2.15
2.9	Instructions for appropriate working clothes?	☐ ☐ ☐		2.16
2.10	Absence of food and drink (chewing gum!) in the working area?	☐ ☐ ☐		2.17
2.11	Measures against contact with open product (gloves etc.)?	☐ ☐ ☐		2.18
2.12	Instructions for hand washing in production?	☐ ☐ ☐		2.19
2.13	Change of clothes when entering and leaving the production area?	☐ ☐ ☐		5.19
2.14	Change rooms and toilets easily within reach?	☐ ☐ ☐		3.31
2.15	Toilets and restrooms sufficiently separated from production areas?	☐ ☐ ☐		3.30/3.31
2.16	Workshops separate from production areas?	☐ ☐ ☐		3.32
2.17	Laboratory animal rooms totally segregated from production rooms?	☐ ☐ ☐		3.33

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
3	WAREHOUSE			
	Rooms, General			
3.1	Suitable for the intended use?	☐ ☐ ☐		3
3.2	• Adequate size?	☐ ☐ ☐		3
3.3	• Clean?	☐ ☐ ☐		3
3.4	Located and designed to exclude external contamination?	☐ ☐ ☐		3.1
3.5	Appropriate level of maintenance?	☐ ☐ ☐		3.2
3.6	Maintenance works possible without contamination risk?	☐ ☐ ☐		3.2
3.7	Appropriate lighting and air-conditioning?	☐ ☐ ☐		3.3
3.8	Recording of temperature and humidity?	☐ ☐ ☐		3.3
3.9	Protection against the entry of insects or other animals?	☐ ☐ ☐		3.4
3.10	Controlled access for authorized personnel only?	☐ ☐ ☐		3.5
	Rooms, Special Requirements			
	Type of warehousing:			
3.11	Separation of goods sufficient?	☐ ☐ ☐		3.18
3.12	Provision for different storage temperatures?	☐ ☐ ☐		3.19
3.13	Goods receiving zone weather protected?	☐ ☐ ☐		3.20
3.14	Cleaning zone for incoming goods?	☐ ☐ ☐		3.20
3.15	Separate quarantine area with controlled access?	☐ ☐ ☐		3.21
3.16	Separate, protected sampling area?	☐ ☐ ☐		3.22
	Separate and safe storage of			
3.17	• Returned goods?	☐ ☐ ☐		3.23
3.18	• Rejected goods?	☐ ☐ ☐		3.23
3.19	Separate and safe storage of highly active, toxic, or dangerous substances?	☐ ☐ ☐		3.24
3.20	Safe storage of narcotics?	☐ ☐ ☐		3.24
3.21	Safe storage of printed packaging materials?	☐ ☐ ☐		3.25
3.22	Security measurements against theft?	☐ ☐ ☐		3.25
3.23	Smoke detectors?	☐ ☐ ☐		3.25
3.24	Fire extinguishing system?	☐ ☐ ☐		3.25
	Operations			
3.25	Reception, sampling, and labeling according to written procedures?	☐ ☐ ☐		5.2
3.26	Is a sampling plan available?	☐ ☐ ☐		Suppl. 4
3.27	Cleaning of incoming containers?	☐ ☐ ☐		5.3
3.28	Investigation and recording of damaged deliveries?	☐ ☐ ☐		5.4
3.29	First In First Out (FIFO) principle?	☐ ☐ ☐		5.7
3.30	Inventory system?	☐ ☐ ☐		5.8
3.31	Can the location of materials be detected at all times?	☐ ☐ ☐		
3.32	Incoming goods: containers and seals intact?	☐ ☐ ☐		5.27
3.33	Incoming goods: conformity with bill of delivery?	☐ ☐ ☐		5.27
	Labeling of incoming containers with			
3.34	• Internal name and code?	☐ ☐ ☐		5.29
3.35	• Allocated batch number?	☐ ☐ ☐		5.29
3.36	• Quarantine status?	☐ ☐ ☐		5.29
3.37	• Expiry date or reanalysis date?	☐ ☐ ☐		5.29
3.38	Identity test for each incoming container?	☐ ☐ ☐		5.29
3.39	Are the sampled containers marked?	☐ ☐ ☐		5.30
3.40	Are reference samples taken?	☐ ☐ ☐		5.30

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
3.41	Safe storage of printed packaging materials?	☐ ☐ ☐		5.41
3.42	Lot tracing of all packaging materials possible?	☐ ☐ ☐		5.42
3.43	Are excessive packaging materials destroyed?	☐ ☐ ☐		5.43
	Release of starting materials by physical/inventory checks on raw materials, packaging materials, and finished goods:			
	Item	Stocks: Physical	Stocks: Inventory	Storage conditions
4	DISPENSING/ASSEMBLING			
	Rooms, General			
4.1	Suitable for the intended use?	☐ ☐ ☐		3
4.2	• Adequate size?	☐ ☐ ☐		3
4.3	• Clean?	☐ ☐ ☐		3
4.4	Located and designed to exclude external contamination?	☐ ☐ ☐		3.1
4.5	Appropriate level of maintenance?	☐ ☐ ☐		3.2
4.6	Maintenance works possible without contamination risk?	☐ ☐ ☐		3.2
4.7	Appropriate lighting and air-conditioning?	☐ ☐ ☐		3.3
4.8	Recording of temperature and humidity?	☐ ☐ ☐		
4.9	Protection against the entry of insects or other animals?	☐ ☐ ☐		3.4
4.10	Controlled access for authorized personnel only?	☐ ☐ ☐		3.5
	Rooms, Special Requirements			
4.11	Segregated from production and warehouse?	☐ ☐ ☐		3.13
4.12	Separate weighing cabins?	☐ ☐ ☐		3.13
4.13	Separate air handling unit (AHU) for each cabin?	☐ ☐ ☐		3.12
	Air pressure gradient from weighing cabin → corridor:			3.3
4.14	Dust extraction systems available?	☐ ☐ ☐		5.11
	Operations			
4.15	Balances regularly calibrated?	☐ ☐ ☐		3.41
4.16	Only pharmaceutical raw materials in this area?	☐ ☐ ☐		5.17
4.17	Check on remains from previous materials before entering of new materials into a weighing cabin?	☐ ☐ ☐		5.9/5.35
4.18	Only one material in one cabin?	☐ ☐ ☐		5.9
4.19	Are dispensed materials correctly labeled?	☐ ☐ ☐		5.29
4.20	Only released products in the dispensing?	☐ ☐ ☐		5.31
4.21	Cleaning SOPs for the dispensing?	☐ ☐ ☐		4.28
4.22	Previously dispensed material recorded on weighing protocol?	☐ ☐ ☐		4.8
4.23	Safety measures against mix-ups during assembling (e.g., cage pallets)?	☐ ☐ ☐		5.32/5.34
5	SOLIDS MANUFACTURING			
	Field of activity:			
	• Granulation	☐		
	• Compression	☐		
	• Encapsulation	☐		
	• Film and sugar coating	☐		

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
	• Visual inspection (capsules, tablets, etc.) • Premix (human)	☐ ☐		
	Rooms, General			
5.1	Suitable for the intended use?	☐ ☐ ☐		3
5.2	• Adequate size?	☐ ☐ ☐		3
5.3	• Clean?	☐ ☐ ☐		3
5.4	Located and designed to exclude external contamination?	☐ ☐ ☐		3.1
5.5	Appropriate level of maintenance?	☐ ☐ ☐		3.2
5.6	Maintenance works possible without contamination risk?	☐ ☐ ☐		3.2
5.7	Appropriate lighting and air-conditioning?	☐ ☐ ☐		3.3
5.8	Recording of temperature and humidity?	☐ ☐ ☐		
5.9	Protection against the entry of insects or other animals?	☐ ☐ ☐		3.4
5.10	Controlled access for authorized personnel only?	☐ ☐ ☐		3.5
	Rooms, Special Requirements			
5.11	Separate manufacturing area for penicillins/cephalosporins or highly sensitizing substances?	☐ ☐ ☐		3.6
5.12	Only for processing of pharmaceuticals?	☐ ☐ ☐		3.6
5.13	Logical flow of materials?	☐ ☐ ☐		3.7
5.14	Walls, floors, and ceilings: smooth surface and free of cracks?	☐ ☐ ☐		3.8
5.15	Easy cleaning possible?	☐ ☐ ☐		3.10
5.16	Adequate drains with traps and grilles?	☐ ☐ ☐		3.11
5.17	Appropriate air handling system?	☐ ☐ ☐		3.12
	Air pressure gradient from working bay → corridor:			
	Classification according to EC guide?			
5.18	Appropriate dust extraction system?	☐ ☐ ☐		3.14
5.19	Appropriate lighting?	☐ ☐ ☐		3.16
5.20	Separate rest rooms?	☐ ☐ ☐		3.30
5.21	Changing rooms designed to avoid contamination?	☐ ☐ ☐		3.31
5.22	Toilets segregated from manufacturing areas?	☐ ☐ ☐		3.31
	Equipment			
5.23	Suitable for the intended use?	☐ ☐ ☐		3.34
5.24	Well maintained?	☐ ☐ ☐		3.34
5.25	Written and validated cleaning procedures?	☐ ☐ ☐		3.36
5.26	Maintenance without contamination risk (separate area)?	☐ ☐ ☐		3.35
5.27	Equipment in contact with product: suitable materials quality?	☐ ☐ ☐		3.39
5.28	Machinery equipped with measuring and control devices?	☐ ☐ ☐		3.40
5.29	Calibration at fixed intervals according to written procedures?	☐ ☐ ☐		3.41
5.30	Calibration records available?	☐ ☐ ☐		3.41
5.31	Contents and flow direction marked on pipes?	☐ ☐ ☐		3.42
5.32	Pipes for distilled and demineralized water regularly monitored and sanitized?	☐ ☐ ☐		3.43
5.33	Not functioning equipment in the production area (if yes: clearly marked)?	Y N ☐ ☐ ☐		3.44
5.34	Status of cleanliness indicated?	☐ ☐ ☐		5.13

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
5.35	Previous product indicated?	☐ ☐ ☐		5.13
	Operations			
5.36	Are written and validated procedures for all manufacturing steps available?	☐ ☐ ☐		5.2
5.37	Are all manufacturing steps recorded with actual parameters?	☐ ☐ ☐		5.2
5.38	Check of each single container of the starting materials (contents, weight, and identity)?	☐ ☐ ☐		5.3
5.39	Limits for yields?	☐ ☐ ☐		5.8
5.40	Only one batch of one product processed?	☐ ☐ ☐		5.9
5.41	Protection against microbial contamination?	☐ ☐ ☐		5.10
5.42	Appropriate measures against generation of dust (e.g., closed systems)?	☐ ☐ ☐		5.11
	Correct labeling of containers, materials, equipment, and rooms with			5.12
5.43	• Product name and batch no.?	☐ ☐ ☐		5.12
5.44	• Quarantine status?	☐ ☐ ☐		5.12
5.45	Deviations from standard procedures recorded and signed by the supervisor?	☐ ☐ ☐		5.14
5.46	Special procedures for the production of antibiotics, hormones, etc.?	☐ ☐ ☐		5.19
5.47	• Campaign production?	☐ ☐ ☐		5.19
5.48	• Special monitoring?	☐ ☐ ☐		5.19
5.49	• Validated decontamination procedure?	☐ ☐ ☐		5.19
5.50	Double check on weight?	☐ ☐ ☐		5.34
5.51	Line clearance before start of production?	☐ ☐ ☐		5.35
5.52	Investigation of deviations in yields?	☐ ☐ ☐		5.39
5.53	Validated procedures for reworking of rejected batches?	☐ ☐ ☐		5.62
5.54	Detailed procedures for the addition of previous batches?	☐ ☐ ☐		5.63
5.55	Special release procedure (QA) for those batches?	☐ ☐ ☐		5.64
5.56	Use of protective clothing (hair cover, shoes, masks, and gloves)?	☐ ☐ ☐		2.16
5.57	Clothing regulation for visitors?	☐ ☐ ☐		2.11
	In-Process Control (IPC)			5.38
	Who performs IPC?			
5.58	Are IPC methods approved by QC?	☐ ☐ ☐		6.18
	Performance of IPCs:	During start-up?	Frequency	Automatic data recording?
		Yes No		Yes No
	Tablets/Kernels			
5.59	Individual weights	☐ ☐		☐ ☐
5.60	Disintegration	☐ ☐		☐ ☐
5.61	Thickness	☐ ☐		☐ ☐
5.62	Hardness	☐ ☐		☐ ☐
5.63	Friability/Abrasion	☐ ☐		☐ ☐
	Sugar-/Film-Coated Tablets			
5.64	Weights	☐ ☐		☐ ☐
5.65	Disintegration	☐ ☐		☐ ☐
5.66	Residual absolute humidity	☐ ☐		☐ ☐
	Capsules			
5.67	Individual weights	☐ ☐		☐ ☐
5.68	Disintegration	☐ ☐		☐ ☐

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
	Validation			
5.69	Validation according to fixed procedures?	☐ ☐ ☐		5.21
5.70	New procedures released only after validation?	☐ ☐ ☐		5.22
	Validation of changes of			
5.71	• Processes?	☐ ☐ ☐		5.23
5.72	• Starting materials?	☐ ☐ ☐		5.23
5.73	• Equipment?	☐ ☐ ☐		5.23
5.74	Revalidation at fixed intervals?	☐ ☐ ☐		5.24
5.75	Procedures for the retrospective validation of old procedures?	☐ ☐ ☐		
6	LIQUIDS MANUFACTURING			
	Operations carried out:			
	• Dispensing (if different from solid)	☐ ☐ ☐		
	• Syrups and suspensions	☐ ☐ ☐		
	• Drops	☐ ☐ ☐		
	• Ointment manufacture	☐ ☐ ☐		
	• Ointment filling	☐ ☐ ☐		
	• Ampoule solution manufacture	☐ ☐ ☐		
	• Sterile or aseptic ampoule filling	☐ ☐ ☐		
	• Sterile freeze drying	☐ ☐ ☐		
	• Sterile powder filling	☐ ☐ ☐		
	Rooms, General			
6.1	Suitable for the intended use?	☐ ☐ ☐		3
6.2	• Adequate size?	☐ ☐ ☐		3
6.3	• Clean?	☐ ☐ ☐		3
6.4	Located and designed to exclude external contamination?	☐ ☐ ☐		3.1
6.5	Appropriate level of maintenance?	☐ ☐ ☐		3.2
6.6	Maintenance works possible without contamination risk?	☐ ☐ ☐		3.2
6.7	Appropriate lighting and air-conditioning?	☐ ☐ ☐		3.3
6.8	Recording of temperature and humidity?	☐ ☐ ☐		
6.9	Protection against the entry of insects or other animals?	☐ ☐ ☐		3.4
6.10	Controlled access for authorized personnel only?	☐ ☐ ☐		3.5
	Rooms, Special Requirements			
6.11	Separate manufacturing area for penicillins/cephalosporins or highly sensitizing substances?	☐ ☐ ☐		3.6
6.12	Only for processing of pharmaceuticals?	☐ ☐ ☐		3.6
6.13	Logical flow of materials?	☐ ☐ ☐		3.7
6.14	Walls, floors, and ceilings: smooth surface and free of cracks?	☐ ☐ ☐		3.8
6.15	Easy cleaning possible?	☐ ☐ ☐		3.10
6.16	Adequate drains with traps and grilles?	☐ ☐ ☐		3.11
6.17	Appropriate air-handling system with filtered air where open products are exposed to the environment?	☐ ☐ ☐		3.12
	Air pressure gradient from working bay → corridor:			
	Classification according to EC guide?			
6.18	Appropriate lighting?	☐ ☐ ☐		3.16
6.19	Separate rest rooms?	☐ ☐ ☐		3.30
6.20	Changing rooms designed to avoid contamination?	☐ ☐ ☐		3.31
6.21	Toilets segregated from manufacturing areas?	☐ ☐ ☐		3.31

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
	Equipment			
6.22	Suitable for the intended use?	☐ ☐ ☐		3.34
6.23	Well maintained?	☐ ☐ ☐		3.34
6.24	Tanks, containers, pipework, and pumps designed for easy cleaning and sanitation (dead legs!)?	☐ ☐ ☐		Suppl. 2
6.25	Written and validated cleaning procedures?	☐ ☐ ☐		3.36
6.26	Maintenance without contamination risk (separate area)?	☐ ☐ ☐		3.35
6.27	Equipment in contact with product: suitable materials quality?	☐ ☐ ☐		3.39
6.28	Machinery equipped with measuring and control devices?	☐ ☐ ☐		3.40
6.29	Calibration at fixed intervals according to written procedures?	☐ ☐ ☐		3.41
6.30	Calibration records available?	☐ ☐ ☐		3.41
6.31	Contents and flow direction marked on pipes?	☐ ☐ ☐		3.42
6.32	Pipes for distilled and demineralized water regularly monitored and sanitized?	☐ ☐ ☐		3.43
6.33	Not functioning equipment in the production area (if yes: clearly marked)?	Y N ☐ ☐ ☐		3.44
6.34	Status of cleanliness indicated?	☐ ☐ ☐		5.13
6.35	Previous product indicated?	☐ ☐ ☐		5.13
	Operations			
6.36	Are written and validated procedures for all manufacturing steps available?	☐ ☐ ☐		5.2
6.37	Are all manufacturing steps recorded with actual parameters?	☐ ☐ ☐		5.2
6.38	Check of each single container of the starting materials (contents, weight, and identity)?	☐ ☐ ☐		5.3
6.39	Limits for yields?	☐ ☐ ☐		5.8
6.40	Only one batch of one product processed?	☐ ☐ ☐		5.9
6.41	Protection against microbial contamination?	☐ ☐ ☐		5.10
	Correct labeling of containers, materials, equipment, and rooms with			5.12
6.42	• Product name and batch no.?	☐ ☐ ☐		5.12
6.43	• Quarantine status?	☐ ☐ ☐		5.12
6.44	Deviations from standard procedures recorded and signed by the supervisor?	☐ ☐ ☐		5.14
6.45	Special procedures for the production of antibiotics, hormones, etc.?	☐ ☐ ☐		5.19
6.46	• Campaign production?	☐ ☐ ☐		5.19
6.47	• Special monitoring?	☐ ☐ ☐		5.19
6.48	• Validated decontamination procedure?	☐ ☐ ☐		5.19
6.49	Double check on weight?	☐ ☐ ☐		5.34
6.50	Line clearance before start of production?	☐ ☐ ☐		5.35
6.51	Investigation of deviations in yields?	☐ ☐ ☐		5.39
6.52	Specification of maximum storage time and storage conditions if products are not immediately filled or packaged?	☐ ☐ ☐		Suppl. 9
6.53	Validated procedures for reworking of rejected batches?	☐ ☐ ☐		5.62
6.54	Detailed procedures for the addition of previous batches?	☐ ☐ ☐		5.63
6.55	Special release procedure (QA) for those batches?	☐ ☐ ☐		5.64

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
6.56	Use of protective clothing (hair cover, shoes, masks, and gloves)?	☐ ☐ ☐		2.16
6.57	Clothing regulation for visitors?	☐ ☐ ☐		2.11
	Water			
6.58	Loop system for purified water?	☐ ☐ ☐		Suppl. 4
6.59	Antimicrobial treatment of purified water?	☐ ☐ ☐		Suppl. 4
6.60	Loop system for water for injection?	☐ ☐ ☐		Suppl. 4
	Storage temperature of water for injection:			Suppl. 4
6.61	Loop system constructed to avoid dead legs?	☐ ☐ ☐		Suppl. 4
6.62	Regular microbiological monitoring?	☐ ☐ ☐		Suppl. 4
6.63	Regular endotoxin control?	☐ ☐ ☐		Suppl. 4
	Special Requirements for Sterile and Aseptic Products			Suppl.
	Rooms and Equipment			
6.64	Access of staff and materials to clean areas <i>only</i> through air locks?	☐ ☐ ☐		1
6.66	Rooms classified according to EC Guide?	☐ ☐ ☐		3
	Classification for products to be sterilized:			
6.67	• Solution preparation (EC: class C, with special precautions class D):	Class:		5
6.68	• Filling (EC: under LF in class C):	Class:		5
	Classification for aseptic products:			
6.69	• Handling of starting materials that can be sterile filtered (EC: class C):	Class:		6
6.70	• Handling of starting materials that cannot be sterile filtered (EC: class A in class B):	Class:		6
6.71	• Handling and filling of bulk (EC: class A in Class B):	Class:		6
6.72	All rooms easy to clean and disinfect?	☐ ☐ ☐		17
6.73	Doors, windows, frames, lighting, etc. without edges?	☐ ☐ ☐		18
6.74	Suspended ceilings (if yes: sealed?)?	☐ ☐ ☐		19
6.75	Traps constructed to avoid microbiological contamination?	☐ ☐ ☐		21
6.76	Appropriately constructed changing rooms?	☐ ☐ ☐		22
6.77	Measures against opening of both doors of air locks?	☐ ☐ ☐		23
6.78	Overpressure gradient from cleanest areas to others?	☐ ☐ ☐		24
6.79	AHU validated and regularly revalidated?	☐ ☐ ☐		25
6.80	@@@Control instruments for pressure gradient?	☐ ☐ ☐		26
6.81	Warning system for errors in air supply?	☐ ☐ ☐		26
6.82	Recording of pressure gradients?	☐ ☐ ☐		26
6.83	Do conveyor belts leave sterile areas?	☐ ☐ ☐		28
6.84	Maintenance works outside clean areas possible?	☐ ☐ ☐		28
6.85	Cleaning and disinfection procedure after maintenance works?	☐ ☐ ☐		29
6.86	Regular revalidation of all equipment and systems?	☐ ☐ ☐		30
6.87	Water prepared, circulated, and stored to exclude microbiological contamination?	☐ ☐ ☐		31
6.88	Cleaning and disinfection of rooms according to validated SOPs?	☐ ☐ ☐		32
	• Disinfection methods?			
6.89	Microbiological monitoring of cleaning and disinfection agents?	☐ ☐ ☐		33

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
6.90	Microbiological monitoring program of production areas?	☐ ☐ ☐		35
6.91	Results recorded and considered for the release?	☐ ☐ ☐		35
	Personnel and Hygiene			
6.92	Minimal number of personnel in clean areas?	☐ ☐ ☐		7
6.93	Special and regular training?	☐ ☐ ☐		8
6.94	Regular medical examinations?	☐ ☐ ☐		10
6.95	Appropriate clean room clothes (material and design)?	☐ ☐ ☐		12
6.96	Protective clothes worn correctly?	☐ ☐ ☐		12
6.97	Prohibition of cosmetics, jewelry, and watches?	☐ ☐ ☐		13
6.98	New clean room clothes for each working cycle?	☐ ☐ ☐		15
6.99	Appropriate washing and sterilization of clothes?	☐ ☐ ☐		16
	Operations			
6.100	Validation (media filling) at regular intervals? Monitoring of water preparation system, frequency:	☐ ☐ ☐		38
6.101	• Microbiological:			40
6.102	• Chemical:			40
6.103	• Particles:			40
6.104	• Endotoxins:			40
6.105	Microbiological monitoring of starting materials?	☐ ☐ ☐		42
6.106	Maximum storage times defined for sterilized equipment?	☐ ☐ ☐		45
6.107	Maximum storage time defined between solution preparation and filtration?	☐ ☐ ☐		46
6.108	Material transfer to clean areas through double door autoclaves?	☐ ☐ ☐		48
	Sterilization Processes			
6.109	All processes validated?	☐ ☐ ☐		50
6.110	Sterilized and nonsterilized materials clearly separated?	☐ ☐ ☐		54
	Trays and boxes clearly labeled with			
6.111	• Product name and code	☐ ☐ ☐		54
6.112	• Batch no.	☐ ☐ ☐		54
6.113	• Status: sterilized or nonsterilized	☐ ☐ ☐		54
	Sterilizers			
6.114	Recording of temperature, pressure, and time?	☐ ☐ ☐		55
6.115	Coldest point determined?	☐ ☐ ☐		55
6.116	Independent counter check probe?	☐ ☐ ☐		55
6.117	Heat-up time for each product determined?	☐ ☐ ☐		56
6.118	Sterile cooling media?	☐ ☐ ☐		57
6.119	Tightness tests for vacuum autoclaves?	☐ ☐ ☐		58
6.120	Clean steam for steam autoclaves?	☐ ☐ ☐		58
6.121	Circulated air with overpressure?	☐ ☐ ☐		61
6.122	Recirculated air: sterile filtered?	☐ ☐ ☐		61
6.123	Ethylene oxide autoclaves: humidity, temperature, and time recorded?	☐ ☐ ☐		69
6.124	Ethylene oxide autoclaves: use of bioindicators?	☐ ☐ ☐		70
	Filtration			
6.125	Double filtration?	☐ ☐ ☐		75
6.126	Integrity testing of filters immediately after use?	☐ ☐ ☐		77
6.127	Are results a part of the batch protocol?	☐ ☐ ☐		77

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
6.128	Optical control of each single container of ampoules, vials, and infusions?	☐ ☐ ☐		82
	IPC			
6.129	Written IPC procedures and SOPs?	☐ ☐ ☐		
	Particle testing of			
6.130	• Rooms?	☐ ☐ ☐		
6.131	• Primary packaging materials?	☐ ☐ ☐		
6.132	• System of warning and action limits?	☐ ☐ ☐		
	Microbiological monitoring of			
6.133	• Rooms?			
6.134	• Personnel?			
6.135	• Equipment?			
6.136	Residual O ₂ of ampoules, infusions, and syrups?	☐ ☐ ☐		
6.137	Endotoxin testing of water and packaging materials?	☐ ☐ ☐		
6.138	Calibration of equipment?	☐ ☐ ☐		
6.139	Regular revalidation of equipment?	☐ ☐ ☐		
7	PACKAGING			
	Operations carried out:			
	• Blistering	☐		
	• Foil packaging	☐		
	• Filling into tablet glasses	☐		
	• Effervescent packaging	☐		
	• Powder filling	☐		
	• Syrup/drops filling	☐		
	• Ointment filling	☐		
	Rooms			
7.1	Suitable for the intended use?	☐ ☐ ☐		3
7.2	• Adequate size?	☐ ☐ ☐		3
7.3	• Clean?	☐ ☐ ☐		3
7.4	Located and designed to exclude external contamination?	☐ ☐ ☐		3.1
7.5	Appropriate level of maintenance?	☐ ☐ ☐		3.2
7.6	Maintenance works possible without contamination risk?	☐ ☐ ☐		3.2
7.7	Appropriate lighting and air-conditioning?	☐ ☐ ☐		3.3
7.8	Recording of temperature and humidity?	☐ ☐ ☐		
7.9	Protection against the entry of insects or other animals?	☐ ☐ ☐		3.4
7.10	Controlled access for authorized personnel only?	☐ ☐ ☐		3.5
7.11	Adequate separation of the packaging lines?	☐ ☐ ☐		3.15
	Operations			
7.12	Only <i>one</i> product per line?	☐ ☐ ☐		5.44
7.13	Check list for clearance before processing a new product/new batch?	☐ ☐ ☐		5.45
7.14	Adequate labeling of the lines (product name and code)?	☐ ☐ ☐		5.46
7.15	Check of all materials delivered to the line (quantity, identity, conformity with order)?	☐ ☐ ☐		5.47
7.16	Cleaning of primary packaging materials?	☐ ☐ ☐		5.48
7.17	Immediate labeling after filling?	☐ ☐ ☐		5.49
7.18	Careful check of all printing processes (code and expiry date)?	☐ ☐ ☐		5.50
7.19	Special safety measures for off-line printing?	☐ ☐ ☐		5.51

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
7.20	Regular checks of all control devices (code reader, counter, etc.)?	☐ ☐ ☐		5.52
7.21	Printings clear and durable?	☐ ☐ ☐		5.53
7.22	Balancing of printed packaging materials and bulk?	☐ ☐ ☐		5.56
7.23	Destruction of excessive coded packaging material after completion of an order?	☐ ☐ ☐		5.57
7.24	Are the finished products kept in quarantine until final release?	☐ ☐ ☐		5.58
7.25	Appropriate storage after release?	☐ ☐ ☐		5.60
	IPC			
7.26	Checks on identity of bulk and packaging materials?	☐ ☐ ☐		5.47
	Regular line checks on			
7.27	• Aspect of the packages?	☐ ☐ ☐		5.54a
7.28	• Completeness?	☐ ☐ ☐		5.54b
7.29	• Conformity of quantity and quality of materials with packaging order?	☐ ☐ ☐		5.54c
7.30	• Correct imprint?	☐ ☐ ☐		5.54d
7.31	• Correct function of control devices?	☐ ☐ ☐		5.54d
	Are the following IPC checks performed?			
7.32	• Leaking	☐ ☐ ☐		
7.33	• Release torque of screw caps	☐ ☐ ☐		
7.34	• pH, density, drop weight, viscosity, and sedimentation	☐ ☐ ☐		
8	DOCUMENTATION			
	Specifications			
8.1	Specifications for raw/packaging materials available?	☐ ☐ ☐		4.10
	Do they include			
8.2	• internal name and code?	☐ ☐ ☐		4.11
8.3	• Name of supplier and/or manufacturer?	☐ ☐ ☐		4.11
8.4	• Reference sample (printed packaging material)?	☐ ☐ ☐		4.11
8.5	• Sampling procedure?	☐ ☐ ☐		4.11
8.6	• Qualitative/quantitative specifications with limits?	☐ ☐ ☐		4.11
8.7	• Storage conditions?	☐ ☐ ☐		4.11
8.8	• Maximum storage period?	☐ ☐ ☐		4.11
	Goods Receiving			
8.9	Written procedures for the reception of deliveries?	☐ ☐ ☐		4.19
	Do the records of receipt include			
8.10	• Product name on labels and delivery note?	☐ ☐ ☐		4.20
8.11	• Internal name and code?	☐ ☐ ☐		4.20
8.12	• Receiving date?	☐ ☐ ☐		4.20
8.13	• Name of supplier and/or manufacturer?	☐ ☐ ☐		4.20
8.14	• Batch number of supplier?	☐ ☐ ☐		4.20
8.15	• Total quantity and number of containers?	☐ ☐ ☐		4.20
8.16	• Allocated internal batch number?	☐ ☐ ☐		4.20
8.17	SOPs for labeling, quarantine, and storage conditions of all incoming goods available?	☐ ☐ ☐		4.21
	SOPs include			
8.18	• authorized sampling personnel?	☐ ☐ ☐		4.22
8.19	• methods, equipment, and quantities?	☐ ☐ ☐		4.22
8.20	• safety measures?	☐ ☐ ☐		4.22

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
	Master Formulae			
8.21	Are master formulae for each product and batch size available?	☐ ☐ ☐		4.3
8.22	Is the master formula approved and signed by the authorized persons?	☐ ☐ ☐		4.3
	The master formula includes			
8.23	• Product name and code?	☐ ☐ ☐		4.14a
8.24	• Description of galenical form, dosage, and batch size?	☐ ☐ ☐		4.14b
8.25	• All active ingredients with name, code, and weight?	☐ ☐ ☐		4.14c
8.26	• All excipients used during manufacture with name, code, and weight?	☐ ☐ ☐		4.14c
8.27	• Yields with limits?	☐ ☐ ☐		4.14d
	Does the working procedure include			
8.28	• The production line?	☐ ☐ ☐		4.15a
8.29	• Equipment to be used?	☐ ☐ ☐		4.15a
8.30	• Reference to methods for cleaning, assembling, and calibration of machines?	☐ ☐ ☐		4.15b
8.31	• Detailed stepwise manufacturing prescription?	☐ ☐ ☐		4.15c
8.32	• IPCs to be performed with limits?	☐ ☐ ☐		4.15d
8.33	• Precautions to be followed?	☐ ☐ ☐		4.15e
8.34	Are batch records kept for each batch processed?	☐ ☐ ☐		4.17
	Do batch records include			
8.35	• Protocol of line clearance?	☐ ☐ ☐		4.17
8.36	• Name of the product and batch no.?	☐ ☐ ☐		4.17a
8.37	• Date and time of start and end of production?	☐ ☐ ☐		4.17b
8.38	• Name and initials of responsible workers for each step?	☐ ☐ ☐		4.17c, d
8.39	• Batch and analytical no. and actual weight of all starting materials?	☐ ☐ ☐		4.17e
8.40	• Equipment used?	☐ ☐ ☐		4.17f
8.41	• Results of IPCs with initials of person who carries them out?	☐ ☐ ☐		4.17g
8.42	• Yields of the relevant manufacturing steps?	☐ ☐ ☐		4.17h
8.43	• Detailed notes on problems and process deviations?	☐ ☐ ☐		4.17i
8.44	Records on reprocessing of batches?	☐ ☐ ☐		
	Packaging Instructions			
8.45	Packaging instructions for each product, package size, and presentation?	☐ ☐ ☐		4.16
	Do they include			
8.46	• Product name?	☐ ☐ ☐		4.16a
8.47	• Description of galenical form and strength?	☐ ☐ ☐		4.16b
8.48	• Package size?	☐ ☐ ☐		4.17c
8.49	• List of all packaging materials with code for a standard batch size?	☐ ☐ ☐		4.17d
8.50	• Samples of printed packaging materials?	☐ ☐ ☐		4.17e
8.51	• Special precautions?	☐ ☐ ☐		4.17f
8.52	• Description of the process and equipment?	☐ ☐ ☐		4.17g
8.53	• IPCs to be performed with sampling instruction?	☐ ☐ ☐		4.17h

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
8.54	Are packaging batch records kept for each batch or part batch?	☐ ☐ ☐		4.18
	Do the packaging batch records include			
8.55	• Protocol of line clearance?	☐ ☐ ☐		4.18
8.56	• Name of the product?	☐ ☐ ☐		4.18a
8.57	• Date and time when operations have been performed?	☐ ☐ ☐		4.18b
8.58	• Name of the responsible person?	☐ ☐ ☐		4.18c
8.59	• Initials of workers carrying out operations?	☐ ☐ ☐		4.18d
8.60	• Notes on identity checks and conformity with packaging instructions?	☐ ☐ ☐		4.18e
8.61	• Results of IPCs?	☐ ☐ ☐		4.18e
8.62	• Details of operations and equipment used?	☐ ☐ ☐		4.18f
8.63	• Samples of printed packaging materials with codes (MFD, EXP, batch no., etc.)?	☐ ☐ ☐		4.18g
8.64	• Record of problems and process deviations?	☐ ☐ ☐		4.18h
8.65	• Quantities of packaging materials delivered, used, destroyed, or returned?	☐ ☐ ☐		4.18i
8.66	• No. of packs consumed?	☐ ☐ ☐		4.18j
	Testing			
	Do the written testing procedures include			
8.67	• Test methods?	☐ ☐ ☐		4.23
8.68	• Equipment for testing?	☐ ☐ ☐		4.23
8.69	Tests documented?	☐ ☐ ☐		4.23
	Others			
8.70	Procedures for release and rejection of materials and finished products?	☐ ☐ ☐		4.24
8.71	Final release by authorized person?	☐ ☐ ☐		4.24
8.72	Records about distribution of each batch?	☐ ☐ ☐		4.25
	Procedures and protocols about			
8.73	• Validation?	☐ ☐ ☐		4.26
8.74	• Setup and calibration of equipment?	☐ ☐ ☐		4.26
8.75	• Maintenance, cleaning, and disinfection?	☐ ☐ ☐		4.26
8.76	• Training records?	☐ ☐ ☐		4.26
8.77	• Environmental monitoring of production areas?	☐ ☐ ☐		4.26
8.78	• Pest control?	☐ ☐ ☐		4.26
8.79	• Complaints?	☐ ☐ ☐		4.26
8.80	• Recalls?	☐ ☐ ☐		4.26
8.81	• Returned goods?	☐ ☐ ☐		4.26
8.82	Instructions for use of manufacturing and testing equipment?	☐ ☐ ☐		4.27
	Log books for major equipment including date and name of persons who performed			
8.83	• Validation?	☐ ☐ ☐		4.28
8.84	• Calibration?	☐ ☐ ☐		4.28
8.85	• Maintenance, cleaning, and repair works?	☐ ☐ ☐		4.28
8.86	Chronological records of use of major equipment and manufacturing areas?	☐ ☐ ☐		4.29
9	QUALITY CONTROL			6
	General Requirements			
9.1	Independent QC department available?	☐ ☐ ☐		6.1
9.2	Head of QC well qualified and sufficiently experienced?	☐ ☐ ☐		6.1
9.3	Qualified personnel available?	☐ ☐ ☐		2.1
9.4	Organization charts available?	☐ ☐ ☐		2.2
9.5	Job descriptions available?	☐ ☐ ☐		2.2

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
9.6	Responsibilities clearly defined?	☐ ☐ ☐		2.2
9.7	Continuous training programs for QC staff?	☐ ☐ ☐		2.2
9.8	Initial job training for all employees?	☐ ☐ ☐		2.9
9.9	Training records?	☐ ☐ ☐		
9.10	QC personnel admitted to the production rooms for sampling, etc.?	☐ ☐ ☐		
	QC Laboratories			
9.11	Suitable for the intended use?	☐ ☐ ☐		3.26
9.12	Laboratories of adequate size?	☐ ☐ ☐		3.26
9.13	Appropriate level of maintenance?	☐ ☐ ☐		3.1
9.14	Adequate separation from the production area?	☐ ☐ ☐		3.26
9.15	Controlled access of authorized personnel only?	☐ ☐ ☐		3.5
9.16	Special laboratory to handle biological samples available?	☐ ☐ ☐		3.29
9.17	Special laboratory to handle radioactive material available?	☐ ☐ ☐		3.29
9.18	Separate recreation rooms for the personnel available?	☐ ☐ ☐		3.30
9.19	Animal laboratories present?	☐ ☐ ☐		3.33
9.20	Animal laboratories separated from other areas?	☐ ☐ ☐		3.33
9.21	Animal laboratories equipped with a separate air-handling system?	☐ ☐ ☐		3.33
	QC Documentation			
9.22	Do procedures exist for			
	• Self inspection?	☐ ☐ ☐		
	• Release or rejection of products or raw material?	☐ ☐ ☐		
	• Product complaints?	☐ ☐ ☐		
	• Product recalls?	☐ ☐ ☐		
	• Local stability testing?	☐ ☐ ☐		
	• Storage of reference samples?	☐ ☐ ☐		
	• Validation of analytical procedures?	☐ ☐ ☐		
9.23	Specifications available for	☐ ☐ ☐		6.7
	• Raw materials?	☐ ☐ ☐		
	• Bulk products?	☐ ☐ ☐		
	• Packaging materials?	☐ ☐ ☐		
9.24	Analytical procedures for every product?	☐ ☐ ☐		
9.25	Are Basel methods followed?	☐ ☐ ☐		
9.26	Validation of locally developed test methods?	☐ ☐ ☐		
9.27	Sampling procedures available for			6.7
	• Raw materials?	☐ ☐ ☐		
	• Bulk products?	☐ ☐ ☐		
	• Packaging materials?	☐ ☐ ☐		
9.28	Suppliers' certificates available?	☐ ☐ ☐		6.7
9.29	Calibration program for analytical instruments installed?	☐ ☐ ☐		6.7
9.30	Maintenance program for analytical instruments?	☐ ☐ ☐		6.7
9.31	Retention system for QC records?	☐ ☐ ☐		6.8
9.32	Batch documents stored for expiry + 1 year or 5 years (EEC 75/319, article 22) minimum?	☐ ☐ ☐		6.8
9.33	Are original data such as notebooks stored in addition to the batch documents?	☐ ☐ ☐		6.10
9.34	Can the original data be traced back easily and quickly from the analytical report number or batch number?	☐ ☐ ☐		6.10

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
9.35	Are trend analyses being performed for			6.9
	• Analytical results?	☐ ☐ ☐		
	• Yields?	☐ ☐ ☐		
	• Environmental monitoring data?	☐ ☐ ☐		
	Sampling			
9.36	Written procedures for taking samples?	☐ ☐ ☐		6.11
9.37	Do procedures define			
	• Method of sampling?	☐ ☐ ☐		
	• Necessary equipment?	☐ ☐ ☐		
	• Quantity of the sample?	☐ ☐ ☐		
	• Subdivision of the sample?	☐ ☐ ☐		
	• Sample container?	☐ ☐ ☐		
	• Labeling of samples?	☐ ☐ ☐		
	• Storage conditions?	☐ ☐ ☐		
	• Cleaning and storage of sampling equipment?	☐ ☐ ☐		
	• Identification of containers sampled?	☐ ☐ ☐		
9.38	Are samples representative of the batch they are taken from (sampling plan)?	☐ ☐ ☐		6.12
9.39	Are critical steps being surveilled and validated by additional sampling (e.g., at the beginning or end of a process)?	☐ ☐ ☐		6.12
9.40	Sample containers labeled with			6.13
	• Name of the content?	☐ ☐ ☐		
	• Batch number?	☐ ☐ ☐		
	• Date of sampling?	☐ ☐ ☐		
	• Batch containers sampled?	☐ ☐ ☐		
9.41	Are samples taken by QC/QA?	☐ ☐ ☐		
9.42	Reference samples retained for validity +1 year?	☐ ☐ ☐		6.14
9.43	Storage of reference samples under the recommended storage conditions?	☐ ☐ ☐		6.14
9.44	Finished products stored in the final packaging?	☐ ☐ ☐		6.14
9.45	Quantity of the reference sample makes one (better two) complete reanalysis possible?	☐ ☐ ☐		6.14
9.46	Sample room secure?	Yes No		6.14
9.47	Sample room neatly organized and not overcrowded?	Yes No		6.14
	Testing			
9.48	Are the applied analytical methods validated?	☐ ☐ ☐		6.15
9.49	Analytical methods in compliance with the registration?	☐ ☐ ☐		6.16
9.50	Are all results recorded and checked for correctness?	☐ ☐ ☐		6.16
9.51	Are all calculations checked?	☐ ☐ ☐		6.16
9.52	Do the testing protocols contain			6.17
	• Name and galenical form of material?	☐ ☐ ☐		
	• Batch number?	☐ ☐ ☐		
	• Supplier if applicable?	☐ ☐ ☐		
	• Specification reference?	☐ ☐ ☐		
	• Method reference?	☐ ☐ ☐		
	• Analytical results?	☐ ☐ ☐		
	• Reference to analytical certificates?	☐ ☐ ☐		
	• Date of the analysis?	☐ ☐ ☐		
	• Name of the analyst?	☐ ☐ ☐		
	• Name of the person verifying the data?	☐ ☐ ☐		
	• Statement of release or rejection?	☐ ☐ ☐		
	• Date and signature of the release person?	☐ ☐ ☐		

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
9.53	Are all IPC methods in production approved by QC?	☐ ☐ ☐		6.18
9.54	Are written methods available for the preparation of reagents and volumetric solutions?	☐ ☐ ☐		6.19
9.55	Is a record maintained of standardization of volumetric solutions?	☐ ☐ ☐		6.2
9.56	Are reagents for prolonged use labeled with			6.20
	• Date of the preparation?	☐ ☐ ☐		
	• Signature of the preparator?	☐ ☐ ☐		
9.57	Are unstable reagents labeled with			6.20
	• Expiry date?	☐ ☐ ☐		
	• Storage conditions?	☐ ☐ ☐		
9.58	Are volumetric solutions labeled with			6.20
	• The last date of standardization?	☐ ☐ ☐		
	• Last current factor?	☐ ☐ ☐		
9.59	Are reference standards labeled with			6.21
	• Name and potency?	☐ ☐ ☐		
	• Supplier's reference?	☐ ☐ ☐		
	• Date of receipt?	☐ ☐ ☐		
	• Date of expiry?	☐ ☐ ☐		
9.60	Are reference standards stored properly and under the control of a designated person?	☐ ☐ ☐		
9.61	Are animals used for testing of components, materials, or products			
	• Quarantined before use?	☐ ☐ ☐		
	• Checked for suitability?	☐ ☐ ☐		
	• Are records maintained showing the history of their use?	☐ ☐ ☐		
10	COMPLAINTS AND PRODUCT RECALLS			8
	Complaints			8.1
10.1	Does a written complaint procedure exist?	☐ ☐ ☐		8.2
10.2	Are product complaints carefully reviewed?	☐ ☐ ☐		8.1
10.3	Is a person designated to handle complaints and to decide on measures to be taken?	☐ ☐ ☐		8.1
10.4	Is each complaint concerning a product recorded with all original details?	☐ ☐ ☐		8.3
10.5	Are product complaints thoroughly investigated?	☐ ☐ ☐		8.3
10.6	Is a responsible QC person involved in the study?	☐ ☐ ☐		8.3
10.7	Is it considered that other batches might be concerned as well?	☐ ☐ ☐		8.4
10.8	Are decisions and measures as a result recorded?	☐ ☐ ☐		8.5
10.9	Is this record added to the corresponding batch documents?	☐ ☐ ☐		8.5
10.10	Are the complaint records regularly revised with respect to specific or recurring problems?	☐ ☐ ☐		8.6
10.11	Are the authorities informed of serious quality problems with a product?	☐ ☐ ☐		8.7
	Recalls			8.8
10.12	Does a written recall procedure exist?	☐ ☐ ☐		8.9
10.13	Is a person nominated responsible for the execution and coordination of a recall?	☐ ☐ ☐		8.8
10.14	Is the responsible person independent of the marketing and sales organization?	☐ ☐ ☐		8.8

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
10.15	Are the competent authorities informed of an imminent recall?	☐ ☐ ☐		8.11
10.16	Does the person responsible for a recall have access to the distribution records?	☐ ☐ ☐		8.12
10.17	Do the distribution records contain sufficient information on customers with • Addresses? • Phone numbers inside or outside working hours? • Batches and amounts delivered? • Medical samples?	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐		8.12
10.18	Are recalled products stored separately in a secure area?	☐ ☐ ☐		8.13
10.19	Is a final record made, including a reconciliation between the delivered and recovered quantities?	☐ ☐ ☐		8.14
10.20	Is the effectiveness of the arrangements for recalls checked critically from time to time?	☐ ☐ ☐		8.15
11	SELF-INSPECTION			9
11.1	Does a self-inspection procedure exist that defines frequency and program?	☐ ☐ ☐		9.1
11.2	Are self-inspections carried out to check compliance with GMP rules?	☐ ☐ ☐		9.1
11.3	Are self-inspections conducted in an independent and detailed way?	☐ ☐ ☐		9.2
	by designated competent persons from the company or external experts?	☐ ☐ ☐		
11.4	Are self-inspections recorded?	☐ ☐ ☐		9.3
11.5	Do reports contain • The observations made during a self-inspection? • Proposals for corrective measures?	☐ ☐ ☐ ☐ ☐ ☐		9.3
11.6	Are actions subsequently taken recorded?	☐ ☐ ☐		9.3
12	CONTRACT MANUFACTURE AND ANALYSIS			7
12.1	Is a written contract between contract giver and contract acceptor available?	☐ ☐ ☐		7.1
12.2	Are responsibilities and duties clearly defined?	☐ ☐ ☐		7
12.3	Are all arrangements in accordance with the marketing authorization of the product concerned?	☐ ☐ ☐		7.2
	The Contract Giver			
12.4	Competence of the acceptor to carry out the work successfully and according to GMP assessed?	☐ ☐ ☐		7.3
12.5	Acceptor provided with all the information necessary to carry out the contract work?	☐ ☐ ☐		7.4
12.6	Acceptor informed of safety aspects?	☐ ☐ ☐		7.4
12.7	Conformance of products supplied by the acceptor ensured?	☐ ☐ ☐		7.5
12.8	Product released by a qualified person on the acceptor's side?	☐ ☐ ☐		7.5
	The Contract Acceptor			
12.9	Does the acceptor have • Adequate premises and equipment? • Knowledge and experience? • Competent personnel? • A manufacturing authorization?	☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐		7.6

(Continued)

		Compliance 1 2 3 ^a	Remarks	EU-Guide
12.10	Does the acceptor ensure that all products or materials delivered to him or her are suitable?	☐ ☐ ☐		7.7
12.11	There must be no work passed to a third party without the permission of the giver.	☐ ☐ ☐		7.8
12.12	If a third party is involved, it must have the necessary manufacturing and analytical information.	☐ ☐ ☐		7.8
The Contract				
12.13	Does the written contract specify the responsibilities?	☐ ☐ ☐		7.10
12.14	Have technical aspects been drawn up by competent persons?	☐ ☐ ☐		7.10
12.15	Release of material and check for compliance with the marketing authorization defined?	☐ ☐ ☐		7.11
12.16	Is it defined who is responsible for			7.12
	• Purchasing of materials?	☐ ☐ ☐		
	• IPC controls?	☐ ☐ ☐		
	• Testing and release of materials?	☐ ☐ ☐		
	• Manufacturing and quality control?	☐ ☐ ☐		
	• Sampling?	☐ ☐ ☐		
	• Storage of batch documentation?	☐ ☐ ☐		
12.17	Are manufacturing, analytical, and distribution records available to the contract giver?	☐ ☐ ☐		7.13
12.18	Does the contract permit the giver to visit the facilities of the acceptor?	☐ ☐ ☐		7.14
12.19	In the case of contract analysis: Does the contract acceptor understand that he or she is subject to inspection by the competent authorities?	☐ ☐ ☐		7.15
13	AUDIT OF SUPPLIERS			2.7
13.1	Supplier audits performed for	☐ ☐ ☐		
	• Excipients?	☐ ☐ ☐		
	• Active substances?	☐ ☐ ☐		
	• Packaging material?	☐ ☐ ☐		

^a 1. Fulfilled or available; 2. partially fulfilled; 3. not fulfilled or not available.

GLOSSARY

Acceptance Criteria: Numerical limits, ranges, or other suitable measures for acceptance of test results.

Active Pharmaceutical Ingredient (API) (or Drug Substance): Any substance or mixture of substances intended to be used in the manufacture of a drug (medicinal) product and that, when used in the production of a drug, becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body.

Air Lock: An enclosed space with two or more doors, which is interposed between two or more rooms, for example, of differing classes of cleanliness, for the purpose of controlling the airflow between those

rooms when they need to be entered. An air lock is designed for use either by people or for goods and/or equipment.

API Starting Material: A raw material, intermediate, or API that is used in the production of an API and that is incorporated as a significant structural fragment into the structure of the API. An API Starting Material can be an article of commerce, a material purchased from one or more suppliers under contract or commercial agreement, or produced in house. API Starting Materials are normally of defined chemical properties and structure.

Authorized Person: The person recognized by the national regulatory authority as having the responsibility for ensuring that each batch of finished product has been manufactured, tested, and approved for release in compliance with the laws and regulations in force in that country.

- Batch (or Lot):** A specific quantity of material produced in a process or series of processes so that it is expected to be homogeneous within specified limits. In the case of continuous production, a batch may correspond to a defined fraction of the production. The batch size can be defined either by a fixed quantity or by the amount produced in a fixed time interval.
- Batch Number (or Lot Number):** A unique combination of numbers, letters, and/or symbols that identifies a batch (or lot) and from which the production and distribution history can be determined.
- Batch Records:** All documents associated with the manufacture of a batch of bulk product or finished product. They provide a history of each batch of product and of all circumstances pertinent to the quality of the final product.
- Bioburden:** The level and type (e.g., objectionable or not) of microorganisms that can be present in raw materials, API starting materials, intermediates, or APIs. Bioburden should not be considered contamination unless the levels have been exceeded or defined objectionable organisms have been detected.
- Bulk Product:** Any product that has completed all processing stages up to, but not including, final packaging.
- Calibration:** The demonstration that a particular instrument or device produces results within specified limits by comparison with those produced by a reference or traceable standard over an appropriate range of measurements. The set of operations that establish, under specified conditions, the relationship between values indicated by an instrument or system for measuring (especially weighing), recording, and controlling, or the values represented by a material measure, and the corresponding known values of a reference standard. Limits for acceptance of the results of measuring should be established.
- Clean Area:** An area with defined environmental control of particulate and microbial contamination, constructed and used in such a way as to reduce the introduction, generation, and retention of contaminants within the area.
- Computer System:** A group of hardware components and associated software designed and assembled to perform a specific function or group of functions. A process or operation integrated with a computer system.
- Consignment (or Delivery):** The quantity of a pharmaceutical(s) made by one manufacturer and supplied at one time in response to a particular request or order. A consignment may comprise one or more packages or containers and may include material belonging to more than one batch.
- Contamination:** The undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or on to a starting material or intermediate during production, sampling, packaging or repackaging, and storage or transport.
- Contract Manufacturer:** A manufacturer performing some aspect of manufacturing on behalf of the original manufacturer.
- Critical:** Describes a process step, process condition, test requirement, or other relevant parameter or item that must be controlled within predetermined criteria to ensure that the API meets its specification.
- Critical Operation:** An operation in the manufacturing process that may cause variation in the quality of the pharmaceutical product.
- Cross-Contamination:** Contamination of a material or product with another material or product. Contamination of a starting material, intermediate product, or finished product with another starting material or product during production.
- Deviation:** Departure from an approved instruction or established standard.
- Drug (Medicinal) Product:** The dosage form in the final immediate packaging intended for marketing. (See ICH Guidance Q1A.)
- Drug Substance:** See Active Pharmaceutical Ingredient.
- Expiry Date (or Expiration Date):** The date placed on the container/labels of an API designating the time during which the API is expected to remain within established shelf-life specifications if stored under defined conditions, and after which it should not be used.
- Finished Product:** A finished dosage form that has undergone all stages of manufacture, including packaging in its final container and labeling.
- Impurity:** Any component present in the intermediate or API that is not the desired entity.
- Impurity Profile:** A description of the identified and unidentified impurities present in an API.
- In-Process Control:** Checks performed during production in order to monitor and if necessary, to adjust the process to ensure that the product conforms to its specifications. The control of the environment or equipment may also be regarded as a part of in-process control.
- Intermediate:** A material produced during steps of the processing of an API that undergoes further molecular change or purification before it becomes an API. Intermediates may or may not be isolated. Partly processed product that must undergo further manufacturing steps before it becomes a bulk product.
- Large-Volume Parenterals:** Sterile solutions intended for parenteral application with a volume of 100 mL or more in one container of the finished dosage form.
- Lot:** See Batch.
- Lot Number:** See Batch Number.
- Manufacture:** All operations of receipt of materials, production, packaging, repackaging, labeling, relabeling, quality control, release, storage, and distribution of APIs and related controls.

- Manufacturer:** A company that carries out operations such as production, packaging, repackaging, labeling, and relabeling of pharmaceuticals.
- Marketing Authorization (Product License, Registration Certificate):** A legal document issued by the competent drug regulatory authority that establishes the detailed composition and formulation of the product and the pharmacopoeial or other recognized specifications of its ingredients and of the final product itself, and includes details of packaging, labeling, and shelf life.
- Master Formula:** A document or set of documents specifying the starting materials with their quantities and the packaging materials, together with a description of the procedures and precautions required to produce a specified quantity of a finished product as well as the processing instructions, including the in-process controls.
- Master Record:** A document or set of documents that serve as a basis for the batch documentation (blank batch record).
- Material:** A general term used to denote raw materials (starting materials, reagents, and solvents), process aids, intermediates, APIs, and packaging and labeling materials.
- Mother Liquor:** The residual liquid that remains after the crystallization or isolation processes. A mother liquor may contain unreacted materials, intermediates, levels of the API, and/or impurities. It may be used for further processing.
- Packaging:** All operations, including filling and labeling, that a bulk product has to undergo in order to become a finished product. Filling of a sterile product under aseptic conditions, or a product intended to be terminally sterilized, would not normally be regarded as part of packaging.
- Packaging Material:** Any material intended to protect an intermediate or API during storage and transport. Any material, including printed material, employed in the packaging of a pharmaceutical, but excluding any outer packaging used for transportation or shipment. Packaging materials are referred to as primary or secondary according to whether or not they are intended to be in direct contact with the product.
- Pharmaceutical Product:** Any material or product intended for human or veterinary use presented in its finished dosage form, or as a starting material for use in such a dosage form, that is subject to control by pharmaceutical legislation in the exporting state and/or the importing state.
- Procedure:** A documented description of the operations to be performed, the precautions to be taken, and measures to be applied directly or indirectly related to the manufacture of an intermediate or API.
- Process Aids:** Materials, excluding solvents, used as an aid in the manufacture of an intermediate or API that do not themselves participate in a chemical or biological reaction (e.g., filter aid, activated carbon, and so on).
- Process Control:** See In-Process Control.
- Production:** All operations involved in the preparation of a pharmaceutical product, from receipt of materials, through processing, packaging and repackaging, and labeling and relabeling, to completion of the finished product.
- Qualification:** Action of proving and documenting that equipment or ancillary systems are properly installed, work correctly, and actually lead to the expected results. Qualification is part of validation, but the individual qualification steps alone do not constitute process validation.
- Quality Assurance (QA):** The sum total of the organized arrangements made with the object of ensuring that all APIs are of the quality required for their intended use and that quality systems are maintained.
- Quality Control (QC):** Checking or testing that specifications are met.
- Quality Unit(s):** An organizational unit independent of production that fulfills both Quality Assurance and Quality Control responsibilities. This can be in the form of separate QA and QC units or a single individual or group, depending upon the size and structure of the organization.
- Quarantine:** The status of starting or packaging materials, intermediates, or bulk or finished products isolated physically or by other effective means while a decision is awaited on their release, rejection, or reprocessing.
- Raw Material:** A general term used to denote starting materials, reagents, and solvents intended for use in the production of intermediates or APIs.
- Reconciliation:** A comparison between the theoretical quantity and the actual quantity.
- Recovery:** The introduction of all or part of previous batches (or of redistilled solvents and similar products) of the required quality into another batch at a defined stage of manufacture. It includes the removal of impurities from waste to obtain a pure substance or the recovery of used materials for a separate use.
- Reference Standard, Primary:** A substance that has been shown by an extensive set of analytical tests to be authentic material that should be of high purity.
- Reference Standard, Secondary:** A substance of established quality and purity, as shown by comparison to a primary reference standard, used as a reference standard for routine laboratory analysis.
- Reprocessing:** Subjecting all or part of a batch or lot of an in-process drug, bulk process intermediate (final biological bulk intermediate), or bulk product of a single batch/lot to a previous step in the validated manufacturing process due to failure to meet predetermined specifications. Reprocessing procedures are foreseen as occasionally necessary for biological

drugs and in such cases, are validated and preapproved as part of the marketing authorization.

Retest Date: The date when a material should be reexamined to ensure that it is still suitable for use.

Reworking: Subjecting an in-process or bulk process intermediate (final biological bulk intermediate) or final product of a single batch to an alternate manufacturing process due to a failure to meet predetermined specifications. Reworking is an unexpected occurrence and is not preapproved as part of the marketing authorization.

Self-Contained Area: Premises that provide complete and total separation of all aspects of an operation, including personnel and equipment movement, with well-established procedures, controls, and monitoring. This includes physical barriers as well as separate air-handling systems but does not necessarily imply two distinct and separate buildings.

Signature (Signed): See definition for signed.

Signed (Signature): The record of the individual who performed a particular action or review. This record can be initials, a full handwritten signature, a personal seal, or an authenticated and secure electronic signature.

Solvent: An inorganic or organic liquid used as a vehicle for the preparation of solutions or suspensions in the manufacture of an intermediate or API.

Specification: A list of detailed requirements with which the products or materials used or obtained during manufacture have to conform. They serve as a basis for quality evaluation.

Standard Operating Procedure (SOP): An authorized written procedure giving instructions for performing

operations not necessarily specific to a given product or material (e.g., equipment operation, maintenance, and cleaning; validation; cleaning of premises and environmental control; sampling and inspection). Certain SOPs may be used to supplement product-specific master and batch production documentation.

Starting Material: Any substance of a defined quality used in the production of a pharmaceutical product, but excluding packaging materials.

Validation: A documented program that provides a high degree of assurance that a specific process, method, or system will consistently produce a result meeting predetermined acceptance criteria. Action of proving, in accordance with the principles of GMP, that any procedure, process, equipment, material, activity, or system actually leads to the expected results (see also Qualification).

Validation Protocol: A written plan stating how validation will be conducted and defining acceptance criteria. For example, the protocol for a manufacturing process identifies processing equipment, critical process parameters/operating ranges, product characteristics, sampling, test data to be collected, number of validation runs, and acceptable test results.

Yield, Expected: The quantity of material or the percentage of theoretical yield anticipated at any appropriate phase of production based on previous laboratory, pilot-scale, or manufacturing data.

Yield, Theoretical: The quantity that would be produced at any appropriate phase of production, based upon the quantity of material to be used, in the absence of any loss or error in actual production.

Appendix B: OTC Process and Ingredients

The Over-the-Counter (OTC) Drug Review was established to evaluate the safety and effectiveness of OTC drug products marketed in the United States before May 11, 1972. It is a three-phase public rulemaking process (each phase requiring a *Federal Register* publication) resulting in the establishment of standards (drug monographs) for an OTC therapeutic drug class.

The first phase was accomplished by advisory review panels. The panels were charged with reviewing the active ingredients in OTC drug products to determine whether these ingredients could be generally recognized as safe and effective for use in self-treatment. They were also charged with reviewing claims and recommending appropriate labeling, including therapeutic indications, dosage instructions, and warnings about side effects and preventing misuse.

The FDA published the panel's conclusions in the *Federal Register* in the form of an advanced notice of proposed rulemaking (ANPR). After publication of the ANPR, a period of time was allotted for interested parties to submit comments or data in response to the proposal.

According to the terms of the review, the panels classified ingredients into three categories as follows:

- Category I: generally recognized as safe and effective for the claimed therapeutic indication
- Category II: not generally recognized as safe and effective or unacceptable indications
- Category III: insufficient data available to permit final classification

The second phase of the OTC Drug Review is the FDA's review of active ingredients in each class of drugs, based on the panel's review of ingredients, on public comment, and on new data that may have become available. The FDA, in turn, publishes its conclusions in the *Federal Register* in the form of a tentative final monograph (TFM). After the publication of the TFM, a period of time is allotted for interested parties to submit comments or data in response to the FDA's proposal.

The publication of final regulations in the form of drug monographs is the third and last phase of the review process. The monographs establish conditions under which certain

OTC drug products are generally recognized as safe and effective. Products containing active ingredients or indications that are nonmonograph require an approved New Drug Application for marketing.

After publication, a final monograph may be amended, either on the Commissioner's own initiative or upon the petition of any interested person. OTC drug monographs are continually updated to add, change, or remove ingredients, labeling, or other pertinent information as needed.

The OTC drug category Web site contains Federal Register notices organized by therapeutic category subtopics. Each Web page also links to therapeutic category pages organized chronologically.

This rulemaking history site is intended as a research aid and is not an official Food and Drug Administration (FDA record). We have tried to make these histories accurate and complete. Should you find an error, however, please let us know so that we can correct it (Table 1).

OTC drugs can be brought to the market following the new drug application (NDA) process as described earlier or under an OTC monograph. Each OTC drug monograph is a kind of "recipe book" covering acceptable ingredients, doses, formulations, labeling, and in some cases, testing parameters. OTC drug monographs are continually updated to add additional ingredients and labeling as needed. Products conforming to a monograph may be marketed without FDA preapproval. The NDA and monograph processes can be used to introduce new ingredients into the OTC marketplace. For example, OTC drug products previously available only by prescription are first approved through the NDA process, and their "switch" to OTC status is approved via the NDA process. OTC ingredients marketed overseas can be introduced into the U.S. market via a monograph under a Time and Extent Application (TEA) as described in 21 CFR 330.14. For a more thorough discussion of how OTC drug products are regulated, visit FDA laws, regulations, and guidances that affect small business. Information is also provided on financial assistance and incentives that are available for drug development. Table 2 shows a comparison of the NDA and the OTC monograph process for approval (Table 3).

TABLE 1

Categories of OTC Products with Monographs (www.fda.gov/drugs/over-the-counter-otc-drugs/status-otc-rulemakings)

Acne	Alcohol	Allergy
Analgesic, External	Analgesic, Internal	Anorectal
Antacid	Anthelmintic	Antibiotic, First Aid
Anticaries	Anticholinergic	Antidiarrheal
Antiemetic	Antiflatulent	Antifungal
Antihistamine	Antimalarial	Antimicrobial
Antiperspirant	Antipyretic	Antirheumatic
Antitussive	Aphrodisiac	Astringent
Benign Prostatic Hypertrophy	Boil Treatment	Bronchodilator
Callus Remover	Camphorated Oil	Category 2/3 Active Ingredients
Cholecystokinetic	Cold and Cough	Colloidal Silver
Corn Remover	Dandruff	Daytime Sedative
Decongestant, Nasal	Dental Care	Deodorant, Internal
Diaper Rash	Digestive Aid	Drink Overindulgence
Exocrine Pancreatic Insufficiency	Expectorant	External Analgesic
Fever Blister	First Aid Antibiotic	Food Overindulgence
General Procedures and Policies	Hair Growth and Loss	Hormone
Hypophosphatemia/Hyperphosphatemia	Ingrown Toenail	Insect Bite and Sting
Insect Repellent, Oral	Internal Analgesic	Internal Deodorant
Labeling	Laxative	Leg Muscle Cramps
Male Genital Desensitizers	Menstrual	Nailbiting
Nasal Decongestant	Nighttime Sleep Aid	Ophthalmic
Oral Health Care	Oral Wound Healing	Otic
Overindulgence, Food and Drink	Pancreatic Insufficiency	Pediatric Dosing Information
Pediculicide	Poison Oak/Ivy	Poison Treatment
Prostatic Hypertrophy	Psoriasis	Seborrheic Dermatitis
Sedative, Daytime	Silver	Skin Bleaching
Skin Protectant	Sleep Aid, Nighttime	Smoking Deterrent
Stimulant	Stomach Acidifier	Sunscreen
Sweet Spirits of Nitre	Thumbsucking	Time and Extent Applications
Topical Analgesic	Vaginal Contraceptive	Vaginal Drug Products
Vitamins and Minerals	Wart Remover	Weight Control

TABLE 2

NDA versus OTC approval of drugs

NDA Approval process

Premarket approval—FDA reviews and approves formulation and labeling prior to marketing.

Confidential filing

Drug product specific

May require a user fee

Potential for marketing exclusivity

FDA review timelines

May require clinical studies, including studies on label comprehension and actual use

Approved labeling is unique to the drug.

Approved NDA is your "license" to market.

Trade name reviewed prior to marketing

OTC Monograph Process

No premarket approval – FDA sets forth specific conditions for generally regarded as safe and effective (GRASE) or in the case of a developing monograph, sets forth conditions that allow continued marketing pending a final monograph. Oversight occurs on a postmarketing basis.

Public process

Active ingredient specific and evaluated by OTC drug category

No user fees

No marketing exclusivity

Manufacturers responsible for ensuring compliant product with no FDA-mandated review (either pre or post market)

Generally, does not require clinical studies. Label comprehension and actual use studies are not required for ingredients already covered by a final or tentative final monograph.

Labeling is defined by the monograph. Once marketed, FDA can review the complete labeling at any time to determine whether it is truthful or misleading.

Final monograph is open to anyone.

No review of trade name prior to marketing. Once marketed, FDA can review the trade name at any time.

TABLE 3
Active Ingredients for OTC Monographs

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
93NOD9WBCS	2-ethylhexyl-4-phenylbenzophenone-2-carboxylic acid	sunscreen		II	IISE		58 FR 28281
36209ITL9D	acetaminophen	internal analgesic		I	I		
36209ITL9D	acetaminophen	menstrual/diuretic	analgesic	I			
36209ITL9D	acetaminophen	nighttime sleep aid		II	IISE		54 FR 6826
36209ITL9D	acetaminophen	overindulgence in alcohol	hangover reliever		I		
SP86R356CC	acetaminophen	internal analgesic		II	IIS		
Q40Q9N063P	acetamide	otic				310.545(a)(15)(i)	
Q40Q9N063P	acetic acid	wart remover		III	IIISE		[55 FR 33254]
Q40Q9N063P	acetic acid	corn/callus remover	II	IIISE			
Q40Q9N063P	acetic acid, glacial	wart remover		III	IIISE		[55 FR 33254]
Q40Q9N063P	acetic acid, glacial	skin protectant	astringent	II			
1364PS73AF	acetone	antiacaries			I	310.545(a)(18)(ii)	
	acidulated phosphate fluoride	antiacaries			I	355.10(a)(3)(i)	
	acidulated phosphate fluoride	antiacaries			I	355.10(a)(3)(ii)	
	agar	laxative	bulk laxative	II	III	310.545(a)(12)(i)	
18B8O9DQA2	alcloxa	acne			II	310.545(a)(1)	
18B8O9DQA2	alcloxa	anorectal		I(e)	I(e)	346.20(a)	
18B8O9DQA2	alcloxa	antifungal	keratolytic	III	III	310.545(a)(22)(ii)	
3K9958V90M	alcohol	digestive aid				310.545(a)(8)(ii)	
3K9958V90M	alcohol	external analgesic	insect bite/sting			310.545(a)(10)(vi)	
3K9958V90M	alcohol	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
3K9958V90M	alcohol	menstrual/diuretic				310.545(a)(24)(i)	
3K9958V90M	alcohol	mercury			I		
3K9958V90M	alcohol	oral health care		III	IIISE		
3K9958V90M	alcohol	skin protectant	astringent	II		310.545(a)(18)(ii)	
3K9958V90M	alcohol	skin protectant	insect bites/stings			310.545(a)(18)(v)(A)	
3K9958V90M	alcohol	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
3K9958V90M	alcohol	skin protectant		II	IISE		
3K9958V90M	alcohol	weight control			II	310.545(a)(20)	
3K9958V90M	alcohol, ethoxylated alkyl	external analgesic	insect bite/sting			310.545(a)(10)(vi)	
3K9958V90M	alcohol, ethoxylated alkyl	skin protectant	insect bites/stings			310.545(a)(18)(v)(A)	
8T66131YNK	aldioxa	skin protectant	diaper rash		IIISE		
SQ12NB Y9KR	alfalfa	weight control			II	310.545(a)(20)	
SQ12NB Y9KR	alfalfa leaves	menstrual/diuretic				310.545(a)(24)(i)	
8C3Z4148WZ	alginic acid	weight control			III	310.545(a)(20)	
	alkyl dimethyl amine oxide and alkyl dimethyl glycine	gingivitis/plaque			IIISE		

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
344S277G0Z	alkyl isoquinolinium bromide	acne		II	II	310.545(a)(1)	
344S277G0Z	alkyl isoquinolinium bromide	dandruff		III	III	310.545(a)(7)	
344S277G0Z	allantoin	dandruff		III	III	310.545(a)(7)	
344S277G0Z	allantoin	external analgesic			IISE		
344S277G0Z	allantoin	skin protectant		I	I	347.10(a)	
344S277G0Z	allantoin (5-ureidohydantoin)	corn/callus remover	II	IISE		[55 FR 33261]	58 FR 28281
344S277G0Z	allantoin (with aminobenzoic acid)	sunscreen		II	IIIE		
344S277G0Z	allantoin (wound healing claims only)	skin protectant			III	310.545(a)(18)(i)(A)	
BN34FX42G3	allyl isothiocyanate	cough/cold					
BN34FX42G3	allyl isothiocyanate	external analgesic	nasal decongestant	I	I	310.545(a)(6)(ii)(A)	
BN34FX42G3	allyl isothiocyanate	external analgesic	counterirritant			pending	
9104833TPA	almadrate sulfate	digestive aid	fever blister/cold sore	III	II	310.545(a)(10)(v)	
V5VD430YW9, ZY	aloe ingredients (aloe, aloe extract, aloe flower extract)	laxative	antacid		I		
09TD8L5SQV	aloe vera (see aloe)	gingivitis/plaque	stimulant laxative		I	310.545(a)(12)(iv)(C)	
V5VD430YW9	aloes	menstrual/diuretic			IIIE		
W41H6S09F4	aloin	laxative	stimulant laxative		III	310.545(a)(24)(i)	
	alpha cellulose	laxative	bulk laxative		III	310.545(a)(12)(iv)(A)	
DPU64XYB1D	alum, ammonium	oral health care	aststringent	I	I		
DPU64XYB1D	alum, ammonium	skin protectant	aststringent	II		310.545(a)(18)(ii)	
1L24V9R23S	alum, potassium	antifungal		III	III	310.545(a)(22)(ii)	
1L24V9R23S	alum, potassium	antiperspirant		IIIE	IIIE	310.545(a)(4)(i)	
1L24V9R23S	alum, potassium	oral health care			I		
1L24V9R23S	alum, potassium	skin protectant	aststringent	II		310.545(a)(18)(ii)	
LM126O6933	alumina powder, hydrated	antidiarrheal		III	III		
80EHD8143D	aluminum acetate	external analgesic			I	347.12(a)	
80EHD8143D	aluminum acetate	skin protectant	aststringent	I	I	347.12(a)	
80EHD8143D	aluminum acetate	skin protectant	diaper rash		IIIE		
	aluminum bromohydrate	antiperspirant		IISE	IISE	310.545(a)(4)(i)	
	aluminum carbonate gel (basic)	antacid			I	331.11(a)(1)	
	aluminum chlorhydroxy complex	skin protectant	aststringent	II		310.545(a)(18)(ii)	
LIF1N9568Y	aluminum chloride (alcoholic solutions)	antiperspirant		IIIS	IIIS	310.545(a)(4)(i)	
LIF1N9568Y	aluminum chloride (aqueous solution) (aerosol only)	antiperspirant				310.545(a)(4)(i)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
LIF1N9568Y	aluminum chloride (nonaerosol aqueous solution)	antiperspirant		I	I	350.10(a)	
LIF1N9568Y	aluminum chloride hexahydrate	external analgesic			IIIE		
HPN8MZWI3M	aluminum chlorohydrate	antiperspirant		I	I	350.10(b)	
	aluminum chlorohydrate	acne		II	II	310.545(a)(1)	
	aluminum chlorohydrate	antiperspirant		I	I	350.10(c)	
	polyethylene glycol	antiperspirant					
	aluminum chlorohydrate	antiperspirant		I	I	350.10(d)	
	propylene glycol	antiperspirant					
	aluminum dichlorohydrate	antiperspirant		I	I	350.10(e)	
	aluminum dichlorohydrate	antiperspirant		I	I	350.10(f)	
	polyethylene glycol	antiperspirant					
	aluminum dichlorohydrate	antiperspirant		I	I	350.10(g)	
	propylene glycol	antiperspirant					
5QB0T2IUN0	aluminum hydroxide	acne		II	II	310.545(a)(1)	
5QB0T2IUN0	aluminum hydroxide	antacid			I	331.11(a)(2)	
5QB0T2IUN0	aluminum hydroxide	antidiarrheal				310.545(a)(3)(i)	
5QB0T2IUN0	aluminum hydroxide	digestive aid	antacid	III	I	310.545(a)(8)(ii)	
5QB0T2IUN0	aluminum hydroxide	overindulgence in alcohol	hangover reliever		I		
5QB0T2IUN0	aluminum hydroxide	skin protectant	diaper rash			310.545(a)(18)(iii)	
5QB0T2IUN0	aluminum hydroxide	skin protectant	diaper rash			310.545(a)(18)(iii)	
5QB0T2IUN0	aluminum hydroxide	topical analgesic	diaper rash			310.545(a)(10)(iv)	
5QB0T2IUN0	aluminum hydroxide gel	anorectal	protectant	I(e,i)	I(e,i)	346.14(a)(1)	
5QB0T2IUN0	aluminum hydroxide gel	overindulgence in alcohol	hangover reliever		I		
5QB0T2IUN0	aluminum hydroxide gel	skin protectant		I	I	347.10(b)	
5QB0T2IUN0	aluminum hydroxide-hexitol, stabilized polymer	antacid			I	331.11(a)(2)	
5QB0T2IUN0	aluminum hydroxide-magnesium carbonate, codried gel	antacid			I	331.11(a)(2)	
5QB0T2IUN0	aluminum hydroxide-magnesium trisilicate, codried gel	antacid			I	331.11(a)(2)	
5QB0T2IUN0	aluminum hydroxide-sucrose powder hydrated	antacid			I	331.11(a)(2)	
F92V3S5210	aluminum phosphate	antacid			I	331.11(i)(1)	
F92V3S5210	aluminum phosphate gel (in combination only)	antacid			I	331.11(a)(4)	
UCN889409V	aluminum sesquichlorohydrate	antiperspirant		I	I	350.10(h)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
	aluminum sesquichlorohydrate	antiperspirant		I	I	350.10(i)	
	polyethylene glycol						
	aluminum sesquichlorohydrate	antiperspirant		I	I	350.10(j)	
	propylene glycol						
34S289N54E	aluminum sulfate	antifungal				310.545(a)(22)(ii)	
34S289N54E	aluminum sulfate	antiperspirant		IIIE	IIIE	310.545(a)(4)(i)	
	aluminum sulfate buffered	antiperspirant	w/ sales less than \$25,000	I	IIIS	310.545(a)(4)(ii)	
	w/ sodium aluminum lactate						
I7T908772F	aluminum sulfate, anhydrous	skin protectant	astringent	I	I	347.12(b)	
	aluminum sulfate, buffered	antiperspirant		I	IIIS	310.545(a)(4)(i)	
	(aerosol only)						
481Y8HDW2B	aluminum zirconium	antiperspirant		I	IIS	350.10(k)	
	octachlorohydrate						
P9D3YP29MY	aluminum zirconium	antiperspirant		I	IIS	350.10(l)	
	octachlorohydrate gly						
15K31617MU	aluminum zirconium	antiperspirant		I	IIS	350.10(m)	
	pentachlorohydrate						
94703016SM	aluminum zirconium	antiperspirant		I	IIS	350.10(n)	
	pentachlorohydrate gly						
8O386558JE	aluminum zirconium	antiperspirant		I	IIS	350.10(o)	
	tetrachlorohydrate						
8O386558JE	aluminum zirconium	antiperspirant		I	IIS	350.10(p)	
	tetrachlorohydrate gly						
T27D6T99LH	aluminum zirconium	antiperspirant		I	IIS	350.10(q)	
	trichlorohydrate						
T27D6T99LH	aluminum zirconium	antiperspirant		I	IIS	350.10(r)	
	trichlorohydrate gly						
376KTP06K8	amiloxate (isoamyl	sunscreen		NA			
	p-methoxycinnamate)						
OR5RM3Q5QL	aminacrine hydrochloride	boil treatment			IIIE	310.531(a)	
TE7660XO1C	aminoacetic acid	antiemetic			II		
TL2TJE8QTX	aminobenzoic acid	internal analgesic		II	II	310.545(a)(23)(i)	
TL2TJE8QTX	aminobenzoic acid (PABA)	sunscreen		I	I	352.10(a)	
27Y3KJK423	aminophylline	cough/cold	bronchodilator	I	II	310.545(a)(6)(iv)	
5138Q19F1X	ammonia solution, strong	skin protectant	insect bites/stings			310.545(a)(18)(v)(A)	
5138Q19F1X	ammonia solution, strong	external analgesic	fever blister/cold sore	I	I	310.545(a)(10)(v)	
	(ammonia water, strong)						
JD546Z56F0	ammoniated mercury	antimicrobial	first aid antiseptic			310.545(a)(27)(i)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
R0JB3224WS	ammonium bromide	nighttime sleep aid	bromide	II	IIIE		[54 FR 6826]
R0JB3224WS	ammonium chloride	cough/cold	expectorant		III	310.545(a)(6)(iii)	
R0JB3224WS	ammonium chloride	menstrual/diuretic	diuretic	I	I		
R0JB3224WS	ammonium chloride	nighttime sleep aid			II		
R0JB3224WS	ammonium chloride	oral health care	expectorant	III			
R0JB3224WS	ammonium chloride	stimulant			IIIE		[39 FR 6104]
5138Q19F1X	ammonium hydroxide	skin protectant	insect bites/stings			310.545(a)(18)(v)(A)	
YOJ58O116E	amylase	digestive aid				310.545(a)(8)(ii)	
	anyltricrosols, secondary	antifungal		III	III	310.545(a)(22)(iii)	
	anyltricrosols, secondary	oral health care			IIIE		
	anion and cation exchange resins buffered	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
6Y89129C8H	anise oil	weight control			II	310.545(a)(20)	
21C2F5E8RE	anise seed	digestive aid				310.545(a)(8)(ii)	
DL6OZ476V3	antimony potassium tartrate	cough/cold	expectorant		II	310.545(a)(6)(iii)	
T3CHA1B5IH	antipyrine	internal analgesic		III	III	310.545(a)(23)(i)	
T3CHA1B5IH	antipyrine	ophthalmic	anesthetic	II	II	310.545(a)(21)(i)	
T3CHA1B5IH	antipyrine	oral health care	anesthetic/analgesic	II	II	310.545(a)(14)	
7C0697DR9I	any atropine ingredient	internal analgesic				310.545(a)(23)(ii)	
7C0697DR9I	any atropine ingredient	menstrual/diuretic				310.545(a)(24)(ii)	
GN83C131XS	any ephedrine ingredient	internal analgesic				310.545(a)(23)(ii)	
GN83C131XS	any ephedrine ingredient	menstrual/diuretic				310.545(a)(24)(ii)	
94ZL A3W45F	arginine	weight control			II	310.545(a)(20)	
	aromatic powder	digestive aid				310.545(a)(8)(ii)	
	aromatics	skin protectant	astringent	II		310.545(a)(18)(ii)	
W9FZA51AS1	asafetida	digestive aid				310.545(a)(8)(ii)	
Y62M9GTW4A	<i>Asclepias tuberosa</i>	menstrual/diuretic	botanical/vegetable herb	II	II	310.545(a)(24)(i)	
PQ6CK8PD0R	ascorbic acid	corn/callus remover	II	IIIE		[55 FR 33261]	
PQ6CK8PD0R	ascorbic acid	wart remover		III			
PQ6CK8PD0R	ascorbic acid	weight control			II	310.545(a)(20)	
Z1EJP3037Z	asparagus	menstrual/diuretic				310.545(a)(24)(i)	
Q6Z8UK5R3G	<i>Aspergillus oryzae</i> enzymes (except lactase enzyme derived from aspe	digestive aid				310.545(a)(8)(ii)	
R16CO5Y76E	aspirin	external analgesic	analgesic and anesthetic	III	III	310.545(a)(10)(i)	
R16CO5Y76E	aspirin	external analgesic	fever blister/cold sore	III	III	310.545(a)(10)(v)	
R16CO5Y76E	aspirin	external analgesic	poison ivy/oak/sumac	III	III	310.545(a)(10)(vii)	
R16CO5Y76E	aspirin	internal analgesic	cardiovascular	I	I	343.12(a)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
R16CO5Y76E	aspirin	internal analgesic	rheumatologic	I	I	343.13(a)	[54 FR 6826]
R16CO5Y76E	aspirin	menstrual/diuretic	analgesic		I		
R16CO5Y76E	aspirin	nighttime sleep aid		II	III		
R16CO5Y76E	aspirin	oral health care	anesthetic/analgesic	I	IIIE		
R16CO5Y76E	aspirin	overindulgence in alcohol	hangover reliever		I		
R16CO5Y76E	aspirin (buffered)	internal analgesic	cardiovascular	I	I	343.12(b)	
R16CO5Y76E	aspirin (buffered)	internal analgesic		I	I	343.13(b)	
R16CO5Y76E	aspirin, aluminum	internal analgesic	rheumatologic	III	III	310.545(a)(23)(i)	
R16CO5Y76E	aspirin, calcium	internal analgesic			I		
R16CO5Y76E	aspirin, calcium	internal analgesic			I		
R16CO5Y76E	aspirin, calcium	menstrual/diuretic			I		
WQZ3G9PF0H	<i>Atropa belladonna</i>	cough/cold	anticholinergic		II	310.53	
7C0697DR9I	atropine	anorectal	anticholinergic	II(e,i)	II(e,i)	310.545(a)(26)(i)	
0315ZE7KA5	atropine sulfate	antidiarrheal		III	III	310.545(a)(3)(i)	
0315ZE7KA5	atropine sulfate	cough/cold	anticholinergic		III	310.53	
U6V729APAM	atapulgit, activated	antidiarrheal	w/ sales less than \$25,000	III	I	310.545(3)(ii)	
G63QQF2NOX	avobenzone	sunscreen				352.10(a)	
58H6RWO52I	<i>Bacillus acidophilus</i>	digestive aid				310.545(a)(8)(ii)	
89Y4M234ES	bacitracin	first aid antibiotic	ointment		I	333.110(a)	
	bacitracin zinc	first aid antibiotic	ointment		I	333.110(b)	
	barosma	menstrual/diuretic		III	III	310.545(a)(24)(i)	
5P5C03819W	basic fuchsin	antifungal			III	310.545(a)(22)(ii)	
	beechwood creosote	cough/cold	expectorant	III	III	310.545(a)(6)(iii)	
8WB9PV3YW5	bean	digestive aid			II	310.545(a)(8)(ii)	
3M5V3D1X36	bearberry	weight control				310.545(a)(20)	
3M5V3D1X36	bearberry (extract of <i>Uva ursi</i>)	menstrual/diuretic				310.545(a)(24)(i)	
3M5V3D1X36	bearberry fluid extract (extract of bearberry)	menstrual/diuretic				310.545(a)(24)(i)	
2ZA36H0S2V	beeswax	skin protectant	insect bites/stings w/ sales less than \$25,000		310.545(a)(18)(v)(B)		
2ZA36H0S2V	beeswax	skin protectant	poison ivy/oak/sumac w/ sales less than \$25,000	310.545(a)(18)(vi)(B)			
2ZA36H0S2V	beeswax	skin protectant	w/ sales less than \$25,000			310.545(a)(18)(i)(B)	
WQZ3G9PF0H	belladonna alkaloids	corn/callus remover	II	IIIE	III	[55 FR 33261]	
WQZ3G9PF0H	belladonna alkaloids	cough/cold	anticholinergic		II	310.53	
WQZ3G9PF0H	belladonna alkaloids	cough/cold	bronchodilator	II	II	310.545(a)(6)(iv)	
WQZ3G9PF0H	belladonna alkaloids	digestive aid				310.545(a)(8)(ii)	
WQZ3G9PF0H	belladonna extract	anorectal	anticholinergic	II(e,i)	II(e,i)	310.545(a)(26)(i)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
6GZW20TIOI	belladonna leaves, powdered extract	digestive aid		NA		310.545(a)(8)(ii)	
PWZ1720CBH	bemotrizinol	sunscreen			I		
F5UM2KM3W7	benzalkonium chloride	antimicrobial			IIIE		
F5UM2KM3W7	benzalkonium chloride	antimicrobial			III		
F5UM2KM3W7	benzalkonium chloride	dandruff		III		310.545(a)(7)	
F5UM2KM3W7	benzalkonium chloride	external analgesic				310.545(a)(10)(vi)	
F5UM2KM3W7	benzalkonium chloride	skin protectant	insect bite/sting			310.545(a)(18)(iii)	
F5UM2KM3W7	benzalkonium chloride	skin protectant	astringent	II		310.545(a)(18)(v)(A)	
PH41D05744	benzalkonium chloride	antifungal	insect bites/stings			310.545(a)(22)(ii)	
PH41D05744	benzethonium chloride	antimicrobial			I		
PH41D05744	benzethonium chloride	antimicrobial			IIIE		
PH41D05744	benzethonium chloride	antimicrobial			IIIE		
PH41D05744	benzethonium chloride	antimicrobial			IIIE		
PH41D05744	benzethonium chloride	antimicrobial			III		
PH41D05744	benzethonium chloride	dandruff		III		310.545(a)(7)	
PH41D05744	benzethonium chloride	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
PH41D05744	benzethonium chloride	skin protectant	astringent	II		310.545(a)(18)(ii)	
PH41D05744	benzethonium chloride	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
U3RSY48JW10	benzocaine	external analgesic			IIIE	IIIE (0.5-1.25%)	
U3RSY48JW11	benzocaine	oral health care	anesthetic/analgesic	I	I		[51 FR 28660]
U3RSY48JW12	benzocaine	otic			IIIE		
U3RSY48JW13	benzocaine	pediculicide			II		
U3RSY48JW14	benzocaine	relief of oral discomfort		II		310.545(a)(25)(i)	
U3RSY48JW15	benzocaine	relief of oral discomfort		I	II		
U3RSY48JW16	benzocaine	skin protectant		IIIIE			
U3RSY48JW17	benzocaine	skin protectant	astringent	II			
U3RSY48JW18	benzocaine	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(ii)	
U3RSY48JW19	benzocaine	wart remover		II	IIIE	310.545(a)(18)(vi)(A)	
U3RSY48JW5	benzocaine	weight control			IIIE		[55 FR 33254]
U3RSY48JW5	benzocaine	acne		II	II		
U3RSY48JW5	benzocaine	external analgesic	male genital desensitizer		II	310.545(a)(1)	
U3RSY48JW6	benzocaine	anorectal	local anesthetic	I	I	348.10(a)(1)	
U3RSY48JW7	benzocaine	dandruff		I(e),III(i)	I(e),III(i)	346.10(a)	
U3RSY48JW9	benzocaine (0.5-1.25%)	external analgesic	poison ivy/oak/sumac	II	IIIIE		[56 FR 63567]
8SKN0B0MIM	benzoic acid	acne		I	I	310.545(a)(10)(vii)	
8SKN0B0MIM	benzoic acid	antifungal		II	II	310.545(a)(1)	
8SKN0B0MIM	benzoic acid	oral health care		III	III	310.545(a)(22)(ii)	
8SKN0B0MIM	benzoic acid	skin protectant	astringent	II	IIIIE	310.545(a)(18)(ii)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
L7J6A1NE81	benzooin preparations (compound tincture of benzooin, tincture of benz	cough/cold	expectorant		III	310.545(a)(6)(iii)	
L7J6A1NE81	benzooin tincture, compound	relief of oral discomfort		I			
5P4DHS6ENR	benzonatate	cough/cold	antitussive		I		
GRE0P19C3Z	benzoxiquine	antifungal		III	III	310.545(a)(22)(ii)	
W9WZN9A0GM	benzoyl peroxide	acne		I	I-> IIS	333.310(a)	75 FR 9767
LKG8494WBH	benzyl alcohol	anorectal	local anesthetic	III(e,i)	I(e),III(i)	346.10(b)	
LKG8494WBH	benzyl alcohol	external analgesic	analgesic and anesthetic	I	I	pending	
LKG8494WBH	benzyl alcohol	external analgesic	male genital desensitizer			310.545(a)(10)(iii)	
LKG8494WBH	benzyl alcohol	oral health care	anesthetic/analgesic	I	I		
LKG8494WBH	benzyl alcohol	pediculicide		II	II	310.545(a)(25)(i)	
LKG8494WBH	benzyl alcohol	relief of oral discomfort		I			
LKG8494WBH	benzyl alcohol	relief of oral discomfort		IIISE			
LKG8494WBH	benzyl alcohol	skin protectant	poison ivy/oak/sumac	II	II	310.545(a)(18)(vi)(A)	
N863NB338G	benzyl benzoate	pediculicide				310.545(a)(25)(i)	
JK8U8K4D6K	betaine hydrochloride	digestive aid				310.545(a)(8)(ii)	
	bicarbonate	antacid				331.11(b)	
	bile salts/acids	laxative	stimulant laxative		III	310.545(a)(12)(iv)(A)	
6SO6U10H04	biotin	weight control			II	310.545(a)(20)	
10X0709Y6I	bisacodyl	laxative			I		
JB5Y63JDHJ	bismuth aluminate	antacid			I	331.11(c)(1)	
M41L2IN55T	bismuth carbonate	antacid			I	331.11(c)(2)	
A614E79QF1	bismuth oxide	anorectal	protectant	III(e,i)	III(e,i)	310.545(a)(26)(viii)	
	bismuth sodium tartrate	digestive aid		II	II	310.545(a)(8)(i)	
M41L2IN55T	bismuth sodium tartrate	external analgesic	fever blister/cold sore			310.545(a)(10)(v)	
M41L2IN55T	bismuth subcarbonate	anorectal	protectant	III(e,i)	III(e,i)	310.545(a)(26)(viii)	
M41L2IN55T	bismuth subcarbonate	antacid			I	331.11(c)(3)	
Y1W503MI7V	bismuth subcarbonate	digestive aid				310.545(a)(8)(ii)	
Y1W503MI7V	bismuth subgallate	anorectal	protectant	III(e,i)	III(e,i)	310.545(a)(26)(viii)	
Y1W503MI7V	bismuth subgallate	antacid			I	331.11(c)(4)	
Y1W503MI7V	bismuth subgallate	deodorants for internal use	III	I	357.810(a)		
Y1W503MI7V	bismuth subgallate	digestive aid				310.545(a)(8)(ii)	
H19J064BA5	bismuth subnitrate	skin protectant		II	IIS		
Y1W503MI7V	bismuth subnitrate	anorectal	protectant	II(e,i)	II(e,i)	310.545(a)(26)(viii)	
Y1W503MI7V	bismuth subnitrate	antacid			I	331.11(c)(5)	
Y1W503MI7V	bismuth subnitrate	antidiarrheal	w/ sales less than \$25,000	III	III	310.545(a)(3)(ii)	
Y1W503MI7V	bismuth subnitrate	skin protectant	fever blister/cold sore		II	310.545(a)(18)(iv)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
Y1W503MI7V	bismuth subnitrate	skin protectant	insect bites/stings w/ sales less than \$2	II	II	310.545(a)(18)(v)(B)	
Y1W503MI7V	bismuth subnitrate	skin protectant	poison ivy/oak/sumac	II	II	310.545(a)(18)(vi)(A)	
Y1W503MI7V	bismuth subnitrate	skin protectant	poison ivy/oak/sumac w/ sales less tha	II	II	310.545(a)(18)(vi)(B)	
Y1W503MI7V	bismuth subnitrate	skin protectant	w/ sales less than \$25,000	II	II	310.545(a)(18)(i)(B)	
62TEY5 IRR1	bismuth subsalicylate	antidiarrheal		III	IIIE	335.10(a)	
62TEY5 IRR2	bismuth subsalicylate	antiemetic			III		
62TEY5 IRR3	bismuth subsalicylate	antimicrobial			IIIE		
62TEY5 IRR4	bismuth subsalicylate	oral health care			IIIE		
62TEY5 IRR5	bismuth subsalicylate	overindulgence in a	overindulgence		I		
8NT850T0YS	bisotrizole	sunscreen		NA			
AMT77LS62O	bithionol	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
AMT77LS62O	bithionol	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
86R5JD01D	black radish powder	digestive aid				310.545(a)(8)(ii)	
6L5ZL09795	blessed thistle (<i>Cnicus benedictus</i>)	digestive aid				310.545(a)(8)(ii)	
6L5ZL09795	blessed thistle (<i>Cnicus benedictus</i>)	menstrual/diuretic				310.545(a)(24)(i)	
R57ZHV85D10	bone marrow, red	weight control			II	310.545(a)(20)	
R57ZHV85D11	boric acid	skin protectant	fever blister/cold sore		II	310.545(a)(18)(iv)	
R57ZHV85D12	boric acid	skin protectant	insect bites/stings w/ sales less than \$2	II	II	310.545(a)(18)(v)(B)	
R57ZHV85D13	boric acid	skin protectant	poison ivy/oak/sumac	II	II	310.545(a)(18)(vi)(A)	
R57ZHV85D14	boric acid	skin protectant	poison ivy/oak/sumac w/ sales less tha	II	II	310.545(a)(18)(vi)(B)	
R57ZHV85D4	boric acid	skin protectant	w/ sales less than \$25,000	II	II	310.545(a)(18)(i)(B)	
R57ZHV85D5	boric acid	acne		II	II	310.545(a)(1)	
R57ZHV85D6	boric acid	anorectal	antiseptic	II(e,i)	II(e,i)	310.545(a)(26)(ii)	
R57ZHV85D7	boric acid	antifungal		III		310.545(a)(22)(ii)	
R57ZHV85D8	boric acid	dandruff		II	II	310.545(a)(7)	
R57ZHV85D9	boric acid	ophthalmic	anti-infective	III	II	310.545(a)(21)(ii)	
LU86E5P72A	boric acid	skin protectant	astringent	II	II	310.545(a)(18)(ii)	
	boromelone	sunscreen		III	IIIE		58 FR 28281
	(5-(3,3-dimethyl-2-norbornyliden)3-pentene-2-one)						
	bonyl acetate (topical)	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(B)	
	boroglycerin	anorectal	antiseptic	II(e,i)	II(e,i)	310.545(a)(26)(ii)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
	boroglycerin	oral health care			IISE		
	bran	laxative			I		
IXA7C9ZN03	brompheniramine maleate	cough/cold	antihistamine	I	I	341.12(a)	
KOS935A04V	buchu	weight control			II	310.545(a)(20)	
KOS935A04V	buchu powdered extract (extract of buchu)	menstrual/diuretic		II	II	310.545(a)(24)(i)	
KOS935A04V	buchu, potassium extract	weight control			II	310.545(a)(20)	
2C5Q57D7Z4	buckthorn	digestive aid				310.545(a)(8)(ii)	
PAU39W3CVB	butacaine sulfate	relief of oral discomfort		I			
PAU39W3CVB	butacaine sulfate	relief of oral discomfort		IIISE			
	butamben picrate	external analgesic		I	I		
3G6A5W338E	caffeine	cough/cold	miscellaneous		IIIIE		
3G6A5W338E	caffeine	internal analgesic		III	IIIIE		
3G6A5W338E	caffeine	menstrual/diuretic	analgesic	III			
3G6A5W338E	caffeine	menstrual/diuretic	diuretic	I	I		
3G6A5W338E	caffeine	nighttime sleep aid	stimulant		I		
3G6A5W338E	caffeine	overindulgence in alcohol	hangover reliever		I		
3G6A5W338E	caffeine	stimulant			I	340.10	
3G6A5W338E	caffeine	weight control			II	310.545(a)(20)	
3G6A5W338E	caffeine	weight control			II	310.545(a)(20)	
U26EO4675Q	caffeine citrate	anorectal	astirgent	I(e,i)	I(e,i)	346.18(a)	
	calamine	external analgesic	insect bite/sting			310.545(a)(10)(vi)	
	calamine	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
	calamine	skin protectant		I	I	347.10(c)	
	calamine (in combination only)	anorectal	protectant	I(e,i)	I(e,i)	346.14(b)(1)	
	calcium	weight control			II	310.545(a)(20)	
SY7Q814VUP	calcium (mono or dibasic salt)	antacid				331.11(i)(2)	
Y882YXF34X	calcium acetate	skin protectant	astirgent	II		310.545(a)(18)(ii)	
H0G9379FGK	calcium carbonate	antacid			I	331.11(d)	
H0G9379FGK	calcium carbonate	digestive aid	antacid	III	I	310.545(a)(8)(i)	
H0G9379FGK	calcium carbonate	weight control			II	310.545(a)(20)	
H0G9379FGK	calcium carbonate precipitated	antidiarrheal		III	III	310.545(a)(3)(i)	
	calcium caseinate	weight control			II	310.545(a)(20)	
SQE6VB453K	calcium gluconate	digestive aid				310.545(a)(8)(ii)	
PF5DZW74VN	calcium hydroxide	antidiarrheal	w/ sales less than \$25,000	III	III	310.545(a)(3)(ii)	
2URQ2N32W3	calcium lactate	menstrual/diuretic				310.545(a)(24)(i)	
2URQ2N32W3	calcium lactate	weight control			II	310.545(a)(20)	
568ET80C3D	calcium pantothenate	laxative	stimulant laxative		III	310.545(a)(12)(iv)(A)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
568ET80C3D	calcium pantothenate	menstrual/diuretic					
568ET80C3D	calcium pantothenate	wart remover		III	IIIE	310.545(a)(24)(i)	[55 FR 33254]
568ET80C3D	calcium pantothenate	weight control			II	310.545(a)(20)	
H0G9379FGK	calcium phosphate	antacid			I	331.11(d)	
	calcium polycarbophil	antidiarrheal	w/ sales less than \$25,000	NC	I	310.545(a)(3)(ii)	
	calcium polycarbophil	laxative	bulk laxative		I		
	calcium polysulfide	acne		II	II	310.545(a)(1)	
	calcium salicylate	internal analgesic				310.545(a)(23)(i)	
	calcium sucrose phosphate	anticaries		II	NC	310.545(a)(2)(ii)	
210100728E	calcium thiosulfate	acne		II	II	310.545(a)(1)	
77YW IRTU8V	calcium undecylenate	antifungal		I	I	333.210(f)	
77YW IRTU8V	calcium undecylenate	antimicrobial			IIIE		
77YW IRTU8V	calcium undecylenate	dandruff				310.545(a)(7)	
J2D46N657D	calomel	laxative	stimulant laxative		II	310.545(a)(12)(iv)(A)	
J2D46N657D	calomel (mercurous chloride)	antimicrobial	first aid antiseptic			310.545(a)(27)(i)	
5TJD82A1ET	camphor	acne		II	II	310.545(a)(1)	
5TJD82A1ET	camphor	anorectal	analgesic, anesthetic, antipruritic		I(e)	346.16(a)	
5TJD82A1ET	camphor	anorectal	counterirritant	II(e,i)	II(e,i)	310.545(a)(26)(iv)	
5TJD82A1ET	camphor	antifungal		II	II	310.545(a)(22)(iii)	
5TJD82A1ET	camphor	cough/cold	antitussive	III	IIIE	341.14(b)(1)	steam inhalation
5TJD82A1ET	camphor	cough/cold	antitussive	III	I	341.14(b)(1)	topical
5TJD82A1ET	camphor	cough/cold	expectorant		III	310.545(a)(6)(iii)	topical/inhalant
5TJD82A1ET	camphor	cough/cold	nasal decongestant	III	IIIE		[59 FR 43408]
5TJD82A1ET	camphor	external analgesic		I	I		
5TJD82A1ET	camphor	external analgesic		I	IIIE		
5TJD82A1ET	camphor	oral health care	anesthetic/analgesic	II	IIIE		
5TJD82A1ET	camphor	oral health care	nonantimicrobial			310.545(a)(14)	
5TJD82A1ET	camphor	relief of oral discomfort		IIIE			
5TJD82A1ET	camphor	skin protectant	insect bites/stings			310.545(a)(18)(v)(A)	
5TJD82A1ET	camphor	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
5TJD82A1ET	camphor	sunscreen		inactive			
5TJD82A1ET	camphor	wart remover		II	IIIE		43 FR 38208
5TJD82A1ET	camphor (exceeding 3 percent)	external analgesic	fever blister/cold sore	I	I	310.545(a)(10)(v)	[55 FR 33254]
5TJD82A1ET	camphor (lozenge)	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(A)	
5TJD82A1ET	camphor gum	skin protectant	astringent	II		310.545(a)(18)(ii)	
	camphorated metacresol	antifungal		III	III	310.545(a)(22)(iv)	
	camphorated metacresol	external analgesic	analgesic and anesthetic	IIIE	I	pending	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
	camphorated metacresol	external analgesic	male genital desensitizer			310.545(a)(10)(iii)	
	candidin	antifungal		II	II	310.545(a)(22)(ii)	
S07O44R1ZM	capsaicin	external analgesic	fever blister/cold sore	I	I	310.545(a)(10)(v)	
S07O44R1ZM	capsicum	digestive aid				310.545(a)(8)(ii)	
S07O44R1ZM	capsicum	external analgesic	fever blister/cold sore	I	I	310.545(a)(10)(v)	
S07O44R1ZM	capsicum	relief of oral discomfort		IIIE			
S07O44R1ZM	capsicum	relief of oral discomfort		IIIE			
S07O44R1ZM	capsicum oleoresin	external analgesic	fever blister/cold sore	I	I	310.545(a)(10)(v)	
S07O44R1ZM	capsicum oleoresin	menstrual/diuretic				310.545(a)(24)(i)	
S07O44R1ZM	capsicum, fluid extract of carbon	digestive aid				310.545(a)(8)(ii)	
	captan	dandruff		III	III	310.545(a)(7)	
09TQU5PG95	caramiphen edisylate	cough/cold	antitussive	III	IIIE		[52 FR 30054]
31PZ2VAU81	carbamide peroxide	oral health care			III		
31PZ2VAU81	carbamide peroxide	oral health care			IIIE		
31PZ2VAU81	carbamide peroxide (in anhydrous glycerin)	oral health care	wound cleansing	I	I		
31PZ2VAU81	carbamide peroxide 6.5% (in anhydrous glycerin)	otic			I	344.10	
N667F17JP1	carbaspirin calcium	internal analgesic		I	I		
N667F17JP1	carbaspirin calcium	menstrual/diuretic	analgesic	I			
4SH0MFJ5HJ	carbetapentane citrate	cough/cold	antitussive	III	IIIE		[52 FR 30054]
2P3VWU3H10	carbon	digestive aid					
142M471B3J	carbon dioxide, released	laxative			I		
K679OBS311	carboxymethylcellulose sodium	antidiarrheal				310.545(a)(3)(i)	
K679OBS311	carboxymethylcellulose sodium	laxative		I	I		
K679OBS311	carboxymethylcellulose sodium	ophthalmic	demulcents	I	I	349.12(a)(1)	
K679OBS311	carboxymethylcellulose sodium	weight control		III	III	310.545(a)(20)	
5C69YCD2YJ	carrageenan	weight control		III	III	310.545(a)(20)	
5C69YCD2YJ	carrageenan (degraded)	laxative	bulk laxative		II	310.545(a)(12)(i)	
5C69YCD2YJ	carrageenan (native)	laxative	bulk laxative		III	310.545(a)(12)(i)	
	casantranol	laxative	stimulant laxative		I	310.545(a)(12)(iv)(C)	
	cascara fluid extract aromatic	laxative	stimulant laxative		I	310.545(a)(12)(iv)(C)	
	cascara fluid extract, aromatic (extract of cascara)	menstrual/diuretic				310.545(a)(24)(i)	
4VBP01X99F	cascara sagrada bark	laxative	stimulant laxative		I	310.545(a)(12)(iv)(C)	
	cascara sagrada extract	digestive aid				310.545(a)(8)(ii)	
	cascara sagrada extract	laxative	stimulant laxative		I	310.545(a)(12)(iv)(C)	
	cascara sagrada fluid extract	laxative	stimulant laxative		I	310.545(a)(12)(iv)(C)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
D5340Y2I9G	castor oil	laxative	stimulant laxative	II	I		[55 FR 33254]
D5340Y2I9G	castor oil	wart remover			IISE		
48300360NZ	catechu, tinctures	digestive aid				310.545(a)(8)(ii)	
7Y51EV0DZW	catnip	digestive aid				310.545(a)(8)(ii)	
BJ169U4NLG	cedar leaf oil (topical)	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(B)	
	cellulase	digestive aid		II/III	III	310.545(a)(8)(i)	
SMD1X3X09M	cellulose, microporous	skin protectant	diaper rash		IIISE		
85474O1N9D	cetalkonium chloride	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
85474O1N9D	cetalkonium chloride	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
9361ST6JCN	cetyl alcohol	skin protectant	insect bites/stings w/ sales less than \$25,000		310.545(a)(18)(v)(B)		
9361ST6JCN	cetyl alcohol	skin protectant	poison ivy/oak/sumac w/ sales less than \$25,000	310.545(a)(18)(vi)(B)			
9361ST6JCN	cetyl alcohol	skin protectant	w/ sales less than \$25,000			310.545(a)(18)(i)(B)	
D9OM4SK49P	cetylpyridinium chloride	oral health care			IIISE		
O2T154T6OG	chamomile flowers	digestive aid				310.545(a)(8)(ii)	
2P3VWU3H10	charcoal (activated)	antidiarrheal	w/ sales less than \$25,000	III	III	310.545(a)(3)(ii)	
2P3VWU3H10	charcoal, activated	acute toxic ingestion		I			
2P3VWU3H10	charcoal, activated	antacid			IIIE		[55 FR 19864]
2P3VWU3H10	charcoal, activated	deodorants for internal use	III	III			
2P3VWU3H10	charcoal, activated	overindulgence in alcohol	hangover minimizer		IIIE		
2P3VWU3H10	charcoal, activated	poison treatment			I		
2P3VWU3H10	charcoal, wood/activated	digestive aid		III	III	310.545(a)(8)(iii)	oral
69QQ58998Y	chlorphedianol hydrochloride	cough/cold	antitussive		I	341.14(a)(1)	
418M5916WG	chloral hydrate	external analgesic	analgesic and anesthetic	II	II	310.545(a)(10)(i)	
418M5916WG	chloral hydrate	external analgesic	counterirritant	I	I	310.545(a)(10)(ii)	
418M5916WG	chloral hydrate	external analgesic	fever blister/cold sore	II	II	310.545(a)(10)(v)	
418M5916WG	chloral hydrate	external analgesic	poison ivy/oak/sumac	II	II	310.545(a)(10)(vii)	
418M5916WG	chloral hydrate	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
NPB7A7874U	chlorcyclizine hydrochloride	cough/cold	antihistamine		I	341.12(b)	
BPF36H1G6S	chlorhydroxyquinoline (cloxyquin)	acne		II	II	310.545(a)(1)	[48 FR 32873]
HM4YQM8WRC	chlorobutanol	corn/callus remover	II	IIISE		[55 FR 33261]	
HM4YQM8WRC	chlorobutanol	external analgesic	analgesic and anesthetic	III	III	310.545(a)(10)(i)	
HM4YQM8WRC	chlorobutanol	external analgesic	fever blister/cold sore	III	III	310.545(a)(10)(v)	
HM4YQM8WRC	chlorobutanol	external analgesic	poison ivy/oak/sumac	III	III	310.545(a)(10)(vii)	
7V31YC746X	chloroform	cough/cold	expectorant		II	310.545(a)(6)(iii)	
7V31YC746X	chloroform	digestive aid				310.545(a)(8)(ii)	(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
CIW5S16655	chlorophenothane (dichlorodiphenyl trichloroethane)	pediculicide				310.545(a)(25)(i)	
	chlorophyllin	relief of oral discomfort		IIIE			
	chlorophyllin copper complex	deodorants for internal use	III	I	357.810(b)		
	chlorophyllin copper complex	oral health care		IIIE			
LJ25TI0CVT	chlorothymol	antifungal		III	III	310.545(a)(22)(ii)	
LJ25TI0CVT	chloroxylenol	antimicrobial		III	III		
LJ25TI0CVT	chloroxylenol	antimicrobial			IIIE		
LJ25TI0CVT	chloroxylenol	acne		II	II	310.545(a)(1)	
LJ25TI0CVT	chloroxylenol	antifungal		III	III	310.545(a)(22)(iv)	
LJ25TI0CVT	chloroxylenol	dandruff		III	III	310.545(a)(7)	
V1Q0090J9Z	chlorpheniramine maleate	cough/cold	antihistamine	I	I	341.12(c)	
V1Q0090J9Z	chlorpheniramine maleate	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
V1Q0090J9Z	chlorpheniramine maleate	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
O1GX33ON8R	chlorphenirpyridamine maleate	menstrual/diuretic				310.545(a)(24)(i)	
1C6V77QF4I	chlortetracycline hydrochloride	first aid antibiotic	ointment	I	I	333.110(c)	
1C6V77QF4I	cholecalciferol	skin protectant	diaper rash	IIIE			
1C6V77QF4I	cholecalciferol	weight control		II	II	310.545(a)(20)	
N91BDP6H0X	cholecalciferol (vitamin D)	anorectal	wound healing	III(e,i)	III(e,i)	310.545(a)(26)(x)	
N91BDP6H0X	choline	weight control		II	II	310.545(a)(20)	
N91BDP6H0X	choline salicylate	internal analgesic		I	I		
N91BDP6H0X	choline salicylate	menstrual/diuretic	analgesic	I			
XR12Z4HLEA	chondrus	weight control		III	III	310.545(a)(20)	
K73E24S6X9	<i>Cimicifuga racemosa</i>	menstrual/diuretic	botanical/vegetable herb	II	II	310.545(a)(24)(i)	
T4B6SPQ0UF	cinnamedrine hydrochloride	menstrual/diuretic	muscle relaxant	III	IIIE		
E5GY4I6YCZ	cinnamon oil	digestive aid				310.545(a)(8)(ii)	
5S29HWU6QB	cinnamon tincture	digestive aid				310.545(a)(8)(ii)	
5437O7N5BH	cinoxate	sunscreen		I	I	352.10(c)	
	citrate (containing active ingredients: citrate ion, as citric acid or salt)	antacid		I	I	331.11(e)	
2968PHW8QP	citric acid	relief of oral discomfort		IIIE			
2968PHW8QP	citric acid	weight control		II	II	310.545(a)(20)	
47EQ08LE7H	citrus pectin	digestive aid				310.545(a)(8)(ii)	
7BHQ856EJ5	clioquinol	antifungal		I	I	333.210(a)	
7BHQ856EJ5	clioquinol (iodochlorhydroxyquin)	antifungal		I	I	333.210(a)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
I5ZZY3DC5G	cloflucarban	antimicrobial			IIIS		
I5ZZY3DC5G	cloflucarban	antimicrobial			IIISE		
I5ZZY3DC5G	cloflucarban	antimicrobial			IISE		
G07GZ97H65	clotrimazole	antifungal			I	333.210(g)	
G07GZ97H65	clotrimazole	n/a			I		[67 FR 5942]
578389D6D0	clove oil	skin protectant	astringent	II		310.545(a)(18)(ii)	
BPF36H1G6S	cloxyquin (chlorhydroxyquinoline)	acne				310.545(a)(1)	
6L5ZL09795	<i>Cnicus benedictus</i>	menstrual/diuretic		II	II		
6L5ZL09795	<i>Cnicus benedictus</i>	weight control			II	310.545(a)(20)	
R533ES02EC	coal tar	acne		II	II	310.545(a)(1)	
R533ES02EC	coal tar	antifungal		II	II	310.545(a)(22)(ii)	
R533ES02EC	coal tar	dandruff	psoriasis	ISIII	I	358.710(c)(1)	
R533ES02EC	coal tar	dandruff	seborrheic dermatitis	ISIII	I	358.710(b)(1)	
R533ES02EC	coal tar	dandruff		ISIII	I	358.710(a)(1)	
512OYT1CRR	cocoa butter	anorectal	protectant	I(e,i)	I(e,i)	346.14(a)(2)	
512OYT1CRR	cocoa butter	skin protectant	diaper rash		III	310.545(a)(18)(iii)	
512OYT1CRR	cocoa butter	skin protectant	fever blister/cold sore		I		
512OYT1CRR	cocoa butter	skin protectant		I	I	347.10(d)	
BBL281NWFG	coconut oil soap, aqueous	pediculicide					
BBL281NWFG	cod liver oil	anorectal	wound healing	II	II	310.545(a)(25)(i)	
BBL281NWFG	cod liver oil	cough/cold	antitussive	III(e,i)	III(e,i)	310.545(a)(26)(x)	
BBL281NWFG	cod liver oil	skin protectant	diaper rash	III	IIIE		[52 FR 30054]
BBL281NWFG	cod liver oil (in combination only)	anorectal	protectant	I(e,i)	I(e,i)	346.14(b)(2)	
Q830PW7520	codeine	cough/cold	antitussive	I	I	341.14(a)(2)(i)	oral
Q830PW7520	codeine	internal analgesic		II	II	310.545(a)(23)(i)	
Q830PW7520	codeine	menstrual/diuretic	analgesic	II		310.545(a)(24)(i)	
GSL05Y1MN6	codeine phosphate	cough/cold	antitussive	I	I	341.14(a)(2)(ii)	oral
GSL05Y1MN6	codeine phosphate	cough/cold					
11QV9BS0CB	codeine sulfate	cough/cold	antitussive	I	I	310.545(a)(23)(i)	oral
11QV9BS0CB	codeine sulfate	internal analgesic					
J9BTD5377V	collinsonia (extract stone root)	menstrual/diuretic	other	II(e,i)	II(e,i)	310.545(a)(26)(vii)	
IOS9HV04K7	collinsonia extract	anorectal		II	II	310.545(a)(7)	
8PI54V663Y	colloidal oatmeal	dandruff	astringent	II		310.545(a)(18)(ii)	
8PI54V663Y	colloidal oatmeal	skin protectant	diaper rash		III		
8PI54V663Y	colloidal oatmeal	skin protectant			I	347.10(f)	
8PI54V663Y	colloidal oatmeal	skin protectant			II	310.545(a)(12)(iv)(A)	
23H32AOH17	colocynth	laxative	stimulant laxative				(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
789U1901C5	copper	weight control			II	310.545(a)(20)	
789U1901C5	copper gluconate	weight control			II	310.545(a)(20)	
789U1901C5	copper oleate	pediculicide		II	II	310.545(a)(25)(i)	
789U1901C5	copper undecylenate	antifungal		I	I	333.210(f)	
8470G57WFM	corn oil	weight control			II	310.545(a)(20)	
	corn oil, aqueous emulsion	cholecystokinetic			I	357.210(a)	
7D3VB244UX	corn silk	menstrual/diuretic		II	II	310.545(a)(24)(i)	
O8232NY3SJ	corn silk, potassium extract	weight control			II	310.545(a)(20)	
9G5L16BK6N	corn starch	skin protectant			I	347.10(q)	
	corn syrup	weight control			II	310.545(a)(20)	
8K1MK5E1FY	cough grass	menstrual/diuretic				310.545(a)(24)(i)	
	creosote	relief of oral discomfort		IIIE			
	creosote	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	[52 FR 30054]
	creosote, beechwood	cough/cold	antitussive	III	IIIE	310.545(a)(10)(vii)	
	creosote, beechwood	external analgesic	poison ivy/oak/sumac				
	creosote, beechwood	relief of oral discomfort		IIIE			
	creosote, beechwood (oral)	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(A)	
	creosote, beechwood (topical)	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(B)	
1MXY2UM8NV	resol	oral health care	anesthetic/analgesic	II	IIIE		
		nonantimicrobial				310.545(a)(14)	
1MXY2UM8NV	resol	oral health care					
1MXY2UM8NV	resol	relief of oral discomfort		IIIE			
1MXY2UM8NV	resol	skin protectant	astringent	II	II	310.545(a)(18)(ii)	
1MXY2UM8NV	resol, saponated	dandruff		II	II	310.545(a)(7)	
LRX7AJI6DT	cupric sulfate	external analgesic					
LRX7AJI6DT	cupric sulfate	skin protectant	astringent	II		310.545(a)(18)(ii)	
LRX7AJI6DT	cupric sulfate	weight control			II	310.545(a)(20)	
P6YC3EG204	cyano cobalamin (vitamin B12)	weight control			II	310.545(a)(20)	
W001NHP4WE	cyclizine hydrochloride	antiemetic			I	336.10(a)	
7323N7T136	cyclomethycaine sulfate	external analgesic	analgesic and anesthetic	III	III	310.545(a)(10)(i)	
7323N7T136	cyclomethycaine sulfate	external analgesic	fever blister/cold sore	III	III	310.545(a)(10)(v)	
7323N7T136	cyclomethycaine sulfate	external analgesic	poison ivy/oak/sumac	III	III	310.545(a)(10)(vii)	
ZT934N0X4W	cysteine hydrochloride	skin protectant	diaper rash			310.545(a)(18)(iii)	
48TCX9A1VT	cystine	weight control			II	310.545(a)(20)	
Z4XE61BF3V	danthron	laxative	stimulant laxative		I	310.545(a)(12)(iv)(B)	
	<i>Datura stramonium</i>	cough/cold	anticholinergic		II	310.53	
NH5000009I	dehydrocholic acid	digestive aid		II	II	310.545(a)(8)(i)	
XY58INN1I6	dequalinium chloride	oral health care		IIIE	IIIE		
BPA9UT29BS	dexbromopheniramine maleate	cough/cold	antihistamine		I	341.12(d)	
B10YD955QW	dexchlorpheniramine maleate	cough/cold	antihistamine		I	341.12(e)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
I06C93RI7Z	dexpantenol	external analgesic	poison ivy/oak/sumac		IIIE	310.545(a)(10)(vii)	
I06C93RI7Z	dexpantenol	external analgesic			IIIE		
I06C93RI7Z	dexpantenol	skin protectant	diaper rash				
7SA290YK68	dextran 70	ophthalmic	demulcents	I	I	349.12(b)	
7355X3ROTS	dextromethorphan	cough/cold	antitussive	I	I	341.14(a)(3)	oral
9D2RT9KYH	dextromethorphan hydrobromide	cough/cold	antitussive	I	I	341.14(a)(4)	oral
IY9XDZ35W2	dextrose	weight control			II	310.545(a)(20)	
	diastase	digestive aid				310.545(a)(8)(ii)	
	diastase malt	digestive aid				310.545(a)(8)(ii)	
Z3D4AJ IR48	dibenzothioephene	acne		II	II	310.545(a)(1)	
L6JW2TJG99	dibucaine	anorectal	local anesthetic	III(e,i)	I(e),III(i)	346.10(c)	
L6JW2TJG99	dibucaine	external analgesic		I	I		
L6JW2TJG99	dibucaine	oral health care	anesthetic/analgesic	II	II	310.545(a)(14)	
Z97702A5DG	dibucaine hydrochloride	anorectal	local anesthetic	III(e,i)	I(e),III(i)	346.10(d)	
Z97702A5DG	dibucaine hydrochloride	external analgesic		I	I		
Z97702A5DG	dibucaine hydrochloride	oral health care	anesthetic/analgesic	II	II	310.545(a)(14)	
O7TSZ97GEP	dicalcium phosphate dihydrate	antiararies		II	NC	310.545(a)(2)(ii)	
O7TSZ97GEP	dicalcium phosphate dihydrate (see calcium phosphate, dibasic)	gingivitis/plaque			IIIE		
	dichlorodiphenyl trichloroethane (DDT)	pediculicide		II	II		
T1J0JOU640	dichlorophen	antifungal		III	III	310.545(a)(22)(ii)	
2UTZ0QC864	diethylhexyl butamido triazone	sunscreens		NA			
PGQ9BY2MDE	digalloyl trioleate	sunscreens		I	I	310.545(a)(29)	
D0250MG0W6	dihydroxyaluminum antacid	antacid			I	331.11(a)(3)	
	aminoacetate						
D0250MG0W6	dihydroxyaluminum aminoacetic acid	antacid				331.11(a)(3)	
84H8Z9550J	dihydroxyaluminum sodium carbonate	antacid			I	331.11(a)(5)	
84H8Z9550J	dihydroxyaluminum sodium carbonate	digestive aid	antacid	III	I	310.545(a)(8)(i)	
JB937PER5C	dimenhydrinate	antiemetic			I		
92RU3N3Y10	dimethicone	skin protectant	diaper rash		I	336.10(b)	
92RU3N3Y10	dimethicone	skin protectant			I		
92RU3N3Y10	dimethicone	skin protectant	fever blister/cold sore		I		
SMP2689462	dimethisoquin hydrochloride	external analgesic		I	I	347.10(g)	
F05Q2T2IA0	diocetyl sodium sulfosuccinate	pediculicide		II	II		

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
	diolamine methoxycinnamate (diethanolamine methoxycinnamate)	sunscreen		I	I	310.545(a)(29)	
B762XZ551X	dioxybenzone	sunscreen		I	I	352.10(e)	
2456GO94TR	dipiperdon	anorectal	anesthetic			310.545(a)(26)(vi)	
5YZSR8173Y	dipiperdon hydrochloride	corn/callus remover	II	IIIE		[55 FR 33261]	
5YZSR8173Y	dipiperdon hydrochloride	external analgesic				310.545(a)(10)(vii)	
5YZSR8173Y	dipiperdon hydrochloride	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
8GTS82S83M	diphenhydramine citrate	cough/cold	antihistamine			341.12(f)	
8GTS82S83M	diphenhydramine citrate	cough/cold	antitussive			341.14(a)(5)	oral
8GTS82S83M	diphenhydramine citrate	nighttime sleep aid				338.10(b)	
TC2D6JAD40	diphenhydramine hydrochloride	antiemetic			IIIIE	336.10(c)	
TC2D6JAD41	diphenhydramine hydrochloride	cough/cold	antihistamine	I	I	341.12(g)	
TC2D6JAD42	diphenhydramine hydrochloride	cough/cold	antitussive	III	IIIIE	341.14(a)(6)	oral
TC2D6JAD43	diphenhydramine hydrochloride	external analgesic		I	I		
TC2D6JAD44	diphenhydramine hydrochloride	nighttime sleep aid	antihistamine	III	IIIIE	338.10(a)	
TC2D6JAD45	diphenhydramine hydrochloride	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
	dipropylene glycol salicylate	sunscreen		III	IIIIE		58 FR 28281
6K7YS03HC	disodium hydrogen phosphate	antiacaries					
	docusate calcium sulfosuccinate	laxative	stool softener	II	NC	310.545(a)(2)(ii)	
CIK9F54ZHR	docusate potassium sulfosuccinate	laxative	stool softener				
	docusate sodium	pediculicide				310.545(a)(25)(i)	
F05Q2T2JA0	docusate sodium	weight control			II	310.545(a)(20)	
F05Q2T2JA0	docusate sodium sulfosuccinate	laxative	stool softener				
	dodecaethylene glycol monolaurate (polyethylene glycol 600 monola	vaginal contraceptive		IIIIE	310.545(a)(28)(i)		
8K1MK5EIFY	dog grass	digestive aid				310.545(a)(8)(ii)	
8K1MK5EIFY	dog grass extract	menstrual/diuretic		II	II	310.545(a)(24)(i)	
R4CY19YS7C	domiphen bromide	oral health care			IIIIE		
V9B19B5Y12	doxylamine succinate	cough/cold	antihistamine		I	341.12(h)	
V9B19B5Y12	doxylamine succinate	nighttime sleep aid	antihistamine	III	IIIE		[5 FR 6828]
5X93W9OFZL	drometrizole trisiloxane	sunscreen		NA			
	duodenal substance	digestive aid		II	II	310.545(a)(8)(i)	
ZEC193879Q	dyclonine hydrochloride	anorectal	local anesthetic		I	346.10(e)	
ZEC193879Q	dyclonine hydrochloride	external analgesic		I	I		
ZEC193879Q	dyclonine hydrochloride	oral health care	anesthetic/analgesic	I	I		(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
M94R1PM439	ecamsule	sunscreen		NA			
7FLD91C86K	edetate disodium	relief of oral discomfort		IIIE			
	elaterin resin	laxative	stimulant laxative		II	310.545(a)(12)(iv)(A)	
E55SMD6DA8	elecampane	digestive aid				310.545(a)(8)(ii)	
91QY4PXU8Q	elm bark	cough/cold	antitussive	III	IIIE		[52 FR 30054]
91QY4PXU8Q	elm bark	oral health care	demulcents	I	I		
9YQ9D11W42	ensulizole (phenylbenzimidazole sulfonic acid)	sunscreen		I	I	352.10(n)	
8I3XWY40L9	enzacamene	sunscreen					
	(4-methylbenzylidene camphor)						
GN83C131XS	ephedrine	cough/cold	bronchodilator	I	I	341.16(a)	
GN83C131XS	ephedrine (aqueous)	cough/cold	nasal decongestant		I	341.20(b)(2)	
GN83C131XS	ephedrine (jelly)	cough/cold	nasal decongestant	I	I	341.20(b)(2)	
GN83C131XS	ephedrine (oral)	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(B)	
NLJ6390P1Z	ephedrine hydrochloride	cough/cold	bronchodilator	I	I	341.16(b)	
NLJ6390P1Z	ephedrine hydrochloride	external analgesic	male genital desensitizer			310.545(a)(10)(iii)	
NLJ6390P1Z	ephedrine hydrochloride	ophthalmic	vasoconstrictor	I	I	349.18(a)	
NLJ6390P1Z	ephedrine hydrochloride (aqueous)	cough/cold	nasal decongestant		I	341.20(b)(3)	
NLJ6390P1Z	ephedrine hydrochloride (jelly)	cough/cold	nasal decongestant	I	I	341.20(b)(3)	
NLJ6390P1Z	ephedrine hydrochloride (oral)	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(B)	
U6X61U5ZEG	ephedrine sulfate	anorectal	vasoconstrictor	I	I	346.12(a)	
U6X61U5ZEG	ephedrine sulfate	cough/cold	bronchodilator	I	I	341.16(c)	
U6X61U5ZEG	ephedrine sulfate (aqueous)	cough/cold	nasal decongestant		I	341.20(b)(4)	
U6X61U5ZEG	ephedrine sulfate (jelly)	cough/cold	nasal decongestant	I	I	341.20(b)(4)	
U6X61U5ZEG	ephedrine sulfate (oral)	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(B)	
YKH834O4BH	epinephrine	anorectal	vasoconstrictor	III(e,i)	I(e),III(i)	346.12(b)	
YKH834O4BH	epinephrine	cough/cold	bronchodilator	I	I	341.16(d)	inhalation
YKH834O4BH	epinephrine	cough/cold	bronchodilator	I	I	341.16(d)	rubber bulb
30Q7K153AK	epinephrine bitartrate	cough/cold	bronchodilator	I	I	341.16(e)	inhalation
30Q7K153AK	epinephrine bitartrate	cough/cold	bronchodilator	I	I	341.16(e)	rubber bulb
WBB047OO38	epinephrine hydrochloride	anorectal	vasoconstrictor	I(e),II(i)	I(e),II(i)	346.12(c)	
WBB047OO38	epinephrine hydrochloride	cough/cold	bronchodilator	I	I		
	epinephrine undecylenate	anorectal	vasoconstrictor	I	I	310.545(a)(26)(ix)	
VS041H42XC	ergocalciferol	weight control			II	310.545(a)(20)	
X3S33EX3KW	ergot fluid extract	skin protectant	insect bites/stings			310.545(a)(18)(v)(A)	
X3S33EX3KW	ergot fluid extract	external analgesic	insect bite/sting			310.545(a)(10)(vi)	
514B9K0L10	<i>Escherichia coli</i> vaccine	anorectal	other			310.545(a)(26)(vii)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
2D19HA706A	estrone	acne		II	II	310.545(a)(1)	
0F5N573A2Y	ether	digestive aid				310.545(a)(8)(ii)	
M9JGK7U88V	ethohexadiol	dandruff		III	III	310.545(a)(7)	
54M9O2520I	ethyl 4-[[bis(hydroxypropyl)]aminobenzoate (roxadimate)	sunscreen		I	I	310.545(a)(29)	64 FR 27670
E1Z7886LR5	ethyl nitrate	menstrual/diuretic				310.545(a)(24)(i)	
MF5450P3T	ethymorphine hydrochloride	cough/cold	antitussive	III	IIIE		[52 FR 30054]
RV6J6604TK	eucalyptol	cough/cold	antitussive		IIIE		[52 FR 30055]
RV6J6604TK	eucalyptol	dandruff		III	III	310.545(a)(7)	
RV6J6604TK	eucalyptol	oral health care	anesthetic/analgesic	III	III	310.545(a)(14)	
RV6J6604TK	eucalyptol (lozenge)	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(A)	
RV6J6604TK	eucalyptol (mouthwash)	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(A)	
2R04ONI662	eucalyptol/eucalyptus oil	cough/cold	expectorant		III	310.545(a)(6)(iii)	
2R04ONI663	eucalyptus oil	cough/cold	antitussive	III	IIIE		[52 FR 30055]
2R04ONI664	eucalyptus oil	cough/cold	antitussive	III	IIIE		[52 FR 30054]
2R04ONI665	eucalyptus oil	cough/cold	antitussive	III	IIIE		[52 FR 30055]
2R04ONI666	eucalyptus oil	cough/cold	nasal decongestant	III	IIIE		[59 FR 43408]
2R04ONI667	eucalyptus oil	external analgesic	counterirritant	I	I	310.545(a)(10)(ii)	
2R04ONI668	eucalyptus oil	external analgesic	fever blister/cold sore	I	I	310.545(a)(10)(v)	
2R04ONI669	eucalyptus oil	external analgesic	poison ivy/oak/sumac	I	I	310.545(a)(10)(vii)	
2R04ONI670	eucalyptus oil	skin protectant	astringent	II		310.545(a)(18)(ii)	
2R04ONI671	eucalyptus oil	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
2R04ONI672	eucalyptus oil (lozenge)	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(A)	
2R04ONI673	eucalyptus oil (mouthwash)	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(A)	
3T8HI794QW	eugenol	external analgesic	analgesic and anesthetic	III	III	310.545(a)(10)(i)	
3T8HI794QW	eugenol	external analgesic	fever blister/cold sore	III	III	310.545(a)(10)(v)	
3T8HI794QW	eugenol	external analgesic	poison ivy/oak/sumac	III	III	310.545(a)(10)(vii)	
3T8HI794QW	eugenol	relief of oral discomfort		IIIE			
L13YF113GN	<i>Euphorbia piliulifera</i>	skin protectant	astringent	II		310.545(a)(18)(ii)	
	fennel acid	cough/cold	bronchodilator	III		310.545(a)(6)(iv)	
	ferric acid	digestive aid				310.545(a)(8)(ii)	
	ferric ammonium citrate	skin protectant	poison ivy/oak/sumac		II	310.545(a)(18)(vi)(A)	
UVP74NG1C5	ferric chloride	weight control	insect bite/sting			310.545(a)(20)	
U38V3ZVV3V	ferric chloride	external analgesic				310.545(a)(10)(vi)	
U38V3ZVV3V	ferric chloride	menstrual/diuretic				310.545(a)(24)(i)	
U38V3ZVV3V	ferric chloride	oral health care		IIIE			
U38V3ZVV3V	ferric chloride	skin protectant	insect bites/stings			310.545(a)(18)(v)(A)	
QK8899250F	ferric pyrophosphate	weight control		II		310.545(a)(20)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
3QJ8W56V8H	ferric subsulfate (Monsel's solution)	skin protectant	astringent	II		310.545(a)(18)(ii)	
R5L488RY0Q	ferrous fumarate	weight control			II	310.545(a)(20)	
U1B11I423Z	ferrous gluconate	weight control			II	310.545(a)(20)	
39R4TANI VT	ferrous sulfate	menstrual/diuretic				310.545(a)(24)(i)	
39R4TANI VT	ferrous sulfate (iron)	weight control			II	310.545(a)(20)	
4110YT348C	flax seed	weight control			II	310.545(a)(20)	
800FG3WPTYD	fluorosalan	antimicrobial			IIS		
935E97BOY8	folic acid	weight control			II	310.545(a)(20)	
1HG84L3525	formaldehyde solution	relief of oral discomfort		IIIE			
0YIW783RG1	formic acid	pediculicide				310.545(a)(25)(i)	
S2D77IH6 IR	frangula	laxative	stimulant laxative		III	310.545(a)(12)(iv)(A)	[48 FR 32873]
6YSS42VSEV	fructose	overindulgence in alcohol	inebriation minimizer		IIIE		
6YSS42VSEV	fructose	weight control			II	310.545(a)(20)	
BIA2SO6F5B	galega	digestive aid				310.545(a)(8)(ii)	
7556HI7587	gamboge	laxative	stimulant laxative		II	310.545(a)(12)(iv)(A)	
V1V998DC17	garlic, dehydrated	digestive aid		II	II	310.545(a)(8)(i)	
2G86QN327L	gelatin	ophthalmic	demulcents	I	I	349.12(c)	
2G86QN327L	gelatin	oral health care	demulcents	I	I		
J4Z741D6O5	gentian violet	oral health care			IIIE		
J4Z741D6O5	gentian violet	anthelmintic		I	II		
S72O3284MS	<i>Gentiana lutea</i> (gentian)	menstrual/diuretic				310.545(a)(24)(i)	
C5529G5JPQ	ginger	digestive aid				310.545(a)(8)(ii)	
ZQH6VH092Z	ginseng	nighttime sleep aid			II		
ZQH6VH092Z	ginseng	stimulant			IIIE		[39 FR 6104]
3KX376GY7L	glutamic acid hydrochloride	digestive aid	stomach acidifier	II	II	310.545(a)(8)(i)	
PDC6A3C00X	glycerin	anorectal	protectant	I(e)	I(c)	346.14(a)(3)	
PDC6A3C00X	glycerin	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
PDC6A3C00X	glycerin	laxative	hyperosmotic		I		
PDC6A3C00X	glycerin	ophthalmic	demulcents	I	I	349.12(d)(1)	
PDC6A3C00X	glycerin	oral health care			I		
PDC6A3C00X	glycerin	otic			IIIE		
PDC6A3C00X	glycerin	skin protectant	diaper rash	I	IIIE	310.545(a)(18)(iii)	
PDC6A3C00X	glycerin	skin protectant	fever blister/cold sore		I		
PDC6A3C00X	glycerin	skin protectant	insect bites/stings		IIIE	310.545(a)(18)(vi)	
PDC6A3C00X	glycerin	skin protectant	skin protectant	I	I	347.10(h)	
PDC6A3C00X	glycerin	otic				310.545(a)(15)(ii)	
PDC6A3C00X	glycerin and anhydrous glycerin	skin protectant	diaper rash		III	310.545(a)(18)(iii)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
PDC6A3C00X	glycerin and anhydrous glycerin	skin protectant	poison ivy/oak/sumac	I	I	310.545(a)(18)(vi)(A)	64 FR 27670
A886B5N1IM	glyceryl aminobenzoate (lisadimate, glyceryl PABA)	sunscreen				310.545(a)(29)	
230OU9XXE4	glyceryl stearate	skin protectant	insect bites/stings w/ sales less than \$25,000		310.545(a)(18)(v)(B)		
230OU9XXE4	glyceryl stearate	skin protectant	poison ivy/oak/sumac w/ sales less than \$25,000	310.545(a)(18)(vi)(B)			
230OU9XXE4	glyceryl stearate	skin protectant	w/ sales less than \$25,000			310.545(a)(18)(i)(B)	
TE7660XO1C	glycine	antidiarrheal		II	II	310.545(a)(3)(i)	
TE7660XO1C	glycine	digestive aid				310.545(a)(8)(ii)	
TE7660XO1C	glycine (aminoacetic acid)	antacid			I	331.11(f)	
	glycol salicylate	external analgesic	fever blister/cold sore	III	III	310.545(a)(10)(v)	
	glycol salicylate	external analgesic	poison ivy/oak/sumac	III	III	310.545(a)(10)(vii)	
61ZBX54883	glycyrrhiza (licorice)	menstrual/diuretic				310.545(a)(24)(i)	
5IE6232IP4	gramicidin	first aid antibiotic			III		
495W7451VQ	guaifenesin	cough/cold	expectorant		IIIE	341.18	
E8911637KE	guar gum	laxative	bulk laxative		III	310.545(a)(12)(i)	
E8911637KE	guar gum	weight control			III	310.545(a)(20)	
AIU7053OWL	haloprogin	antifungal		I	I	333.210(b)	
8334LX7S21	hard fat	anorectal	protectant			346.14(a)(4)	
8334LX7S21	hard fat	skin protectant				347.10(i)	
	hectorite	digestive aid				310.545(a)(8)(ii)	
	hectorite	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
	hectorite	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
IWW5FV6NK2	hemicellulase	digestive aid		III	III	310.545(a)(8)(i)	[37 FR 20163]
R9QTB5E82N	hexachlorophene	antimicrobial			I		
R9QTB5E82N	hexylresorcinol	antimicrobial			III		
R9QTB5E82N	hexylresorcinol	antimicrobial			IIIE		
R9QTB5E82N	hexylresorcinol	antimicrobial			IIIE		
R9QTB5E82N	hexylresorcinol	external analgesic	analgesic and anesthetic	III	III	310.545(a)(10)(i)	
R9QTB5E82N	hexylresorcinol	external analgesic	fever blister/cold sore	III	III	310.545(a)(10)(v)	
R9QTB5E82N	hexylresorcinol	external analgesic	poison ivy/oak/sumac	III	III	310.545(a)(10)(vii)	
R9QTB5E82N	hexylresorcinol	oral health care	anesthetic/analgesic	I	I		
R9QTB5E82N	hexylresorcinol	external analgesic	fever blister/cold sore			310.545(a)(10)(v)	
3POAQ0644U	histamine dihydrochloride	weight control			II	310.545(a)(20)	
4QD397987E	histidine	antidiarrheal		III	III	310.545(a)(3)(i)	
68JRS2HC1C	homatropine methylbromide	digestive aid		II/III	III	310.545(a)(8)(i)	
68JRS2HC1C	homatropine methylbromide	menstrual/diuretic	muscle relaxant	II	II	310.545(a)(24)(i)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
V06SV4M95S	homosalate	sunscreen		I	I	352.10(f)	
Y9H1V576FH	honey	skin protectant	astringent	II		310.545(a)(18)(ii)	[52 FR 30054]
7A72MUN24Z	horehound	cough/cold	antitussive	III	IIIE		
7A72MUN24Z	horehound	cough/cold	expectorant			310.545(a)(6)(iii)	
7A72MUN24Z	horehound	oral health care	expectorant	III			
SC52PT1846	horsetail	digestive aid				310.545(a)(8)(ii)	
9P2U39H18W	huckleberry	digestive aid				310.545(a)(8)(ii)	
65806T0WXX	hydrastis	anorectal	antiseptic	II(e.i)	II(e.i)	310.545(a)(26)(ii)	
65806T0WXX	hydrastis	anorectal	counterirritant	II(e.i)	II(e.i)	310.545(a)(26)(iv)	
S1EFO94F35	<i>Hydrastis canadensis</i>	weight control			II	310.545(a)(20)	
ZW3Z11D0JV	<i>Hydrastis canadensis</i> (golden seal)	digestive aid				310.545(a)(8)(ii)	
ZW3Z11D0JV	<i>Hydrastis canadensis</i> (golden seal)	menstrual/diuretic		II	II	310.545(a)(24)(i)	
1E8C2W13Z0	hydrastis fluid extract	digestive aid					
	hydrate magnesium aluminate	antacid				310.545(a)(8)(ii)	
	activated sulfate					331.11(g)(1)	
QTT17582CB	hydrochloric acid	digestive aid					
NO70W886KK	hydrocodone bitartrate	cough/cold	antitussive	II	IIS	310.545(a)(8)(ii)	[52 FR 30054]
W14X0X7BPJ	hydrocortisone	external analgesic		I	I		
W14X0X7BPJ	hydrocortisone (0.25-5%)	external analgesic		I	I		
W14X0X7BPJ	hydrocortisone (0.5-1%)	external analgesic			IIISE		
W14X0X7BPJ	hydrocortisone (combination)	anorectal				310.545(a)(26)(xi)	
3X7931PO74	hydrocortisone acetate	external analgesic		I	I		
3X7931PO75	hydrocortisone acetate	external analgesic		I	I		
3X7931PO76	hydrocortisone acetate (0.25-5.0%)	external analgesic		I	I		
3X7931PO77	hydrocortisone acetate (0.25%-0.5%)	external analgesic		I	I		
	hydrocortisone preparations						
RGL5YE86CZ	hydrogen fluoride	dandruff					
BBX060AN9V	hydrogen peroxide	antiacaries		III	IS	310.545(a)(2)(i)	
BBX060AN9V	hydrogen peroxide	antimicrobial		NC	III		
BBX060AN9V	hydrogen peroxide	external analgesic			I		
BBX060AN9V	hydrogen peroxide	oral health care				310.545(a)(10)(vii)	
BBX060AN9V	hydrogen peroxide	oral health care		I	I		
BBX060AN9V	hydrogen peroxide	oral health care		III	III		
BBX060AN9V	hydrogen peroxide	oral health care		IIIE	IIIE		
BBX060AN9V	hydrogen peroxide	skin protectant				310.545(a)(18)(vi)(A)	
BBX060AN9V	hydrogen peroxide and povidone iodine	gingivitis/plaque			IIISE		

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
BBX060AN9V	hydrogen peroxide and sodium bicarbonate	gingivitis/plaque			IIISE		
BBX060AN9V	hydrogen peroxide, sodium citrate, sodium lauryl sulfate, and zinc ch	gingivitis/plaque			IIISE		
XV74CIN1AE	hydroquinone	skin bleach			I		
273FM27VK1	hydroxyethylcellulose	ophthalmic	demulcents	I	I	349.12(a)(2)	
F2R8V82B84	hydroxypropyl methylcellulose	ophthalmic	demulcents	I	I		
F2R8V82B84	hyoscamine sulfate	antidiarrheal		III	III	310.545(a)(3)(i)	
3NXW29V3WO	hyoscamine sulfate	menstrual/diuretic				310.545(a)(24)(i)	
WK2XY110QM	hypromellose	ophthalmic	demulcents		I	349.12(a)(3)	
	ibuprofen	internal analgesic			I		[67 FR 54139]
	ichthammol	corn/callus remover	II	IIISE		[55 FR 33261]	
SY15A62UPX	<i>Impatiens biflora</i> tincture	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
SY15A62UPX	<i>Impatiens biflora</i> tincture	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
969IQCSYJU	infusion of rose petals	ophthalmic	astringent	III	III	310.545(a)(21)(iii)	
4L6452S749	inositol	weight control			II	310.545(a)(20)	
	iodides (calcium iodide anhydrous, hydriodic acid syrup, iodized lim	cough/cold	expectorant		II	310.545(a)(6)(iii)	
9679TC07X4	iodine	corn/callus remover	II	IIISE		[55 FR 33261]	
9679TC07X5	iodine	digestive aid				310.545(a)(8)(ii)	
9679TC07X6	iodine	oral health care			IIISE		
9679TC07X7	iodine	wart remover		II	IISE		[55 FR 33254]
9679TC07X8	iodine	weight control			II	310.545(a)(20)	
	iodine complex/phosphate ester of alkylaryl/oxyl polyethylene	antimicrobial			IIISE		
	iodine complex/phosphate ester of alkylaryl/oxyl polyethylene	antimicrobial			IISE		
9679TC07X10	iodine tincture	antimicrobial			IISE		
9679TC07X11	iodine tincture	antimicrobial			IISE		
9679TC07X4	iodine tincture	antimicrobial			I		
9679TC07X5	iodine tincture	antimicrobial			I		
9679TC07X6	iodine tincture	antimicrobial			IIIS		
9679TC07X7	iodine tincture	antimicrobial			IIIS		
9679TC07X8	iodine tincture	antimicrobial			IIISE		
9679TC07X9	iodine tincture	antimicrobial			IIIS		
9679TC07X4	iodine topical solution	antimicrobial			I		

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
V30V6H1QX4	idoantipyrene (idopyrine)	internal analgesic		II	II	310.545(a)(23)(i)	
62I3C8233L	ipecac	cough/cold	expectorant			310.545(a)(6)(iii)	
62I3C8233L	ipecac fluid extract	cough/cold	expectorant		II	310.545(a)(6)(iii)	
62I3C8233L	ipecac fluid extract	poison treatment			II	310.545(a)(16)	
62I3C8233L	ipecac syrup	cough/cold	expectorant		III	310.545(a)(6)(iii)	
62I3C8233L	ipecac syrup	emetic			I	337.10	
62I3C8233L	ipecac syrup	poison treatment			I		
62I3C8233L	ipecac tincture	poison treatment			II	310.545(a)(16)	
62I3C8233L	ipomea	laxative	stimulant laxative		II	310.545(a)(12)(iv)(A)	
	iron ox bile	digestive aid				310.545(a)(8)(ii)	
1K09F3G675	iron oxide	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
1K09F3G675	iron oxide	skin protectant	poison ivy/oak/sumac	II	II	310.545(a)(18)(vi)(A)	
	isobornyl thiocyanacetate	pediculicide				310.545(a)(25)(i)	
04Y7590D77	isoleucine	weight control		I	II	310.545(a)(20)	
ND2M416302	isopropyl alcohol	alcohols (topical)	poison ivy/oak/sumac	I	I	310.545(a)(10)(vii)	
ND2M416303	isopropyl alcohol	external analgesic					
ND2M416304	isopropyl alcohol	mercury				344.12	
ND2M416305	isopropyl alcohol	otic				310.545(a)(15)(ii)	
ND2M416306	isopropyl alcohol	otic				310.545(a)(18)(ii)	
ND2M416307	isopropyl alcohol	skin protectant	astrigent	II			
ND2M416308	isopropyl alcohol	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
8CRQ2TH63M	isopropyl palmitate	skin protectant	insect bites/stings w/ sales less than \$25,000		310.545(a)(18)(v)(B)		
8CRQ2TH63M	isopropyl palmitate	skin protectant	poison ivy/oak/sumac w/ sales less than \$25,000	310.545(a)(18)(vi)(B)			
8CRQ2TH63M	isopropyl palmitate	skin protectant	w/ sales less than \$25,000				
4UDO46YBK2	jalap	laxative	stimulant laxative		II	310.545(a)(18)(i)(B)	
XK4IUX8MNB	johnswort	digestive aid				310.545(a)(12)(iv)(A)	
YNW2QPG8YK	juniper oil (oil of juniper)	menstrual/diuretic		II	II	310.545(a)(8)(ii)	
	juniper tar	anorectal	analgesic, anesthetic, antipruritic	III(e.i)	I(e)	346.16(b)	
	juniper tar	dandruff		III	III	310.545(a)(7)	
	juniper tar	digestive aid				310.545(a)(8)(ii)	
	juniper tar	external analgesic		I	I		
	juniper, potassium extract	weight control			II	310.545(a)(20)	
24H4NWX5C0	kaolin	anorectal	protectant	I(e.i)	I(e.i)	346.14(a)(5)	
24H4NWX5C0	kaolin	antidiarrheal		III	III	335.10(b)	
24H4NWX5C0	kaolin	skin protectant	diaper rash		I		

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
24H4NWX5CO	kaolin	skin protectant		I	I	347.10(j)	
24H4NWX5CO	kaolin, colloidal	digestive aid				310.545(a)(8)(ii)	
	karaya gum	laxative			I		
	karaya gum	weight control			III	310.545(a)(20)	
	kelp	weight control			III	310.545(a)(20)	
64Y2IV7284	knotgrass	digestive aid				310.545(a)(8)(ii)	
33X04XA5AT	lactic acid	digestive aid				310.545(a)(8)(ii)	
33X04XA5AT	lactic acid	wart remover				310.545(a)(8)(ii)	
	<i>Lactobacillus acidophilus</i>			III	IIIE		[55 FR 33254]
J2B2A4N98G	<i>Lactobacillus bulgaricus</i>	antidiarrheal		III	III	310.545(a)(3)(i)	
J2B2A4N98G		antidiarrheal		III	III	310.545(a)(3)(i)	
7EV65EAW6H		digestive aid		III	III	310.545(a)(8)(ii)	
7EV65EAW6H		weight control			II	310.545(a)(20)	
7EV65EAW6H		anorectal	protectant	I(e,i)	I(e,i)	346.14(a)(6)	
7EV65EAW6H		external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
7EV65EAW6H		skin protectant	diaper rash		I		
7EV65EAW6H		skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
7EV65EAW6H		skin protectant	poison ivy/oak/sumac		IIE	310.545(a)(18)(vi)	
7EV65EAW6H		skin protectant				347.10(k)	
7EV65EAW6H		ophthalmic	emollient	I	I	349.14(a)(2)	
	lanolin (in combination)	ophthalmic	protectant	I(e,i)	III(e,i)	310.545(a)(26)(viii)	
	lanolin alcohols	anorectal		I	I	349.14	
	lanolin nonionic derivatives	ophthalmic		I	I		
	lanolin, anhydrous (in combination)	ophthalmic	emollient	I	I	349.14(a)(1)	
	lappa extract	anorectal	other	II(e,i)	II(e,i)	310.545(a)(26)(vii)	
	laureth 10S	vaginal contraceptive		IIIE	310.545(a)(28)(i)		
09TM5K0O34	lauryl isoquinolinium bromide	dandruff		III	III	310.545(a)(7)	
9YT4B7IU8P	lavender compound, tincture of	digestive aid				310.545(a)(8)(ii)	
TLH4A6LV1W	lawsone (w/ dihydroxyacetone)	sunscreen		I	I	310.545(a)(29)	
RX077P88RY	lead acetate	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
RX077P88RY	lead acetate	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
	lecithin	weight control			II	310.545(a)(20)	
	leptandra extract	anorectal	other	II(e,i)	II(e,i)	310.545(a)(26)(vii)	
GMW67QNF9C	leucine	weight control			II	310.545(a)(20)	
Y24T9BT2Q2	levmetamfetamine	cough/cold	nasal decongestant		I	341.20(b)(1)	inhalant
Y24T9BT2Q2	levmetamfetamine	cough/cold	nasal decongestant		I	341.20(b)(1)	topical
98PI200987	lidocaine	anorectal	local anesthetic	III(e,i)	I(e),III(i)	346.10(f)	
98PI200988	lidocaine	external analgesic	male genital desensitizer		I	348.10(a)(2)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
98PL200989	lidocaine	external analgesic		I	I		
98PL200990	lidocaine	oral health care	anesthetic/analgesic	II	II	310.545(a)(14)	
98PL200991	lidocaine	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
V13007Z41A	lidocaine hydrochloride	external analgesic		I	I		
V13007Z41A	lidocaine hydrochloride	oral health care	anesthetic/analgesic	II	II	310.545(a)(14)	
CFN6G1F6YK	linden	digestive aid				310.545(a)(8)(ii)	
	lipase	digestive aid				310.545(a)(8)(ii)	
3NY3SM6B8U	live yeast cell derivative	anorectal	other			310.545(a)(26)(vii)	
3NY3SM6B8U	live yeast cell derivative	anorectal	wound healing	III(e,i)	III(e,i)	310.545(a)(26)(x)	
3NY3SM6B8U	live yeast cell derivative	skin protectant	insect bites/stings w/ sales less than \$2	III	III	310.545(a)(18)(v)(B)	
3NY3SM6B8U	live yeast cell derivative	skin protectant	poison ivy/oak/sumac w/ sales less than \$2	III	III	310.545(a)(18)(vi)(B)	
3NY3SM6B8U	live yeast cell derivative	skin protectant	w/ sales less than \$25,000	III	III	310.545(a)(18)(i)(B)	
K3Z4F929H6	lysine	weight control		II	II	310.545(a)(20)	
	lysine aspirin	weight control		II	II	310.545(a)(20)	
JN123Q2COM	lysine hydrochloride	internal analgesic				310.545(a)(23)(i)	
JN123Q2COM	lysine hydrochloride	digestive aid				310.545(a)(8)(ii)	
GG04Y809LO	lysine hydrochloride	weight control		II	II	310.545(a)(20)	
	m-cresol	antifungal				310.545(a)(22)(iv)	
	magaldrate	antacid		I	I	331.11(g)(2)	
I38ZP9992A	magnesium	weight control		II	II	310.545(a)(20)	
6M2P64V0NC	magnesium aluminosilicate	antacid		I	I	331.11(g)(3)	
6M2P64V0NC	magnesium aluminosilicate	antacid		I	I	331.11(l)(1)	
6M2P64V0NC	magnesium aluminum silicate	acne		I	I	310.545(a)(1)	
0E53J927NA	magnesium carbonate	antacid		I	I	331.11(g)(4)	
0E53J927NA	magnesium carbonate	overindulgence in alcohol	hangover reliever	I	I		
RHO2601T9V	magnesium citrate (oral)	laxative	saline laxative	I	I		
IFN18A4Y6B	magnesium glycinate	antacid		I	I	331.11(g)(5)	
NBZ3QY004S	magnesium hydroxide	antacid		I	I	331.11(g)(6)	
NBZ3QY004S	magnesium hydroxide	digestive aid	antacid	III	I	310.545(a)(8)(i)	
NBZ3QY004S	magnesium hydroxide	laxative	saline laxative	I	I		
3A3U0G171G	magnesium oxide	antacid		I	I	331.11(g)(7)	
3A3U0G171G	magnesium oxide	weight control		II	II	310.545(a)(20)	
41728CY7UX	magnesium salicylate	internal analgesic		I	I		
41728CY7UX	magnesium salicylate	menstrual/diuretic	analgesic	I	I		
DE08037SAB	magnesium sulfate	acne		II	II	310.545(a)(1)	
DE08037SAB	magnesium sulfate	laxative	saline laxative	I	I		

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
DE08037SAB	magnesium sulfate	menstrual/diuretic				310.545(a)(24)(i)	
C2E1C1501T	magnesium trisilicate	antacid			I	331.11(g)(8)	
C2E1C1501T	magnesium trisilicate	antacid			I	331.11(l)(2)	
C2E1C1501T	magnesium trisilicate	digestive aid	antacid	III	I	310.545(a)(8)(i)	
C2E1C1501T	magnesium trisilicate	overindulgence in alcohol	hangover reliever		I		
	malt	weight control			II	310.545(a)(20)	
R3NBG8914U	malt soup extract	laxative			I		
7CVR7L4A2D	maltodextrin	weight control			II	310.545(a)(20)	
4Z20A6A13N	manganese citrate	weight control			II	310.545(a)(20)	
3OWL53L36A	mannitol	digestive aid				310.545(a)(8)(ii)	
3OWL53L36A	mannitol	weight control			II	310.545(a)(20)	
HDP7W44C1O	meclizine hydrochloride	antiemetic			I	336.10(d)	
	menfegol	vaginal contraceptive		I			
L7T10EIP3A	menthol	antifungal		II	II	310.545(a)(22)(ii)	
L7T10EIP3A	menthol	dandruff		III	III	310.545(a)(7)	
L7T10EIP3A	menthol	skin protectant	astringent	II		310.545(a)(18)(ii)	
LT10EIP3A	menthol	anorectal	analgesic, anesthetic, antipruritic		I(e)	346.16(c)	
LT10EIP3A	menthol	anorectal	counterirritant	II(e.i)	II(e.i)	310.545(a)(26)(iv)	steam inhalation
LT10EIP3A	menthol	cough/cold	antitussive		IIIE	341.14(b)(2)	lozenge
LT10EIP3A	menthol	cough/cold	antitussive	III	IIIE	341.14(b)(2)	lozenge
LT10EIP3A	menthol	cough/cold	antitussive	III	I	341.14(b)(2)	lozenge
LT10EIP3A	menthol	cough/cold	antitussive	III	I	341.14(b)(2)	topical
LT10EIP3A	menthol	cough/cold	nasal decongestant	III	IIIE		[59 FR 43408]
LT10EIP3A	menthol	external analgesic		I	I		
LT10EIP3A	menthol	oral health care	anesthetic/analgesic	I	I		
LT10EIP3A	menthol	relief of oral discomfort		IIS			
LT10EIP3A	menthol	skin protectant	insect bites/stings			310.545(a)(18)(v)(A)	
LT10EIP3A	menthol	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
LT10EIP3A	menthol	wart remover		II	IIIE		[55 FR 33254]
LT10EIP3A	menthol (0.1 to 1.0%)	external analgesic		I	I		
LT10EIP3A	menthol (mouthwash)	cough/cold	antihistamine	III	III	310.545(a)(6)(ii)(A)	
LT10EIP3A	menthol exceeding 1%	external analgesic	fever blister/cold sore			310.545(a)(10)(v)	
L7T10EIP3A	menthol/peppermint oil	cough/cold	expectorant		III	310.545(a)(6)(iii)	
J9QG600UZZ	meradimate (menthyl anthranilate)	sunscreen		I	I	352.10(h)	
	meralein sodium	oral health care			IIIE		
M0T18YH28D	merbromin	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
M0T18YH28D	metbromin	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
M0T18YH28D	metbromin (mercuochrome)	antimicrobial	first aid antiseptic			310.545(a)(27)(i)	
	merufenol chloride	antimicrobial	first aid antiseptic			310.545(a)(27)(i)	
	(ortho)chloromercuriphenol, orthohydroxyphenyl						
53GH7MZT1R	mercuric chloride	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
53GH7MZT1R	mercuric chloride	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
53GH7MZT1R	mercuric chloride (bichloride of mercury, mercury chloride)	antimicrobial	first aid antiseptic			310.545(a)(27)(i)	
IY191986AO	mercuric oxide, yellow	antimicrobial	first aid antiseptic			310.545(a)(27)(i)	
	mercuric salicylate	antimicrobial	first aid antiseptic			310.545(a)(27)(i)	
	mercuric sulfide, red	antimicrobial	first aid antiseptic			310.545(a)(27)(i)	
FXS1BY2PGL	mercury	antimicrobial	first aid antiseptic			310.545(a)(17)	
	mercury, ammoniated	skin bleach				310.545(a)(27)(i)	
	mercury oleate	antimicrobial	first aid antiseptic	II	II	310.545(a)(7)	
	mercury oleate	dandruff				310.545(a)(27)(i)	
	mercury sulfide	antimicrobial	first aid antiseptic			310.545(a)(27)(i)	
	mercury-containing ingredient	antimicrobial	diaper rash		310.545(a)(28)(i)	310.545(a)(27)(iii)	
	mercury-containing ingredients	vaginal contraceptive					
GJ20H50YF0	metaproterenol sulfate	cough/cold	antihistamine	I	I	310.545(a)(6)(iv)	
KJ5I25TXYL	methapyrilene fumarate	cough/cold	antihistamine	I	II	310.545(a)(6)(i)	
KJ5I25TXYL	methapyrilene fumarate	internal analgesic		III	II	310.545(a)(23)(i)	
KJ5I25TXYL	methapyrilene fumarate	nighttime sleep aid	antihistamine	II	IIS		[54 FR 6826]
00S42N58OM	methapyrilene hydrochloride	cough/cold	antihistamine	I	II	310.545(a)(6)(i)	
00S42N58OM	methapyrilene hydrochloride	external analgesic	analgesic and anesthetic	I	II	310.545(a)(10)(i)	
00S42N58OM	methapyrilene hydrochloride	external analgesic	fever blister/cold sore	I	II	310.545(a)(10)(v)	
00S42N58OM	methapyrilene hydrochloride	external analgesic	poison ivy/oak/sumac	I	II	310.545(a)(10)(vii)	
00S42N58OM	methapyrilene hydrochloride	menstrual/diuretic				310.545(a)(24)(i)	
00S42N58OM	methapyrilene hydrochloride	nighttime sleep aid	antihistamine	II	IIS		[54 FR 6826]
J50OIX95QV	methenamine	menstrual/diuretic				310.545(a)(24)(i)	
AE28F7PNPL	methionine	weight control			II	310.545(a)(20)	
52V8BVV7FX	methoxyphenamine	cough/cold	bronchodilator	I	II	310.545(a)(6)(iv)	
	hydrochloride						
	methoxypolyoxyethyleneglycol	vaginal contraceptive		IIIE	310.545(a)(28)(i)		
7B1AVU9DJN	550 laurate						
LAV5U5022Y	methyl nicotinate	external analgesic	fever blister/cold sore			310.545(a)(10)(v)	
	methyl salicylate	corn/callus remover	II	IIIE		[55 FR 33261]	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
LAV5U5022Y	methyl salicylate	dandruff		III	III	310.545(a)(7)	
LAV5U5022Y	methyl salicylate	external analgesic	fever blister/cold sore			310.545(a)(10)(v)	
LAV5U5022Y	methyl salicylate	oral health care	anesthetic/analgesic	III	III	310.545(a)(14)	
LAV5U5022Y	methyl salicylate	relief of oral discomfort		IISE			
LAV5U5022Y	methyl salicylate	skin protectant	astringent			310.545(a)(18)(ii)	
	methy/benzethonium chloride	antimicrobial			I		
	methy/benzethonium chloride	antimicrobial			IIIE		
	methy/benzethonium chloride	antimicrobial			IIISE		
	methy/benzethonium chloride	antimicrobial			IISE		
	methy/benzethonium chloride	corn/callus remover	II	IISE		[55 FR 33261]	
	methy/benzethonium chloride	dandruff		III	III	310.545(a)(7)	
4GFU244C4J	methy/ce/lululose	laxative		I	I	349.12(a)(4)	
4GFU244C4J	methy/ce/lululose	ophthalmic	demulcents		I	310.545(a)(20)	
4GFU244C4J	methy/ce/lululose	weight control		III	III	310.545(a)(24)(i)	
T42P99266K	methy/ene blue	menstrual/diuretic				310.545(a)(22)(ii)	
A28C7HI9T	methy/lparaben	antifungal		III	III	333.210(c)	
VW4HI1CYW1K	miconazole nitrate	antifungal		I	I	310.545(a)(21)(ii)	
	mild silver protein	ophthalmic	anti-infective	III	II	331.11(h)	
917J3173FT	milk solids, dried	antacid			I		
N6K5787QVP	mineral oil	skin protectant	diaper rash		I		
T5L8T28FGP	mineral oil	anorectal	protectant	I(e,i)	I(e,i)	346.14(a)(7)	
T5L8T28FGP	mineral oil	laxative	lubricant	I	I		
T5L8T28FGP	mineral oil	ophthalmic	emollient	I	I	349.14(b)(2)	
T5L8T28FGP	mineral oil	skin protectant			I	347.10(l)	
T5L8T28FGP	mineral oil, light	ophthalmic	emollient	I	I	349.14(b)(l)	
	mono- and diglycerides	weight control			II	310.545(a)(20)	
9936O846LI	mullein	anorectal	other	II(e,i)	II(e,i)	310.545(a)(26)(vii)	
N4G8379626	mustard oil (allitishthiocyanate) (topical/inhalant)	cough/cold	nasal decongestant	II	II		
	mycozyme	digestive aid				310.545(a)(8)(ii)	
JC71GJ1F3L	myrrh	relief of oral discomfort		IIISE			
JC71GJ1F3L	myrrh, fluid extract of	digestive aid				310.545(a)(8)(ii)	
JC71GJ1F3L	myrrh tincture	oral health care	astringent	II	II	310.545(a)(14)	
MZ1131787D	naphazoline hydrochloride	cough/cold	nasal decongestant		I	341.20(b)(6)	
MZ1131787D	naphazoline hydrochloride	ophthalmic	vasoconstrictor	I	I	349.18(b)	
MZ1131787D	naphazoline hydrochloride (jelly)	cough/cold	nasal decongestant	I	I	341.20(b)(6)	
	natural estrogenic hormone	menstrual/diuretic				310.545(a)(24)(i)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
I16QD7X297	neomycin ointment (combination only)	first aid antibiotic			I	333.120	
057Y626693	neomycin sulfate	first aid antibiotic	ointment		I	333.110(d)	
057Y626693	neomycin sulfate cream	first aid antibiotic			I	333.110(e)	
0GG6WU2KW	nettle	digestive aid				310.545(a)(8)(ii)	
25X51I8RD4	niacinamide	menstrual/diuretic				310.545(a)(24)(i)	
25X51I8RD4	niacinamide	nighttime sleep aid			II		
25X51I8RD4	niacinamide	weight control			II	310.545(a)(20)	
	nickel-pectin	digestive aid				310.545(a)(8)(ii)	
RU6242GP15	nitromersol	antimicrobial	first aid antiseptic		IISE	310.545(a)(27)(i)	
RU6242GP15	nitromersol	oral health care		I			
nonylphenoxypoly	nonoxynol 9	vaginal contraceptive					
	nonylphenoxypoly (ethylenedioxy)	antimicrobial			IIIE		
	ethanol iodine	antimicrobial			IIIE		
	nonylphenoxypoly (ethylenedioxy)	antimicrobial			IIIE		
	ethanol iodine	antimicrobial			IIIE		
	noscipine	cough/cold	antitussive	III	IIIIE		[52 FR 30054]
	noscipine hydrochloride	cough/cold	antitussive	III	IIIIE		[52 FR 30054]
AEE24M3MQ9	nutmeg oil (oil of nutmeg)	menstrual/diuretic				310.545(a)(24)(i)	
269XH13919	<i>Nux vomica</i> extract	digestive aid				310.545(a)(8)(ii)	
BDF1O1C72E	nystatin	antifungal		I	III	310.545(a)(22)(iv)	
	obundia surgical dressing	external analgesic			IIIE		
	obundia surgical dressing	skin protectant			IIIE		
4Y5P7MUD51	octinoxate (octyl methoxycinnamate; ethylhexyl methoxycinnamate)	sunscreen	insect bites/stings	I	I	352.10(j)	
	octisalate (octyl salicylate; ethylhexyl salicylate)	sunscreen		I	I	352.10(k)	
4X49Y0596W	octocrylene	sunscreen		I	I	352.10(i)	
5A68WGF6WM	octoxynol 9	vaginal contraceptive		I	310.545(a)(28)(ii)		
7JPC6Y25QS	octyl triazone (ethylhexyl triazone)	sunscreen		NA			
	oil of erigeron	menstrual/diuretic				310.545(a)(24)(i)	
	opium powder	antidiarrheal	I	III		310.545(a)(3)(i)	
	opium tincture	antidiarrheal	I	III		310.545(a)(3)(i)	
	organic vegetables	weight control		II		310.545(a)(20)	
E4GA8884NN	orthophosphoric acid	digestive aid				310.545(a)(8)(ii)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
	ox bile	laxative	stimulant laxative		III	310.545(a)(12)(iv)(A)	
950O87VE0Y	ox bile extract	digestive aid		II	II	310.545(a)(8)(i)	
K89MJ0S5VY	oxybenzone (benzophenone-3)	sunscreen		I	I	352.10(i)	
	oxymetazoline hydrochloride (aqueous)	cough/cold	nasal decongestant		I	341.20(b)(7)	
K89MJ0S5VY	oxymetazoline hydrochloride (jelly)	cough/cold	nasal decongestant	I	I	341.20(b)(7)	
5UTX5635HP	oxyquinoline	antifungal		III	III	310.545(a)(22)(iii)	
5UTX5635HP	oxyquinoline	antimicrobial			III/SE		
5UTX5635HP	oxyquinoline	oral health care			III/SE		
61VUG75Y3P	oxyquinoline sulfate	antifungal		III	III	310.545(a)(22)(ii)	
61VUG75Y3P	oxyquinoline sulfate	skin protectant	astringent	II		310.545(a)(18)(ii)	
4U7K4N52ZM	oxytetracycline hydrochloride (combination only)	first aid antibiotic	ointment		I	333.120	
0462U14DUI	p-t-butyl-m-cresol	skin protectant	astringent			310.545(a)(18)(ii)	
77FU10423X	padimate A (5 percent or higher)	sunscreen			I/SE		
77FU10423X	padimate A (up to 5 percent)	sunscreen		I	III/SE		
Z11006CMUZ	padimate O	sunscreen		I	I	352.10(m)	
UA8U0KJM72	pamabrom	menstrual/diuretic	antihistamine	I	I		
FQ3DRG0N5K	pancreatin	digestive aid	exocrine pancreatic insufficiency	II/III	I	310.545(a)(8)(i)	
FQ3DRG0N5K	pancreatin	weight control			II	310.545(a)(20)	
FQ3DRG0N5K	pancrelipase	digestive aid	exocrine pancreatic insufficiency	II/III	I	310.545(a)(8)(i)	
WV9CM0O67Z	panthenol	corn/callus remover				[55 FR 33261]	
WV9CM0O67Z	panthenol	external analgesic	II	I/SE		310.545(a)(10)(vi)	
WV9CM0O67Z	panthenol	external analgesic	insect bite/sting			310.545(a)(10)(vii)	
WV9CM0O67Z	panthenol	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
19F5HK2737	pantothenic acid	weight control	poison ivy/oak/sumac		II	310.545(a)(20)	
A236A06Y32	papain	digestive aid			II	310.545(a)(8)(i)	
A236A06Y32	papain	weight control		II	II	310.545(a)(20)	
KU94FY6JB	papaya enzymes	weight control			II	310.545(a)(20)	
KU94FY6JB	papaya, natural	digestive aid			II	310.545(a)(8)(ii)	
3JJ4O33LAY	para-chloromercuriphenol	antimicrobial	diaper rash			310.545(a)(27)(ii)	
3JJ4O33LAY	para-chloromercuriphenol	antimicrobial	first aid antiseptic			310.545(a)(27)(i)	
I900E3H2ZE	paraffin	ophthalmic	emollient	I	I	349.14(b)(3)	
	paregoric	antidiarrheal		I	III	310.545(a)(3)(i)	
414P5USJ7F	parethoxycaine hydrochloride	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
68E52E5J67	parethoxycaine hydrochloride	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
58FMD0Q0EV	parsley	menstrual/diuretic		II		310.545(a)(24)(i)	
SY49TH8VUA	passion flower extract	nighttime sleep aid					
89NA02M4RX	pectin	antidiarrheal	w/ sales less than \$25,000	III	III	310.545(a)(3)(ii)	
89NA02M4RX	pectin	digestive aid				310.545(a)(8)(ii)	
89NA02M4RX	pectin	external analgesic	fever blister/cold sore			310.545(a)(10)(v)	
89NA02M4RX	pectin	oral health care	demulcents	I	I		
V95R5KMY2B	peppermint	digestive aid				310.545(a)(8)(ii)	
V95R5KMY2B	peppermint oil	cough/cold	antitussive		IIIE		[52 FR 30054]
V95R5KMY2B	peppermint oil	cough/cold	nasal decongestant		IIIE		[59 FR 43408]
V95R5KMY2B	peppermint oil	digestive aid		III	III	310.545(a)(8)(i)	
V95R5KMY2B	peppermint oil	external analgesic	insect bite/sting			310.545(a)(10)(vi)	
V95R5KMY2B	peppermint oil	skin protectant	astringent	II		310.545(a)(18)(ii)	
V95R5KMY2B	peppermint oil	skin protectant	insect bites/stings			310.545(a)(18)(v)(A)	
V95R5KMY2B	peppermint oil	cough/cold	antihistamine		IIIE	310.545(a)(6)(ii)(A)	
V95R5KMY2B	peppermint oil (mouthwash)	gingivitis/plaque				310.545(a)(8)(ii)	
V95R5KMY2B	peppermint oil and sage oil	digestive aid				310.545(a)(24)(i)	
V95R5KMY2B	peppermint spirit	menstrual/diuretic		II	II	310.545(a)(8)(i)	
V95R5KMY2B	peppermint spirit	digestive aid			II	310.545(a)(20)	
	pepsin	weight control	wound healing	III(e.i)	III(e.i)	310.545(a)(24)(i)	
367E55FXGW	pepsin, essence	menstrual/diuretic	diaper rash		IIIE	310.545(a)(26)(x)	
367E55FXGW	Peruvian balsam	anorectal			I		
367E55FXGW	Peruvian balsam	skin protectant	diaper rash		III		
367E55FXGW	Peruvian balsam oil	ophthalmic	protectant		I(e.i)	346.14(a)(8)	
367E55FXGW	Peruvian balsam oil	skin protectant	emollient	NA		349.14(b)(4)	
4T6H12BN9U	petrolatum	anorectal		I	I	347.10(m)	
4T6H12BN9U	petrolatum	ophthalmic		I	I	349.14(b)(6)	
4T6H12BN9U	petrolatum, white	skin protectant	emollient	I	I	347.10(r)	
4T6H12BN9U	petrolatum, white	anorectal	anesthetic	II(e.i)	II(e.i)	310.545(a)(26)(vi)	
70C1507JU9	phenacaine hydrochloride	digestive aid				310.545(a)(8)(ii)	
ER0CTH01H9	phenacetin	internal analgesic		II	II	310.545(a)(23)(i)	
ER0CTH01H9	phenacetin	menstrual/diuretic				310.545(a)(24)(i)	
ER0CTH01H9	phenacetin	weight control	antihistamine		II	310.545(a)(20)	
28725X3PV8	phenindamine tartrate	cough/cold		I	I	341.12(i)	
28725X3PV8	phenindamine tartrate	menstrual/diuretic				310.545(a)(24)(i)	
NYW905655B	pheniramine maleate	cough/cold	antihistamine		I	341.12(j)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
NYW905655B	pheniramine maleate	internal analgesic		III	III	310.545(a)(23)(i)	
YQE403BP4D	phenobarbital	cough/cold	miscellaneous		IIS		
339NCG44TV	phenol	acne		II	II	310.545(a)(1)	
339NCG44TV	phenol	anorectal	antiseptic	II(e.i)	II(e.i)	310.545(a)(26)(ii)	
339NCG44TV	phenol	antifungal		II	III	310.545(a)(22)(ii)	
339NCG44TV	phenol	antimicrobial			I		
339NCG44TV	phenol	antimicrobial			III		
339NCG44TV	phenol	antimicrobial			IIS		
339NCG44TV	phenol	antimicrobial			III		
339NCG44TV	phenol	dandruff		III	III	310.545(a)(7)	
339NCG44TV	phenol	external analgesic		I	I		
339NCG44TV	phenol	oral health care	anesthetic/analgesic	I	I		
339NCG44TV	phenol	relief of oral discomfort		I			
339NCG44TV	phenol	relief of oral discomfort		IIISE			
339NCG44TV	phenol	skin protectant	astringent	II		310.545(a)(18)(ii)	
339NCG44TV	phenol	skin protectant	insect bites/stings			310.545(a)(18)(v)(A)	
339NCG44TV	phenol	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
4NCOT56V35	phenolate sodium	acne		II	II	310.545(a)(1)	
4NCOT56V35	phenolate sodium	antifungal		II	III	310.545(a)(22)(ii)	
4NCOT56V35	phenolate sodium	dandruff		III	III	310.545(a)(7)	
4NCOT56V35	phenolate sodium	external analgesic		I	I		
4NCOT56V35	phenolate sodium	oral health care	anesthetic/analgesic	I	I		
4NCOT56V35	phenolate sodium	relief of oral discomfort		I			
4NCOT56V35	phenolate sodium	relief of oral discomfort		IIISE			
6QK969R2IF	phenolphthalein	laxative	stimulant laxative		I	310.545(a)(12)(iv)(B)	
YRC253429Q	phenoxyacetic acid	corn/callus remover	III	IIIE		[55 FR 33261]	
28A37T47QO	phenyl salicylate	corn/callus remover	II	II			
28A37T47QO	phenyl salicylate	acne		II	II	310.545(a)(1)	
28A37T47QO	phenyl salicylate	antiemetic			II		
28A37T47QO	phenyl salicylate	antifungal		III	III	310.545(a)(22)(ii)	
28A37T47QO	phenyl salicylate	menstrual/diuretic				310.545(a)(24)(i)	
28A37T47QO	phenyl salicylate	antidiarrheal		III	III	310.545(a)(3)(i)	
47E5O17Y3R	phenyl salicylate (salo)	weight control			II	310.545(a)(20)	
27O3Q5ML57	phenylalanine	cough/cold	nasal decongestant			341.20(a)(4)	
	phenylephrine bitartrate (effervescent)						
04JA59TNSJ	phenylephrine hydrochloride	anorectal	vasoconstrictor		I	346.12(d)	
04JA59TNSJ	phenylephrine hydrochloride	cough/cold	nasal decongestant		I	341.20(a)(1)	oral
04JA59TNSJ	phenylephrine hydrochloride	ophthalmic	vasoconstrictor	III	III	310.545(a)(21)(v)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
04JA59TNSJ	phenylephrine hydrochloride	oral health care		III			
04JA59TNSJ	phenylephrine hydrochloride (0.08 to 0.2%)	ophthalmic	vasoconstrictor	I	I	349.18(c)	
04JA59TNSJ	phenylephrine hydrochloride (aqueous)	cough/cold	nasal decongestant	I	I	341.20(b)(8)	
04JA59TNSJ	phenylephrine hydrochloride (jelly)	cough/cold	nasal decongestant	I	I	341.20(b)(8)	
OSX8836IUX	phenylmercuric acetate	vaginal contraceptive		IIS	310.545(a)(28)(i)		
CG8692ZNI4	phenylmercuric nitrate	antimicrobial	first aid antiseptic			310.545(a)(27)(i)	
CG8692ZNI4	phenylmercuric nitrate	vaginal contraceptive		IIS	310.545(a)(28)(i)		
B48FTC099P	phenylpropanolamine bitartrate	cough/cold		I			
8D5163UEIQ	phenylpropanolamine hydrochloride	oral health care	nasal decongestant	III			
8D5163UEIQ	phenylpropanolamine hydrochloride	weight control			I/IIS		
8D5163UEIQ	phenylpropanolamine hydrochloride (oral)	cough/cold	nasal decongestant	I			
8D5163UEIQ	phenylpropanolamine hydrochloride (topical)	cough/cold	nasal decongestant	III			
8UE48MJH8M	phenylpropanolamine maleate	cough/cold	nasal decongestant	I	IIIE		
8UE48MJH8M	phenyltoloxamine citrate	internal analgesic					
8UE48MJH8M	phenyltoloxamine citrate	menstrual/diuretic	antihistamine	NA	III		
8UE48MJH8M	phenyltoloxamine dihydrogen citrate	cough/cold	antihistamine			310.545(a)(6)(i)	
8UE48MJH8M	phenyltoloxamine dihydrogen citrate	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
8UE48MJH8M	phenyltoloxamine dihydrogen citrate	internal analgesic		III	III		
8UE48MJH8M	phenyltoloxamine dihydrogen citrate	nighttime sleep aid	antihistamine	III	IISE		[54 FR 6826]
8UE48MJH8M	phenyltoloxamine dihydrogen citrate	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
8UE48MJH8M	phenyltoloxamine hydrochloride	cough/cold	antihistamine			310.545(a)(6)(i)	
E4GA884NN	phosphorated carbohydrate	antiemetic			III		
27YLU75U4W	phosphoric acid	antacids		II	NC	310.545(a)(2)(ii)	
11E6V18VEG	phosphorus	weight control			II	310.545(a)(20)	
	phytolacca	weight control			II	310.545(a)(20)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
ZLT174DL7U	picrotoxin	pediculicide		II	II	310.545(a)(25)(i)	
	pine tar	dandruff		III	III	310.545(a)(7)	
	pine tar preparations (extract	cough/cold	expectorant		III	310.545(a)(6)(iii)	
	white pine compound, pine tar,						
	syrup of						
	pineapple enzymes	weight control			II	310.545(a)(20)	
63KP7FXF2I	piperazine citrate	anthelmintic		II	IIS		[51 FR 27758]
Q2RH0XR1MB	piperocaine hydrochloride	ophthalmic	anesthetic	II	II	310.545(a)(21)(i)	
LWK91TU9AH	piperonyl butoxide (combination)	pediculicide				310.545(a)(25)(ii)	
	piptsissewa	menstrual/diuretic		II	II	310.545(a)(24)(i)	
58JV0P12FY	<i>Piscidia erythrina</i>	menstrual/diuretic	botanical/vegetable herb	II	II	310.545(a)(24)(i)	
	<i>Plantago ovata</i> husks	laxative	bulk laxative		I		
9C60Y73166	plantago seed	laxative	bulk laxative		I		
9C60Y73166	plantago seed	weight control			III	310.545(a)(20)	
9C60Y73166	plantago seed husks (see	laxative			IISE		
	psyllium seed husks)						
9C60Y73166	plantago seed, blond (see	laxative			IISE		
	plantago seed)						
	podophyllum resin (podophyllin)	laxative	stimulant laxative		II	310.545(a)(12)(iv)(A)	
	poloxamer	laxative	stool softener		III	310.545(a)(12)(iii)	
LQA7B6G8JG	poloxamer 188	antimicrobial			I		
TUF21VW3M2	poloxamer 407	relief of oral discomfort		IIIE			
	poloxamer–iodine complex	antimicrobial			IISE		
	poloxamer–iodine complex	antimicrobial			IISE		
	polycarbophil	antidiarrheal	w/ sales less than \$25,000	I	I	310.545(a)(3)(ii)	
	polycarbophil	laxative			I		
	polydimethylsiloxane and	gingivitis/plaque			IIIE		
	poloxamer						
5655G9Y8AQ	polyethylene glycol 300	ophthalmic	demulcents	I	I	349.12(d)(2)	
B697894SGQ	polyethylene glycol 400	ophthalmic	demulcents	I	I	349.12(d)(3)	
30IQX730WE	polyethylene glycol 6000	ophthalmic	demulcents	NA	III	310.545(a)(21)(iv)	
19371312D4	polymyxin B sulfate	first aid antibiotic	ointment		I	333.120	
	(combination only)						
	polyols, liquid	ophthalmic	demulcents			349.12(d)	
60ZP39ZG8H	polyoxyethylene laurate	skin protectant	astringent	II		310.545(a)(18)(ii)	
532B59J990	polysorbate 80	ophthalmic	demulcents	I	I	349.12(d)(4)	
M911911U02	polyvinyl alcohol	ophthalmic	demulcents	I	I	349.12(e)	
	potassium acetate	menstrual/diuretic				310.545(a)(24)(i)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
HM5Z15LEBN	potassium bicarbonate	antacid				331.11(j)(1)	
HM5Z15LEBN	potassium bicarbonate	digestive aid				310.545(a)(8)(ii)	
OSD7855ZM	potassium bromide	nighttime sleep aid	bromide	II	IISE		[54 FR 6826]
BQN1B9B9HA	potassium carbonate	antacid				331.11(j)(1)	
BQN1B9B9HA	potassium carbonate	antidiarrheal	w/ sales less than \$25,000	II	II	310.545(a)(3)(ii)	
BQN1B9B9HA	potassium carbonate	digestive aid				310.545(a)(8)(ii)	
H35KS68EE7	potassium chlorate	oral health care			IISE		
EE90ONI6FF	potassium citrate	weight control			II	310.545(a)(20)	
GTP1P30292	potassium ferrocyanide	skin protectant				310.545(a)(18)(ii)	
TTK33Z47F1	potassium guaiacolsulfonate	cough/cold			III	310.545(a)(6)(iii)	
1C4QK22F9J	potassium iodide	oral health care	expectorant	II			
RU45X2JN0Z	potassium nitrate	oral health care	expectorant				
K91YT16P5M	potassium salicylate	menstrual/diuretic				310.545(a)(24)(i)	
FZ989GH94E	povidone	internal analgesic			III		
85H0HZU99M	povidone–iodine	ophthalmic	demulcents	I	I	349.12(f)	
85H0HZU99M	povidone–iodine	acne		III	III	310.545(a)(1)	
85H0HZU99M	povidone–iodine	antifungal		III	I	333.210(d)	
85H0HZU99M	povidone–iodine	antimicrobial			I		
85H0HZU99M	povidone–iodine	antimicrobial			IIISE		
85H0HZU99M	povidone–iodine	dandruff		III	III	310.545(a)(7)	
85H0HZU99M	povidone–iodine	oral health care			IIISE		
85H0HZU99M	povidone–iodine	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
	povidone–vinylacetate copolymers						
	povidone–vinylacetate copolymers	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
88AYB867L5	pramoxine hydrochloride	anorectal					
88AYB867L5	pramoxine hydrochloride	external analgesic	local anesthetic	I(e),III(i)	I(e),III(i)	346.10(g)	
88AYB867L5	pramoxine hydrochloride	skin protectant		I	I		
88AYB867L5	pramoxine hydrochloride (combination)	anorectal	diaper rash				
70FD1KFU70	precipitated sulfur	anorectal				310.545(a)(26)(xi)	
	prolase	digestive aid	keratolytic	III(e),II(i)	III(e),II(i)	310.545(a)(26)(v)	
JHU490RVYR	propionic acid	antifungal				310.545(a)(8)(ii)	
6DC9Q167V3	propylene glycol	ophthalmic	demulcents	III	III	310.545(a)(22)(ii)	
6DC9Q167V3	propylene glycol	pediculicide		I	I	349.12(d)(5)	
LQU92IU8LL	propylhexedrine	cough/cold		II	II	310.545(a)(25)(i)	
Z81X2SC1OH	propylparaben	antifungal	nasal decongestant	I	I	341.20(b)(9)	inhalant
	protease	digestive aid		III	III	310.545(a)(22)(ii)	
	protein hydrolysate	skin protectant	diaper rash		III	310.545(a)(8)(ii)	
						310.545(a)(18)(iii)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
S800I19YLZ	prune concentrate dehydrate	laxative	stimulant laxative		III	310.545(a)(12)(iv)(A)	
S800I19YLZ	prune powder	laxative	stimulant laxative		III	310.545(a)(12)(iv)(A)	
6V9V2RYJ8N	pseudoephedrine hydrochloride	cough/cold	bronchodilator	II	II	310.545(a)(6)(iv)	
6V9V2RYJ8N	pseudoephedrine hydrochloride	cough/cold	nasal decongestant	I	I	341.20(a)(2)	oral
Y9DL7QPE6B	pseudoephedrine sulfate	cough/cold	bronchodilator	II	II	310.545(a)(6)(iv)	
Y9DL7QPE6B	pseudoephedrine sulfate	cough/cold	nasal decongestant		I	341.20(a)(3)	oral
Y9DL7QPE6B	pseudoephedrine sulfate (oral)	cough/cold	nasal decongestant	I	I		
9C60Y73166	psyllium (hemicellulose) (see plantago seed)	laxative			IISE		
	psyllium hydrophilic mucilloid	laxative			I		
9C60Y73166	psyllium seed	laxative			I		
	psyllium seed (blond)	laxative			I		
	psyllium seed husks	laxative			I		
	psyllium (hemicellulose)	laxative	bulk laxative		I		
81BK194Z5M	pyrantel pamoate	anthelmintic		I	I	357.11	
ZUM06L90GV	pyrethrum extract (combination)	pediculicide	aerosol		I	310.545(a)(25)(ii)	
ZUM06L90GV	pyrethrum extract (combination)	pediculicide	nonaerosol	I	I	358.61	
68Y4CF58BV	pyridoxine hydrochloride	menstrual/diuretic	vitamin	III	IIIE		
68Y4CF58BV	pyridoxine hydrochloride	skin protectant	fever blister/cold sore			310.545(a)(18)(iv)	
68Y4CF58BV	pyridoxine hydrochloride (vitamin B6)	weight control			II	310.545(a)(20)	
R35D29L3ZA	pyrilamine maleate	acne		II	II	310.545(a)(1)	
R35D29L3ZA	pyrilamine maleate	cough/cold	antihistamine	I	I	341.12(k)	
R35D29L3ZA	pyrilamine maleate	external analgesic	insect bite/sting			310.545(a)(10)(vi)	
R35D29L3ZA	pyrilamine maleate	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
R35D29L3ZA	pyrilamine maleate	internal analgesic		III	III	310.545(a)(23)(i)	
R35D29L3ZA	pyrilamine maleate	menstrual/diuretic	antihistamine	I	IIIE		
R35D29L3ZA	pyrilamine maleate	nighttime sleep aid	antihistamine	III	IIIE		[54 FR 6826]
R35D29L3ZA	pyrilamine maleate	oral health cure	anesthetic/analgesic	II	II	310.545(a)(14)	
R35D29L3ZA	pyrilamine maleate	skin protectant	insect bites/stings			310.545(a)(18)(v)(A)	
R35D29L3ZA	pyrilamine maleate	skin protectant	insect bites/stings		IIIE	310.545(a)(18)(v)(A)	
R35D29L3ZA	pyrilamine maleate	skin protectant	poison ivy/oak/sumac				
R35D29L3ZA	pyrilamine maleate	dandruff	dandruff (wash-off)	I	I	358.710(a)(2)	
R953O2RHZ5	pyrithione zinc	dandruff	dandruff (leave-on)	I	I	358.710(a)(3)	
R953O2RHZ6	pyrithione zinc	dandruff	seborrheic dermatitis (wash-off)	I	I	358.710(b)(2)	
R953O2RHZ7	pyrithione zinc	dandruff	seborrheic dermatitis (leave-on)	I	I	358.710(b)(3)	
R953O2RHZ8	pyrithione zinc	dandruff				310.547	
A7V27PHC7A	quinine	antimalarial					

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
A7V27PHC7A	quinine	internal analgesic		II	II	310.545(a)(23)(i)	
73JW72K6T3	racemethionine	skin protectant	diaper rash		III	310.545(a)(18)(iii)	
43SK4LA07D	racepinephrine hydrochloride	cough/cold	bronchodilator		I	341.16(f)	
43SK4LA07D	racepinephrine hydrochloride (oral/topical)	cough/cold	nasal decongestant	I	I	310.545(a)(6)(ii)(B)	
43SK4LA07D	racepinephrine hydrochloride	cough/cold	bronchodilator	I	I	341.16(g)	inhalation
43SK4LA07D	red petrolatum	cough/cold	bronchodilator	I	I	341.16(g)	rubber bulb
	red petrolatum	sunscreen		I	I	310.545(a)(29)	
	reosote	relief of oral discomfort		IIISE			
YUL4LO94HK	resorcinol	anorectal		III(e),II(i)	III(e),II(i)	310.545(a)(26)(ii)	
YUL4LO94HK	resorcinol	anorectal	antiseptic	I(e),II(i)	I(e),II(i)	346.20(b)	
YUL4LO94HK	resorcinol	antifungal	keratolytic	II	II	310.545(a)(22)(ii)	
YUL4LO94HK	resorcinol	antimicrobial			IISE		
YUL4LO94HK	resorcinol	dandruff		II	II	310.545(a)(7)	56 FR 63567
YUL4LO94HK	resorcinol	external analgesic		I	I		
YUL4LO94HK	resorcinol	skin protectant	diaper rash				
YUL4LO94HK	resorcinol (as single ingredient only)	acne		III	II	310.545(a)(1)	
YUL4LO94HK	resorcinol (when combined with sulfur)	acne				333.310(b)	
YUL4LO94HK	resorcinol monoacetate (as single ingredient only)	acne		III	II	310.545(a)(1)	
YUL4LO94HK	resorcinol monoacetate (when combined with sulfur)	acne				333.310(c)	
G280W4MW6E	rhubarb fluid extract	digestive aid				310.545(a)(8)(ii)	
G280W4MW6E	rhubarb fluid extract	antidiarrheal	w/ sales less than \$25,000	II	II	310.545(a)(3)(ii)	
	rhubarb, Chinese	laxative	stimulant laxative		III	310.545(a)(12)(iv)(A)	
TLM2976OFR	riboflavin	menstrual/diuretic			II	310.545(a)(24)(i)	
TLM2976OFR	riboflavin	weight control			II	310.545(a)(20)	
	rice polishings	weight control			II	310.545(a)(20)	
6NAF1689JO	sabadilla, alkaloids	pediculicide			II	310.545(a)(25)(i)	
FST467XS7D	saccharin	weight control		II	II	310.545(a)(20)	
U27K0H1H2O	sage oil	skin protectant	astringent	II	II	310.545(a)(18)(ii)	
FA IN0842KB	salicyl alcohol	oral health care		I	I		
EM8BM710ZC	salicylamide	external analgesic	analgesic and anesthetic	III	III	310.545(a)(10)(i)	
EM8BM710ZC	salicylamide	external analgesic	fever blister/cold sore	III	III	310.545(a)(10)(v)	
EM8BM710ZC	salicylamide	external analgesic	poison ivy/oak/sumac	III	III	310.545(a)(10)(vii)	
EM8BM710ZC	salicylamide	internal analgesic		III	IIISE		

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
EM8BM710ZC	salicylamide	menstrual/diuretic		II	II/ISE		[54 FR 6826]
EM8BM710ZC	salicylamide	nighttime sleep aid		III	III		
O414PZ4LPZ	salicylic acid	acne		III	I	333.310(d)	
O414PZ4LPZ	salicylic acid	antifungal		III	III	310.545(a)(22)(ii)	
O414PZ4LPZ	salicylic acid	corn/callus remover	collodion-like vehicle	I	I	358.510(b)	
O414PZ4LPZ	salicylic acid	corn/callus remover	plaster vehicle	I	I	358.510(a)	
O414PZ4LPZ	salicylic acid	dandruff	dandruff	I	I	358.710(a)(4)	
O414PZ4LPZ	salicylic acid	dandruff	psoriasis	I	I	358.710(c)(2)	
O414PZ4LPZ	salicylic acid	dandruff	seborrheic dermatitis	I	I	358.710(b)(4)	
O414PZ4LPZ	salicylic acid	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
O414PZ4LPZ	salicylic acid	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
O414PZ4LPZ	salicylic acid	wart remover	collodion-like vehicle	I	I	358.110(b)	
O414PZ4LPZ	salicylic acid	wart remover	karaya gum, glycol plaster vehicle	I	I	358.110(c)	
O414PZ4LPZ	salicylic acid	wart remover	plaster vehicle		II/SE	358.110(a)	
O414PZ4LPZ	salicylic acid (over 2 up to 5%)	acne		III	III	310.545(a)(1)	
V9MO595C9I	salsalate	internal analgesic		III	III	310.545(a)(23)(i)	
N9288CD508	sanguinaria extract	gingivitis/plaque			III/IE		[54 FR 6826]
J7WW9H9M8QS	saw palmetto	menstrual/diuretic				310.545(a)(24)(i)	
	scopolamine aminoxide hydrobromide	nighttime sleep aid	scopolamine compound	II	IIS		
451IFR0GXB	scopolamine hydrobromide	antidiarrheal		II	II	310.545(a)(3)(i)	
451IFR0GXB	scopolamine hydrobromide	antiemetic			III		
451IFR0GXB	scopolamine hydrobromide	nighttime sleep aid	scopolamine compound	II	IIS		
	sea minerals	weight control			II	310.545(a)(20)	
Z69D9E381Q	selenium sulfide	dandruff	dandruff	I	I	358.710(a)(5)	
Z69D9E381Q	selenium sulfide	dandruff	seborrheic dermatitis	I	I	358.710(b)(5)	
Z69D9E381Q	selenium sulfide, micronized	dandruff	dandruff	I	I	358.710(a)(6)	
5WS1632J8W	<i>Senecio aureus</i>	menstrual/diuretic	botanical/vegetable herb	II	II	310.545(a)(24)(i)	
AK7JF626KX	senna	digestive aid				310.545(a)(8)(ii)	
AK7JF626KX	senna fluid extract	laxative			I/IIIS		
S8SJ19N2NX	senna pod concentrate	laxative			I/IIIS		
	senna syrup	laxative			I/IIIS		
	sennosides A and B	laxative			I		
7Y1255HVXNR	sesame seed	weight control			II	310.545(a)(20)	(Continued)
4B24275HEU	shark liver oil	anorectal	wound healing	III(e,i)	III(e,i)	310.545(a)(26)(x)	
4B24275HEU	shark liver oil	antimicrobial			n/a		

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
4B24275HEU	shark liver oil	skin protectant	insect bites/stings w/ sales less than \$2	I	I	310.545(a)(18)(v)(B)	
4B24275HEU	shark liver oil	skin protectant	poison ivy/oak/sumac w/ sales less tha	I	I	310.545(a)(18)(vi)(B)	
4B24275HEU	shark liver oil	skin protectant	w/ sales less than \$25,000	I	I	310.545(a)(18)(i)(B)	
4B24275HEU	shark liver oil (combination only)	anorectal	protectant	I(c,i)	I(c,i)	346.14(b)(3)	
95T3W8IZE	silver nitrate	skin protectant	astringent	II		310.545(a)(18)(ii)	
TYU5GP6XGE	simethicone	antiflatulent			I	332.10	[58 FR 54454]
TYU5GP6XGE	simethicone	digestive aid	antiflatulent	III	I		
TYU5GP6XGE	simethicone	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
TYU5GP6XGE	simethicone	skin protectant	poison ivy/oak/sumac		II	310.545(a)(18)(vi)(A)	
25K35WQ32Q	sodium	weight control			II	310.545(a)(20)	[64 FR 27682]
	sodium	sunscreen		II	IISE		
	3,4-dimethylphenyl-glyoxylate						
	sodium acetylsalicylate (in solution)	overindulgence in alcohol	hangover reliever		I		
	sodium aluminum chlorohydroxy lactate	antiperspirant		IIISE	IIISE	310.545(a)(4)(i)	
OI245FE5EU	sodium benzoate	menstrual/diuretic					
8MDF5V39QO	sodium bicarbonate	antacid			I	310.545(a)(24)(i)	
8MDF5V39QO	sodium bicarbonate	anticaries		II	II	331.11(k)(1)	
8MDF5V39QO	sodium bicarbonate	digestive aid	antacid	III	I	310.545(a)(8)(i)	
8MDF5V39QO	sodium bicarbonate	external analgesic			n/a		
8MDF5V39QO	sodium bicarbonate	gingivitis/plaque			IIIE		
8MDF5V39QO	sodium bicarbonate	oral health care	wound cleansing	I	I		
8MDF5V39QO	sodium bicarbonate	skin protectant		I	NA	347.10(o)	
8MDF5V39QO	sodium bicarbonate	weight control		II	III	310.545(a)(20)	
91MBZ8H3QO	sodium borate	acne		II	II	310.545(a)(1)	
91MBZ8H3QO	sodium borate	antifungal		III		310.545(a)(22)(ii)	
91MBZ8H3QO	sodium borate	dandruff		II	II	310.545(a)(7)	
91MBZ8H3QO	sodium borate	external analgesic	insect bite/sting			310.545(a)(10)(vi)	
91MBZ8H3QO	sodium borate	oral health care			IISE		
91MBZ8H3QO	sodium borate	skin protectant	astringent	II		310.545(a)(18)(ii)	
91MBZ8H3QO	sodium borate	skin protectant	insect bites/stings			310.545(a)(18)(v)(A)	
91MBZ8H3QO	sodium borate monohydrate	oral health care			IISE		
LC1V549NOM	sodium bromide	daytime sedative			IISE	310.519(a)	
LC1V549NOM	sodium bromide	nighttime sleep aid	bromide	II	IISE		[54 FR 6826]
9XTM81VK2B	sodium caprylate	antifungal		III	III	310.545(a)(22)(ii)	
9XTM81VK2B	sodium caprylate	oral health care			IIIE		

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
45P3261C7T	sodium carbonate	antacid			I	331.11(k)(1)	
45P3261C7T	sodium carbonate	antacids				310.545(a)(2)(i)	
	sodium carboxymethylcellulose	antidiarrheal		III	III		
	sodium carboxymethylcellulose	laxative	bulk laxative		I		
747P669E	sodium caseinate	weight control			II	310.545(a)(20)	
451W471Q8X	sodium chloride	digestive aid				310.545(a)(8)(ii)	
451W471Q8X	sodium chloride	ophthalmic		I	I	349.16	
451W471Q8X	sodium chloride (salt)	weight control	hypertonic agent		II	310.545(a)(20)	
1Q73Q2JULR	sodium citrate	cough/cold	expectorant		III	310.545(a)(6)(iii)	
1Q73Q2JULR	sodium citrate	digestive aid	antacid	III	I	310.545(a)(8)(i)	
1Q73Q2JULR	sodium citrate	relief of oral discomfort		IIIE			
1Q73Q2JULR	sodium citrate in solution	relief of oral discomfort	hangover reliever/ overindulgence		I		
	sodium citrate in solution	overindulgence in alcohol	aststringent				
26WJH3CS0B	sodium diacetate	skin protectant				310.545(a)(18)(ii)	
	sodium dichromate	oral health care			IIIE		
3980JH2SW	sodium dihydrogen phosphate	antacids		II	NC	310.545(a)(2)(ii)	
	sodium dihydrogen phosphate monohydrate	antacids		II	NC	310.545(a)(2)(ii)	
8ZYQ1474W7	sodium fluoride	relief of oral discomfort		IIIE			
8ZYQ1474W7	sodium fluoride	relief of oral discomfort		IIIE			
8ZYQ1474W7	sodium fluoride (aqueous)	antacids		I/NC	I	355.10(a)(3)(iii)–(v)	
8ZYQ1474W7	sodium fluoride (aqueous)	antacids		NC	I		
	(acidulated phosphate fluoride with 0.01 % f						
8ZYQ1474W7	sodium fluoride (aqueous)	antacids		I	I		
	(acidulated phosphate fluoride with 0.02 % f						
8ZYQ1474W7	sodium fluoride gel or paste	antacids	dentifrices	I	I	355.10(a)(1)	
8ZYQ1474W7	sodium fluoride powder	antacids	dentifrices	I	I	355.10(a)(2)	
C810JCZ56Q	sodium monofluorophosphate	antacids				310.545(a)(2)(i)	
C810JCZ56Q	sodium monofluorophosphate (rinse)	antacids		II	II		
C810JCZ56Q	sodium monofluorophosphate	relief of oral discomfort		IIIE			
C810JCZ56Q	sodium monofluorophosphate (gel or paste)	antacids	dentifrices	I	I	355.10(b)(1)	
C810JCZ56Q	sodium monofluorophosphate (gel or paste)	antacids	dentifrices		I	355.10(b)(2)	
8M4L3H2ZVZ	sodium nitrate	menstrual/diuretic				310.545(a)(24)(i)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
399SL044HN	sodium oleate	laxative	stimulant laxative		III	310.545(a)(12)(iv)(A)	
75UI7QUZ5J	sodium para-aminobenzoate	internal analgesic		II	II	310.545(a)(23)(i)	
Y52BK1W96C	sodium perborate	oral health care			IIISE		
Y9UKD0XE6F	sodium perborate monohydrate	oral health care	wound cleansing	II	I		
SE337SVY37	sodium phosphate	antiacaries		II	NC	310.545(a)(2)(i)	
SE337SVY37	sodium phosphate	antiacaries		II	NC	310.545(a)(2)(ii)	
SE337SVY37	sodium phosphate, dibasic	laxative	saline laxative		I		
SE337SVY37	sodium phosphate, monobasic	laxative	saline laxative		I		
QH257BPV3J	sodium potassium tartrate	antacid			I	331.11(j)(2)	
QH257BPV3J	sodium potassium tartrate	antacid			I	331.11(k)(2)	
DK6Y9P42IN	sodium propionate	antifungal		III	III	310.545(a)(22)(iii)	
DK6Y9P42IN	sodium propionate	antimicrobial			IIISE		
W1QIH85SYP	sodium salicylate	dandruff		III	III	310.545(a)(7)	
W1QIH85SYP	sodium salicylate	digestive aid			III	310.545(a)(8)(ii)	
W1QIH85SYP	sodium salicylate	internal analgesic		I	I		
W1QIH85SYP	sodium salicylate	menstrual/diuretic	analgesic	I			
W1QIH85SYP	sodium salicylate	overindulgence in alcohol/ food		I			
W1QIH85SYP	sodium salicylic acid phenolate	anorectal	antiseptic	II(e.i)	II(e.i)	310.545(a)(26)(ii)	
C02T02993U	sodium sulfide (aqueous)	ingrown toenail	gel vehicle		I	538.31	
HX1032V43M	sodium thiosulfate	acne		II	II	310.545(a)(1)	
506T60A25R	sorbitol	digestive aid		II	II	310.545(a)(8)(i)	
506T60A25R	sorbitol	laxative	hyperosmotic		I		
506T60A25R	sorbitol	oral health care	demulcents		III	310.545(a)(14)	
	soy meal	weight control			II	310.545(a)(20)	
241ATL177A	soybean oil, hydrogenated (powder)	cholecystokinetic				357.210(b)	
R441WB3RN5	soybean protein	weight control			II	310.545(a)(20)	
3629601H5D	squill preparations (squill, squill extract)	cough/cold	expectorant		II	310.545(a)(6)(iii)	
3FTR44B32Q	stannous fluoride	antiacaries	dentifrices	I	I	355.10(c)(1)(i)	
3FTR44B32Q	stannous fluoride	relief of oral discomfort		IIIE			
3FTR44B32Q	stannous fluoride (gel)	antiacaries		I	I	355.10(c)(2)	
3FTR44B32Q	stannous fluoride (rinse)	antiacaries		I	I	355.10(c)(3)	
	stannous pyrophosphate and zinc citrate	gingivitis/plaque			IIIE		
2KR89J4H1Y	stearyl alcohol	skin protectant	insect bites/stings w/ sales less than \$25,000		310.545(a) (18)(v)(B)		

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
2KR89J4H1Y	stearyl alcohol	skin protectant	poison ivy/oak/sumac w/ sales less than \$25,000	310.545(a)(18)(vi)(B)			
2KR89J4H1Y	stearyl alcohol	skin protectant	w/ sales less than \$25,000			310.545(a)(18)(i)(B)	
ZLM4P8929R	stem bromelain	digestive aid				310.545(a)(8)(ii)	
4J2TY8Y81V	strawberry	digestive aid				310.545(a)(8)(ii)	
5R78837D4A	strontium chloride	relief of oral discomfort		III E			
5R78837D4A	strontium chloride	relief of oral discomfort		II SE			
H9Y79VD43J	strychnine	digestive aid					
70FD1KFU70	sublimed sulfur	anorectal	keratolytic	III(e),II(i)		310.545(a)(8)(ii)	
C15IH8M554	sucrose	menstrual/diuretic				310.545(a)(26)(v)	
C15IH8M554	sucrose	weight control			II	310.545(a)(24)(i)	
	sugars	oral health care	demulcents		III	310.545(a)(20)	
4NRT660KJQ	sulfacetamide sodium	ophthalmic	anti-infective	II		310.545(a)(14)	
70FD1KFU70	sulfur	acne		I		333.310(e)	
70FD1KFU70	sulfur	antifungal		III		310.545(a)(22)(ii)	
70FD1KFU70	sulfur	dandruff	dandruff	I		358.710(a)(7)	
70FD1KFU70	sulfur	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
70FD1KFU70	sulfur	skin protectant	diaper rash	II		310.545(a)(18)(iii)	
70FD1KFU70	sulfur	skin protectant	fever blister/cold sore	II		310.545(a)(18)(iv)	
70FD1KFU70	sulfur	skin protectant		II		310.545(a)(18)(i)(A)	
70FD1KFU70	sulfur (when combined w/ resorcinol, resorcinol monoacetate)	acne		I		333.310(f)	
70FD1KFU70	sulfur, sublimed	pediculicide		II			
	sulfurated oils of turpentine	menstrual/diuretic			II	310.545(a)(25)(i)	
1W6L629B4K	sulisobenzon	sunscreen		I		310.545(a)(24)(i)	
7SEV7J4R1U	talc	skin protectant	astringent	I		352.10(o)	
7SEV7J4R1U	talc	skin protectant	astringent	II		310.545(a)(18)(ii)	
7SEV7J4R1U	talc	skin protectant	diaper rash	II	II SE	310.545(a)(18)(ii)	
28F9E0DJY10	tannic acid	skin protectant	poison ivy/oak/sumac		I		
28F9E0DJY11	tannic acid	external analgesic	diaper rash			310.545(a)(10)(vii)	
28F9E0DJY12	tannic acid	skin protectant	fever blister/cold sore	II		310.545(a)(18)(iii)	
28F9E0DJY13	tannic acid	skin protectant	poison ivy/oak/sumac	II		310.545(a)(18)(iv)	
28F9E0DJY14	tannic acid	skin protectant	diaper rash	II		310.545(a)(18)(vi)(A)	
28F9E0DJY14	tannic acid	skin protectant	wound healing	II		310.545(a)(18)(iii)	
28F9E0DJY6	tannic acid	anorectal	astringent	II		310.545(a)(18)(i)(A)	
28F9E0DJY7	tannic acid	antifungal		II(e,i)		310.545(a)(26)(iii)	
28F9E0DJY8	tannic acid	digestive aid		II		310.545(a)(22)(ii)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
28F9E0DJY9	tannic acid	external analgesic	fever blister/cold sore			310.545(a)(10)(v)	
28F9E0DJY15	tannic acid glycerite	skin protectant	astringent	II		310.545(a)(18)(ii)	
	<i>Taraxacum officinale</i>	menstrual/diuretic	botanical/vegetable herb	II	II	310.545(a)(24)(i)	
	tartaric acid	laxative	saline laxative		I	310.545(a)(12)(ii)	
	tartrate (acid or salt)	antacid			III	331.11 (m)	
	terpin hydrate preparations (terpin hydrate, terpin hydrate elixer)	cough/cold	expectorant			310.545(a)(6)(iii)	
0619F35CGV	tetracaine	anorectal	local anesthetic	III(e,i)	I(e),III(i)	346.10(h)	
0619F35CGV	tetracaine	external analgesic	anesthetic and anesthetic	I	I	pending	
0619F35CGV	tetracaine	oral health care	anesthetic/analgesic	II	II	310.545(a)(14)	
5NF5D4OPCI	tetracaine hydrochloride	acne		II	II	310.545(a)(1)	
5NF5D4OPCI	tetracaine hydrochloride	anorectal	local anesthetic	III(e,i)	I(e),III(i)	346.10(i)	
5NF5D4OPCI	tetracaine hydrochloride	external analgesic		I	I		
5NF5D4OPCI	tetracaine hydrochloride	oral health care	anesthetic/analgesic	II	II	310.545(a)(14)	
5NF5D4OPCI	tetracycline hydrochloride	first aid antibiotic	ointment		I	333.110(f)	
0YZT43HS7D	tetrahydrozoline hydrochloride	ophthalmic	vasoconstrictor	I	I	349.18(d)	
M572600E5P	thiamine hydrochloride (vitamin B1)	weight control			II	310.545(a)(20)	
8K0I04919X	thiamine mononitrate (vitamin B1 mononitrate)	weight control			II	310.545(a)(20)	
7ZQC1892H9	thényldiamine hydrochloride	cough/cold	antihistamine	III	III	310.545(a)(6)(i)	
7ZQC1892H9	thényldiamine hydrochloride	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(A)	
7ZQC1892H9	thényldiamine hydrochloride	cough/cold	nasal decongestant	III	III		[59 FR 43408]
	theobromine sodium salicylate	menstrual/diuretic	antihistamine	III	III	310.545(a)(24)(i)	
C137DTR5RG	theophylline	menstrual/diuretic	antihistamine	III	III	310.545(a)(24)(i)	
C137DTR5RG	theophylline (in combination)	cough/cold	bronchodilator			310.545(a)(6)(iv)(B)	
	theophylline calcium salicylate	cough/cold	bronchodilator	I	II	310.545(a)(6)(iv)	
	theophylline sodium glycinate	cough/cold	bronchodilator	I	II	310.545(a)(6)(iv)	
0I551281YK	theophylline, anhydrous	cough/cold	bronchodilator	I	II	310.545(a)(6)(iv)	
M572600E5P	thiamine hydrochloride	menstrual/diuretic				310.545(a)(24)(i)	
M572600E5P	thiamine hydrochloride	nighttime sleep aid					
2225PI3MOV	thimerosal	antimicrobial	first aid antiseptic	II	II	310.545(a)(27)(i)	
	thiocyanacetate	pediculicide					
6K9YKD48Y4	thonylamine hydrochloride	cough/cold	antihistamine	II	II	310.545(a)(25)(i)	
2ZD004190S	threonine	weight control		I	I	341.12(l)	
3I50XA376E	thymol	acne		II	II	310.545(a)(20)	
3I50XA376E	thymol	antifungal		III	III	310.545(a)(1)	
3I50XA376E	thymol	cough/cold	nasal decongestant	II	II	310.545(a)(22)(ii)	
				III	III	310.545(a)(6)(ii)(A)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
3J50XA376E	thymol	dandruff		III	III	310.545(a)(7)	
3J50XA376E	thymol	external analgesic	analgesic and anesthetic	III	III	310.545(a)(10)(i)	
3J50XA376E	thymol	external analgesic	fever blister/cold sore	III	III	310.545(a)(10)(v)	
3J50XA376E	thymol	external analgesic	poison ivy/oak/sumac	III	III	310.545(a)(10)(vii)	
3J50XA376E	thymol	oral health care	anesthetic/analgesic	III	III	310.545(a)(14)	
3J50XA376E	thymol	relief of oral discomfort		IIIE			
3J50XA376E	thymol	skin protectant	astringent	II		310.545(a)(18)(ii)	
3J50XA376E	thymol (lozenge)	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(A)	
3J50XA376E	thymol (mouthwash)	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(A)	
3J50XA376E	thymol iodide	oral health care			IIISE		
3J50XA376E	thymol iodide	relief of oral discomfort		IIIE			
15FIX9V2JP	titanium dioxide	sunscreen		I	I	352.10(p)	
5236RK32KG	tolindate	antifungal		II	II	310.545(a)(22)(ii)	
06KB629TKV	tolnaftate	antifungal		I	I	333.210(e)	
TD2LE9IMBE	tolu balsam	oral health care		III			
TD2LE9IMBE	tolu preparations (tolu, tolu balsam, tolu balsam tincture)	cough/cold	expectorant		III	310.545(a)(6)(iii)	
08232NY3SJ	topical starch	anorectal	protectant	I(e.i)	I(e.i)	346.14(a)(9)	
08232NY3SJ	topical starch	external analgesic			IISE		
08232NY3SJ	topical starch	skin protectant	astringent	II		310.545(a)(18)(iii)	
08232NY3SJ	topical starch	skin protectant	diaper rash		I		
08232NY3SJ	topical starch	skin protectant	fever blister/cold sore			310.545(a)(18)(iv)	
08232NY3SJ	topical starch	skin protectant	poison ivy/oak/sumac		I	310.545(a)(18)(vi)(A)	
08232NY3SJ	topical starch	skin protectant			IISE	347.10(q)	
08232NY3SJ	topical starch	skin protectant		III	III	310.545(a)(18)(iv)	
08232NY3SJ	topical starch	skin protectant				331.11(i)(3)	
XHX3C3X673	triacetin	antifungal				310.545(a)(20)	
K4C08XP666	tricalcium phosphate	antacid					
K4C08XP666	tricalcium phosphate	weight control			II		
BGG1Y1ED0Y	triclocarban	antimicrobial			IIIE		
BGG1Y1ED0Y	triclocarban	antimicrobial			IIISE		
BGG1Y1ED0Y	triclocarban	antimicrobial			IISE		
4NM5039Y5X	triclosan	antimicrobial			IIIE		
4NM5039Y5X	triclosan	antimicrobial			IIISE		
FWV8GJ56ZN	tripelennamine hydrochloride	digestive aid				310.545(a)(8)(ii)	
FWV8GJ56ZN	tripelennamine hydrochloride	external analgesic	fever blister/cold sore		I	310.545(a)(10)(v)	
	triple dye	external analgesic			I		
	triple dye	antimicrobial			IIISE		
YAN7R5L890	triprolidine hydrochloride	antimicrobial			IISE		
8K1MK5E1FY	triticeum	cough/cold	antihistamine		I	341.12(m)	
903K93S3TK	trolamine	menstrual/diuretic		II	II	310.545(a)(24)(i)	
		external analgesic			IISE		

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
903K93S3TK	trolamine	skin protectant	fever blister/cold sore			310.545(a)(18)(iv)	
903K93S3TK	trolamine	skin protectant	insect bites/stings			310.545(a)(18)(v)(A)	
903K93S3TK	trolamine	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
H8O4040BHD	trolamine salicylate	sunscreen		I	I	352.10(q)	
H8O4040BHD	trolamine salicylate	external analgesic	fever blister/cold sore	III	III	310.545(a)(10)(v)	
	(triethanolamine salicylate)						
H8O4040BHD	trolamine salicylate	external analgesic	insect bite/sting	III	III	310.545(a)(10)(vi)	
	(triethanolamine salicylate)						
H8O4040BHD	trolamine salicylate	external analgesic	poison ivy/oak/sumac	III	III	310.545(a)(10)(vii)	
	(triethanolamine salicylate)						
8DUH1N1BX	tryptophan	weight control			II	310.545(a)(20)	
XJ6RUH004G	turpentine oil	external analgesic	fever blister/cold sore	I	I	310.545(a)(10)(v)	
XJ6RUH004G	turpentine oil	external analgesic	insect bite/sting			310.545(a)(10)(vi)	
XJ6RUH004G	turpentine oil	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
XJ6RUH004G	turpentine oil	skin protectant	insect bites/stings			310.545(a)(18)(v)(A)	
XJ6RUH004G	turpentine oil	skin protectant	poison ivy/oak/sumac	III	IISE	310.545(a)(18)(vi)(A)	
XJ6RUH004G	turpentine oil (oral)	cough/cold	antitussive				
XJ6RUH0046	turpentine oil (rectified)	anorectal	counterirritant	II(e,i)	II(e,i)	310.545(a)(26)(iv)	
XJ6RUH004G	turpentine oil (spirits of turpentine)	cough/cold	expectorant			310.545(a)(6)(iii)	
XJ6RUH004G	turpentine oil (spirits of turpentine) (oral)	cough/cold	nasal decongestant	II	II	310.545(a)(6)(ii)(A)	
XJ6RUH004G	turpentine oil (spirits of turpentine) (topical)	cough/cold	nasal decongestant	III	III	310.545(a)(6)(ii)(A)	
XJ6RUH004G	turpentine oil (topical/inhalant)	cough/cold	antitussive	III	IIIE		[52 FR 30055]
AD8LJ73GQF	turpentine, Venice (Venice turpentine)	menstrual/diuretic				310.545(a)(24)(i)	
42HK56048U	tyrosine	weight control			II	310.545(a)(20)	
	undecylium chloridiodine complex	antimicrobial			IIIE		
	undecylium chloridiodine complex	antimicrobial			IIISE		
	undecylium chloridiodine complex	antimicrobial			IISE		
	undecylenic acid	antifungal		I	I	333.210(f)	(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
K3D86KJ24N	undecylenic acid	dandruff		III	III	310.545(a)(7)	
8W8T17847W	urea	menstrual/diuretic				310.545(a)(24)(i)	
3M5V3DIX36	<i>Uva ursi</i> , extract of	menstrual/diuretic		II	II		
	<i>Uva ursi</i> , potassium extract	weight control					
HG18B9YRS7	valine	weight control			II	310.545(a)(20)	
9ZP99WL196	vegetable (green)	weight control			II	310.545(a)(20)	
81G40H8B0T	vitamin A	anorectal	wound healing	III(e,i)	III(e,i)	310.545(a)(26)(x)	
81G40H8B0T	vitamin A	corn/callus remover	II	IISE		[55 FR 33261]	
81G40H8B0T	vitamin A	skin protectant	diaper rash				
81G40H8B0T	vitamin A	weight control			II	310.545(a)(20)	
	vitamin A acetate	weight control			II	310.545(a)(20)	
	vitamin A palmitate	weight control			II	310.545(a)(1)	
H4N855PNZ1	vitamin E	acne		II	II		
H4N855PNZ1	vitamin E	nighttime sleep aid			II	310.545(a)(20)	
H4N855PNZ1	vitamin E	stimulant			III	310.545(a)(20)	
H4N855PNZ1	vitamin E	weight control			II	310.545(a)(20)	
	vitromersol	antimicrobial	first aid antiseptic				[39 FR 6104]
059QF0K00R	water and additives	ophthalmic			I	310.545(a)(20)	
7G1J5DA97F	water, purified	ophthalmic				349.20	
2ZA36H0S2V	wax, white	ophthalmic	emollient	I	I	349.14(b)(7)	
YR3G369F5A	wax, yellow	ophthalmic	emollient	NA	I	349.14(b)(8)	
	wheat germ	weight control			II	310.545(a)(20)	
	white ointment	ophthalmic	emollient	I	I	349.14(b)(5)	
4T6H12BN9U	white petrolatum	anorectal	protectant	I(e,i)	I(e,i)	346.14(a)(10)	
101I4J0U34	witch hazel	skin protectant	astringent	I	I	347.12(c)	
1014J0U34	witch hazel (hamamelis water)	anorectal	astringent	I(e)	I(e)	346.18(b)	
N8C4A9A49H	woodruff	digestive aid				310.545(a)(8)(ii)	
TTV12P4NEE	xanthan gum	weight control			III	310.545(a)(20)	
X5S84033NZ	xylometazoline hydrochloride (aqueous)	cough/cold	nasal decongestant		I	341.20(b)(10)	
X5S84033NZ	xylometazoline hydrochloride (jelly)	cough/cold	nasal decongestant	I	I	341.20(b)(10)	
3NY3SM6B8U	yeast	weight control			II	310.545(a)(20)	
3NY3SM6B8U	yeast cell derivative, live	skin protectant	diaper rash		III		
3NY3SM6B8U	yeast cell derivative, live	skin protectant	wound healing agent		III	310.545(a)(18)(i)(B)	
IY191986AO	yellow mercuric oxide	ophthalmic	anti-infective	III	II	310.545(a)(21)(ii)	
FM5526K07A	zinc acetate	external analgesic			IISE		
FM5526K07A	zinc acetate	skin protectant	diaper rash		III	310.545(a)(18)(iii)	
FM5526K07A	zinc acetate	skin protectant	wound healing agent	I	I	310.545(a)(18)(i)(A)	

(Continued)

TABLE 3 (CONTINUED)
Active Ingredients for OTC Monographs.

UNII Code	Active Ingredient	Monograph	Subcategory	Panel	Pending	Final	FR Citation
FM5526K07A	zinc acetate	skin protectant		I	I	347.10(s)	
QL5435GI2S	zinc caprylate	antifungal		III	III	310.545(a)(22)(ii)	
EQR32Y7H0M	zinc carbonate	skin protectant	diaper rash		III	310.545(a)(18)(iii)	
EQR32Y7H0M	zinc carbonate	skin protectant		I	I	347.10(t)	
86Q357L16B	zinc chloride	corn/callus remover	III	III E		[55 FR 33261]	
86Q357L16B	zinc chloride	oral health care		I	I	310.545(a)(18)(ii)	
86Q357L16B	zinc chloride	skin protectant	astringent	II			
K72I3DEX9B	zinc citrate	gingivitis/plaque			III E		
SOI2LOH54Z	zinc oxide	acne		II	II	310.545(a)(1)	
SOI2LOH54Z	zinc oxide	anorectal	astringent	I(e,i)	I(e,i)	346.18(c)	
SOI2LOH54Z	zinc oxide	external analgesic	insect bite/sting			310.545(a)(10)(vi)	
SOI2LOH54Z	zinc oxide	external analgesic			II SE		
SOI2LOH54Z	zinc oxide	n/a			I	352.10(r)	
SOI2LOH54Z	zinc oxide	skin protectant	astringent	II	II	310.545(a)(18)(ii)	
SOI2LOH54Z	zinc oxide	skin protectant		I	I	347.10(u)	
SOI2LOH54Z	zinc oxide	sunscreen			III	352.10(r)	
SOI2LOH54Z	zinc oxide	anorectal	protectant	I(e,i)	I(e,i)	346.14(b)(4)	
4O7IYT5YB5	zinc oxide (combination only)	antidiarrheal		III	III	310.545(a)(3)(i)	
4O7IYT5YB5	zinc phenolsulfonate	antiemetic			II		
4O7IYT5YB5	zinc phenolsulfonate	skin protectant	astringent	II		310.545(a)(18)(ii)	[64 FR 27682]
4O7IYT5YB5	zinc phenolsulfonate	sunscreen					
	zinc propionate	antifungal					
H92E6QA4FV	zinc stearate	acne					
H92E6QA4FV	zinc stearate	skin protectant	astringent	III	III	310.545(a)(22)(ii)	
89DS0H96TB	zinc sulfate	external analgesic	fever blister/cold sore	II	II	310.545(a)(1)	
89DS0H96TB	zinc sulfate	ophthalmic	astringent	II		310.545(a)(18)(ii)	
89DS0H96TB	zinc sulfate	poison treatment		I	I	349.10	
89DS0H96TB	zinc sulfate	skin protectant	astringent	II	II	310.545(a)(16)	
89DS0H96TB	zinc sulfate	skin protectant	fever blister/cold sore			310.545(a)(18)(ii)	
89DS0H96TB	zinc sulfate	skin protectant		II	II	310.545(a)(18)(iv)	
89DS0H96TB	zinc sulfide	acne		II	II	310.545(a)(1)	
388VZ25DUR	zinc undecylenate	antifungal		I	I	333.210(f)	
	zirconium oxide	external analgesic	insect bite/sting			310.545(a)(10)(vi)	
	zirconium oxide	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
	zirconium oxide	skin protectant	insect bites/stings			310.545(a)(18)(v)(A)	
	zirconium oxide	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	
	zyloxin	antimicrobial	first aid antiseptic			310.545(a)(27)(i)	
	zyloxin	external analgesic	poison ivy/oak/sumac			310.545(a)(10)(vii)	
	zyloxin	skin protectant	poison ivy/oak/sumac			310.545(a)(18)(vi)(A)	

Category II are not considered safe and effective; category III are drugs for which a status has not been established. Multiple entries indicate different uses or combinations.



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Part II

Manufacturing Formulations



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Over-the-Counter Formulations

ACETAMINOPHEN AND CAFFEINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Acetaminophen (fine powder)	500.00
65.00	2	Anhydrous caffeine	65.00
15.00	3	Maize starch	15.00
10.00	4	Povidone (PVP K-30)	10.00
5.00	5	Croscarmellose sodium (Ac-Di-Sol)	5.00
33.00	6	Maize starch	33.00
8.00	7	Povidone (PVP K-90)	8.00
1.00	8	Polysorbate 80 (Tween 80)	1.00
10.00	9	Microcrystalline cellulose (Avicel™ PH102)	10.00
7.00	10	Sodium starch glycolate (Primojel®)	7.00
5.00	11	Croscarmellose sodium (Ac-Di-Sol)	5.00
2.00	12	Stearic acid (fine powder)	2.00
4.00	13	Talc (fine powder)	4.00
–	14	Purified water	155.00

MANUFACTURING DIRECTIONS

1. Sift items 1 to 5 through a stainless steel 630 µm sieve. Load into mixer. Mix for 5 minutes at low speed.
2. Dissolve items 7 and 8 in 115 g of purified water (80–90°C) in a vessel.
3. Prepare slurry of item 6 in 40 g of purified water (25–30°C).
4. Add the slurry to the vessel to make a translucent paste. Cool to 45°C to 50°C.
5. Add the binder (item 4) to the paste.
6. Mix at low speed over a period of 3 minutes. Scrape sides and blades. Mix and chop at low speed for 1 to 2 minutes.
7. Check the end point of granulation. If required, add additional purified water to obtain the end point. (The end point of granulation occurs when the wet mass consists of few or no lumps.) Unload the wet granules into stainless steel trays for drying.

8. Dry the wet granules at 55°C for 8 hours. After 2 hours of drying, scrape the semidried granules to break up the lumps to promote uniform drying. Check the loss on drying (LOD limit: 1.5–2.0%). If required, dry further at 55°C for 1 hour.
9. Grind the dried granules through a 1.25 mm sieve using a granulator at medium speed. Collect in stainless steel drums.
10. Load the granules into blender. Sift items 9, 10, and 11 through a 500 µm sieve using a suitable sifter, and add to the blender. Mix for 2 minutes.
11. Sift items 12 and 13 through a 500 µm sieve.
12. Add 5 to 10 g granules from bulk. Mix in.
13. Check temperature and humidity before start of compression (recommended: relative humidity [RH] 55–60% at a temperature not exceeding 27°C).
14. Compress the granules using a rotary tableting machine. Average weight of tablet is 665 mg.

ACETAMINOPHEN AND CAFFEINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Acetaminophen (crystalline)	500
50.00	2	Caffeine (Knoll)	50
90.00	3	Avicel™ PH101	90
10.00	4	Kollidon® 30	10
20.00	5	Kollidon® CL	20
10.00	6	Polyethylene glycol (PEG-6000) (powder)	10

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with high compression force.
2. Compress into 683 mg tablets using 12 mm biplanar punches.
3. If the flowability of the powder mixture for tableting is not high enough, some Aerosil® 200 should be added.

ACETAMINOPHEN AND DIPHENHYDRAMINE HYDROCHLORIDE HOT THERAPY SACHETS

Bill of Materials			
Scale (mg/ sachet)	Item	Material Name	Qty/1000 Sachets (g)
1650.00	1	Acetaminophen (micronized)	1650.00
250.00	2	Diphenhydramine hydrochloride	250.00
0.90	3	FD&C Yellow No. 10 Lake	0.90
0.0005	4	FD&C Red No. 40	0.0005
18,081.10	5	Castor sugar	18,081.10
200.00	6	Aspartame	200.00
250.00	7	Maize starch (dried)	250.00
180.00	8	Citric acid	180.00
38.00	9	Sodium citrate	38.00
200.00	10	Sodium chloride	200.00
240.00	11	Honey flavor (dry)	240.00
100.00	12	Lemon flavor (dry)	100.00
QS	13	Purified water	QS

MANUFACTURING DIRECTIONS

1. Mix items 1 and 2 well; then, pass through 0.8 mm sieves.
2. Mix items 3, 5, and 13 to make a clear solution.
3. Add mixture of items 1 and 2 to second step mixture, and mix well.
4. Add this mixture to item 4, and mix. Take care to avoid lump formation.
5. Dry in an oven, maintaining a constant temperature.
6. Sieve and add items 6 to 12. Mix well. Make sure all the solids added are in fine powder form.
7. Fill 20 g of powder into sachets, and seal.

ACETAMINOPHEN AND PSEUDOEPHEDRINE HYDROCHLORIDE HOT THERAPY SACHETS

Bill of Materials			
Scale (mg/ sachet)	Item	Material Name	Qty/1000 Sachets (g)
650.00	1	Acetaminophen (micronized)	650.00
260.00	2	Pseudoephedrine hydrochloride	260.00
0.90	3	FD&C Yellow No. 10 Lake	0.90
18,081.10	4	Castor sugar	18,081.10
200.00	5	Aspartame	200.00
250.00	6	Maize starch (dried)	250.00
180.00	7	Citric acid	180.00
38.00	8	Sodium citrate	38.00
200.00	9	Sodium chloride	200.00
240.00	10	Apple flavor (dry)	240.00
100.00	11	Cinnamon flavor (dry)	100.00
QS	12	Purified water	QS

MANUFACTURING DIRECTIONS

1. Mix item 1 and 2 well, pass through a 0.8 mm sieve, and add to items 3 and 12, which have been mixed together.
2. Make into a clear solution. Take care to avoid lump formation.
3. Dry in an oven, maintaining constant moisture.
4. Using a 500 mm sieve, add items 6 to 11. Mix well. Make sure all the solids added are in fine powder form.
5. Fill 20 g of powder into sachets, and seal.

ACETAMINOPHEN AND DIPHENHYDRAMINE HYDROCHLORIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
325.00	1	Acetaminophen (fine powder)	325.00
26.00	2	Diphenhydramine HCl	26.00
50.00	3	Maize starch	50.00
07.00	4	Povidone (PVP K-30)	7.00
50.00	5	Microcrystalline cellulose (Avicel™ PH101)	50.00
42.00	6	Cornstarch	42.00
10.00	7	Povidone (PVP K-30)	10.00
09.50	8	Cellulose (powdered)	9.50
65.50	9	Cellulose (microcrystalline) (Avicel™ PH102)	65.50
20.00	10	Sodium starch glycolate (Primojel®)	20.00
08.00	11	Stearic acid (fine powder)	8.00
05.00	12	Talc (fine powder)	5.00
02.00	13	Magnesium stearate	2.00
—	14	Purified water	180.00

MANUFACTURING DIRECTIONS

1. Sift items 1 to 5 through a 630 µm stainless steel sieve.
2. Load into mixer. Mix for 5 minutes at low speed.
3. Dissolve item 7 in 135 g of purified water (80–90°C) in a vessel.
4. Prepare a slurry of item 6 in 45 g of purified water (25–30°C).
5. Add the slurry to the vessel to make a translucent paste.
6. Cool to 45°C to 50°C.
7. Add the binder (item 4).
8. Mix at low speed over a period of 3 minutes. Scrape sides and blades. Mix and chop at low speed for 1 to 2 minutes. Check the end point of granulation. If required, add additional purified water to obtain the end point. (The end point of granulation occurs when the wet mass consists of few or no lumps.)

9. Unload the wet granules into stainless steel trays for drying.
10. Dry the wet granules in an oven at 55°C for 10 hours. After 2 hours of drying, scrape the semidried granules to break up the lumps to promote uniform drying. Check the LOD (limit: 1–2%). If required, dry further at 55°C for 1 hour.
11. Grind the dried granules through a 1.25 mm sieve at medium speed.
12. Collect in stainless steel drums. Load the granules into blender.
13. Sift items 8, 9, and 10 through a 500 μm sieve using a suitable sifter, and add mixture to blender. Mix for 2 minutes.
14. Sift items 11, 12, and 13 through a 500 μm sieve. Add 5 to 10 g of granules from bulk.
15. Mix in polyethylene bag for 1 minute. Add to blender. Blend for 1 minute.
16. Check temperature and humidity before start of compression (limit: temperature not exceeding 27°C, RH 55–65%).
17. Compress the granules using a rotary tableting machine. Compress average tablet weight of 620 mg.
18. Disintegration time is not more than (NMT) 15 minutes; friability NMT is 1%.
19. Coating: Use one of the HPMC aqueous formulations in part III, such as yellow Opadry.

ACETAMINOPHEN SUSTAINED-RELEASE TABLETS

MANUFACTURING DIRECTIONS

1. 300 g acetaminophen and 60 g hydroxypropylmethylcellulose were dissolved in a mixture of 720 g methanol and 720 g dichloromethane.
2. 300 g Celphere 102 (mean particle diameter of approximately 127 μm , particle diameter of approximately 50–150 μm) was introduced to a fluidized-bed granulator and coated with the solution by the side-spraying method (spraying liquid volume 14 g/min, spraying air pressure 3 kg/cm^2 , product temperature 32°C, inlet temperature 45°C) to obtain acetaminophen particles.
3. Separately, 48 g ethyl cellulose and 12 g hydroxypropylmethylcellulose were dissolved in a mixture of 57 g purified water and 1083 g methanol.
4. 300 g acetaminophen particles were introduced to a fluidized-bed granulator and coated with this solution by side spraying (spraying liquid volume 8 g/min, spraying air pressure 3 kg/cm^2 , product temperature 38°C, inlet temperature 67°C) to obtain sustained-release fine particles.
5. 66.00 g of these sustained-release fine particles and 314.25 g mannitol that had been pulverized by a pin-mill pulverizing device were granulated (spraying liquid volume 15 g/min, spraying air pressure 1.1 kg/cm^2 , product temperature 30°C, inlet

temperature 38°C, spraying cycle 30 seconds spraying/30 seconds drying) with an aqueous 30% w/w solution containing 67.5 g maltose in a fluidized bed granulator to obtain the final composition.

6. After further mixing 2.25 g magnesium stearate with the composition that was obtained, 450 mg tablets containing 25 mg acetaminophen per tablet were made under a tableting pressure of 25 kg/punch and an initial hardness of 2 kp using a rotary tableting machine.
7. Next, these tablets were kept for 24 hours while heating and humidifying at 25°C and 75% RH using a thermostatic chamber at constant humidity. Then, they were dried for 3 hours at 30°C and 40% RH.
8. The tablets that were obtained showed a hardness of 3.5 kp and disintegration time in the buccal cavity of 12 seconds.

ACETAMINOPHEN AND PSEUDOEPHEDRINE HYDROCHLORIDE TABLETS

Bill of Materials			
Scale (mg/ caplet)	Item	Material Name	Qty/1000 Caplets (g)
325.00	1	Acetaminophen (fine powder)	325.00
31.50	2	Pseudoephedrine HCl	31.50
50.00	3	Cornstarch	50.00
7.00	4	Povidone (PVP K-30)	7.00
50.00	5	Microcrystalline cellulose (Avicel™ PH101)	50.00
42.00	6	Cornstarch	42.00
10.00	7	Povidone (PVP K-30)	10.00
9.50	8	Cellulose (powdered)	9.50
60.00	9	Cellulose (microcrystalline) (Avicel™ PH102)	60.00
20.00	10	Sodium starch glycolate (Primojel®)	20.00
8.00	11	Stearic acid (fine powder)	8.00
5.00	12	Talc (fine powder)	5.00
2.00	13	Magnesium stearate	2.00
—	14	Purified water	180.00

MANUFACTURING DIRECTIONS

1. Sift items 1 to 5 through a stainless steel 630 μm sieve.
2. Load into mixer. Mix for 5 minutes at low speed.
3. Dissolve item 7 in 135 g of purified water (80–90°C) in a vessel.
4. Prepare a slurry of item 6 in 45 g of purified water (25–30°C).
5. Add the slurry to the vessel to make a translucent paste. Cool to 45°C to 50°C. Add the binder (item 4).

6. Mix at low speed over a period of 3 minutes. Scrape sides and blades. Mix and chop at low speed for 1 to 2 minutes. Check the end point of granulation. If required, add additional purified water to obtain the end point. (The end point of granulation occurs when the wet mass consists of few or no lumps.) Unload the wet granules into stainless steel trays for drying.
7. Dry the wet granules in oven at 55°C for 10 hours.
8. After 2 hours of drying, scrape the semidried granules to break up the lumps for uniform drying.
9. Check the LOD (limit: 1–2%). If required, dry further at 55°C for 1 hour.
10. Transfer the dried granules to stainless steel drums.
11. Grind the dried granules through a 1.25 mm sieve using granulator at medium speed. Collect in stainless steel drums. Load the granules into blender.
12. Sift items 8, 9, and 10 through a 500 μ m sieve using a suitable sifter, and add to blender. Mix for 2 minutes.
13. Sift items 11, 12, and 13 through a 500 μ m sieve.
14. Add 5 to 10 g of granules.
15. Mix in polyethylene bag for 1 minute. Add to blender. Blend for 1 minute. Unload in stainless steel drums.
16. Compress 620 mg in 6 mm capsule-shaped punches.
17. Coat. The formula for the coating solution is determined to obtain a weight gain of 10 mg per caplet considering evaporation and loss during the coating operation.

ACETAMINOPHEN CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
300.00	1	Acetaminophen, milled (Hoechst)	300.00
600.00	2	Sucrose, milled	600.00
550.00	3	Kollidon® CL-M	550.00
30.00	4	Orange flavor (FDO)	30.00
30.00	5	Strawberry flavor (FDO)	30.00
60.00	6	Kollidon® 30	60.00
QS	7	Ethanol (96%)	~425.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 5 with solution of items 6 and 7, pass through a sieve, and press with medium compression force.
2. Average weight of tablet is 1620 mg using a 20 mm biplanar punch.
3. Taste is sweet, fruity, and only slightly bitter.

ACETAMINOPHEN, CHLORPHENIRAMINE, AND PSEUDOPHEDRINE SYRUP

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
24.00	1	Acetaminophen (fine powder)	24.00
3.00	2	Pseudoephedrine HCl	3.00
0.44	3	Chlorpheniramine maleate (10% excess)	0.44
14.00	4	Ascorbic acid	14.00
2.40	5	Sodium hydroxide	2.40
1.00	6	Edetate disodium (sodium EDTA)	1.00
0.50	7	Saccharin sodium	0.50
2.00	8	Sodium metabisulfite (sodium disulfite)	2.00
80.00	9	Alcohol (ethanol, 95%)	80.00
100.00	10	Propylene glycol	100.00
100.00	11	Sorbitol (70% solution)	100.00
250.00	12	Glycerin (glycerol)	250.00
300.00	13	Sucrose	300.00
0.04	14	Quinoline yellow	0.04
0.25	15	Pineapple flavor	0.25
QS	16	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Add 200 g of item 16 to the manufacturing vessel, and heat to 90°C to 95°C.
2. Add item 13 while mixing at slow speed at a temperature of 90°C to 95°C.
3. Mix for 1 hour at high speed.
4. Add items 10, 11, and 12 to the manufacturing vessel while mixing at high speed. Mix for 10 minutes.
5. Cool the temperature to 50°C while mixing at slow speed.
6. Add 70 g of item 9 to the syrup solution while mixing at slow speed.
7. Load item 1 into the manufacturing vessel while mixing at high speed.
8. Mix for 30 minutes to obtain a clear solution. Check the clarity of the solution.
9. Flush the solution with nitrogen gas for 5 minutes at 1 bar.
10. Add items 2, 4, 6, and 8 to the manufacturing vessel while mixing at slow speed.
11. Dissolve item 3 in 2 g of item 16 (25°C), and check that the solution is complete.
12. Add the solution to the manufacturing vessel while mixing at slow speed.

13. Dissolve item 15 in 10 g of item 9 in a stainless steel container, and add to the manufacturing vessel while mixing at slow speed.
14. Dissolve items 5 and 7 in 20 g of item 16 (25°C), and add to the manufacturing vessel while mixing at slow speed.
15. Dissolve item 14 in 2 g of item 16 (25°C).
16. Transfer the color solution to the manufacturing vessel while mixing at slow speed.
17. Rinse the container of color solution with 2 g of item 16 (25°C); then, transfer the rinsings to the manufacturing vessel, and mix for 5 minutes at high speed.
18. Bring the volume up to 1 L with item 16, and finally, mix for 15 to 20 minutes at high speed.
19. Check and record the pH (limit: 5.1–5.2). If required, adjust pH with 10% citric acid or 10% sodium citrate solution.
20. Assemble the filter press with 13.1 T 1000 12 sheets (K 800 14 sheets). Use changeover plate. Wash the filters using purified water (25°C) by passing through filters at 0.2 bar. Discard the washings. Filter the syrup at 1.5 bar. Recirculate approximately 20 to 30 mL syrup.
21. Connect the hose to the manufacturing vessel, and transfer the filtered syrup to the storage vessel.

ACETAMINOPHEN, CHLORPHENIRAMINE MALEATE, AND PSEUDOEPHEDRINE CAPLETS

Bill of Materials

Scale (mg/ caplet)	Item	Material Name	Qty/1000 Caplets (g)
325.00	1	Acetaminophen (fine powder)	325.00
31.50	2	Pseudoephedrine HCl	31.50
2.10	3	Chlorpheniramine maleate	2.10
50.00	4	Cornstarch	50.00
7.00	5	Povidone (PVP K-30)	7.00
50.00	6	Cellulose (microcrystalline) (Avicel™ PH101)	50.00
42.00	7	Cornstarch	42.00
10.00	8	Povidone (PVP K-30)	10.00
9.50	9	Powdered cellulose	9.50
77.90	10	Cellulose (microcrystalline) (Avicel™ PH102)	77.90
20.00	11	Sodium starch glycolate (Primojel®)	20.00
8.00	12	Stearic acid (fine powder)	8.00
5.00	13	Talc (fine powder)	5.00
2.00	14	Magnesium stearate	2.00
–	15	Purified water	180.00

MANUFACTURING DIRECTIONS

1. Sift items 1 to 6 through a 630 µm stainless steel sieve.
2. Load into mixer. Mix for 5 minutes at low speed.
3. Dissolve item 8 in 135 g of item 15 (80–90°C) in a vessel.
4. Prepare a slurry of item 7 in 45 g of item 15 (25–30°C). Add the slurry to the vessel to make a translucent paste. Cool to 45°C to 50°C.
5. Add the binder (item 5) to preceding step.
6. Mix at low speed over a period of 3 minutes. Scrape sides and blades.
7. Mix and chop at low speed for 1 to 2 minutes. Check the end point of granulation. If required, add additional item 15 to obtain the end point. (The end point of granulation occurs when the wet mass consists of few or no lumps.) Unload the wet granules in stainless steel trays for drying.
8. Dry the wet granules at 55°C for 10 hours. After 2 hours of drying, scrape the semidried granules to break up the lumps to promote uniform drying. Check the LOD (limit: 1.0–2.0%). If required, dry further at 55°C for 1 hour.
9. Grind the dried granules through a 1.25 mm sieve at medium speed. Collect in stainless steel drums.
10. Load the granules into blender.
11. Sift items 9, 10, and 11 through a 500 µm sieve using suitable sifter, and add mixture to blender. Mix for 2 minutes.
12. Sift items 12, 13, and 14 through a 500 µm sieve.
13. Add 5 to 10 g of granules from bulk. Mix in polyethylene bag for 1 minute.
14. Add to blender. Blend for 1 minute.
15. Check temperature and humidity before start of compression. Temperature should not exceed 27°C, and recommended RH is 55% to 65%.
16. Compress the granules using rotary tableting machine. Tablet weight is 640 mg.
17. Coating: Select an appropriate coating, such as Opadry HPMC. The formula for the coating solution is determined to obtain a weight gain of 10 mg per caplet considering evaporation and loss during coating operation.

ACETAMINOPHEN, DEXTROMETHORPHAN, AND PSEUDOEPHEDRINE CAPLETS

Bill of Materials			
Scale (mg/ caplet)	Item	Material Name	Qty/1000 Caplets (g)
325.00	1	Acetaminophen (fine powder)	325.00
31.50	2	Pseudoephedrine HCl	31.50
15.50	3	Dextromethorphan HBr	15.50
50.00	4	Cornstarch	50.00
7.00	5	Povidone (PVP K-30)	7.00
50.00	6	Cellulose (microcrystalline) (Avicel™ PH101)	50.00
42.00	7	Cornstarch	42.00
10.00	8	Povidone (PVP K-30)	10.00
9.50	9	Cellulose (powdered)	9.50
64.50	10	Cellulose (microcrystalline) (Avicel™ PH102)	64.50
20.00	11	Sodium starch glycolate (Primojel®)	20.00
8.00	12	Stearic acid (fine powder)	8.00
5.00	13	Talc (fine powder)	5.00
2.00	14	Magnesium stearate	2.00
–	15	Purified water	180.00

MANUFACTURING DIRECTIONS

Follow manufacturing directions provided for acetaminophen, chlorpheniramine, and pseudoephedrine caplets.

ACETAMINOPHEN, DOXYLAMINE, AND CAFFEINE EFFERVESCENT GRANULES

Bill of Materials			
Scale (mg/ sachet)	Item	Material Name	Qty/1000 Sachets (g)
500.00	1	Acetaminophen (powder)	500.00
5.00	2	Doxylamine succinate	5.00
33.00	3	Caffeine (Knoll)	33.00
391.00	4	Tartaric acid	391.00
417.00	5	Sodium hydrogen carbonate	417.00
6.00	6	Kollidon® 30	6.00
–	7	Isopropanol (or ethanol)	QS
30.00	8	Sodium citrate	30.00
707.00	9	Sugar	707.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 5 with solution of items 6 and 7, dry at 60°C under vacuum conditions through 0.8 mm sieve, and mix with items 8 and 9.
2. Fill 2.1 g in sachets at maximum relative atmospheric humidity of 30%.
3. Granules are free flowing.
4. If the solvent isopropanol is replaced by water, the granulation should be done in a fluidized bed.

ACETAMINOPHEN DROPS

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
739.00	1	Propylene glycol	739.00
90.00	2	Acetaminophen	90.00
17.50	3	Saccharin sodium	17.50
8.75	4	Sodium chloride	8.75
0.05	5	FD&C Red No. 40 ^a	0.05
2.50	6	Purified water, USP	2.50
2.00	7	Wild cherry artificial flavor	2.00
65.00	8	Alcohol (ethanol, 190 proof, nonbeverage), USP	65.00
QS	9	Deionized purified water, USP	QS to 1 L

^a Check for local regulatory allowance to use red dyes.

MANUFACTURING DIRECTIONS

Caution: Ensure that solution in tank never exceeds 65°C.

1. Add 739 g of propylene glycol to jacketed mixing tank, and start heating with slow mixing.
2. Dissolve dye in 2.5 mL of purified water, and add to tank while mixing.
3. Rinse container with small amount of purified water, and add to tank.
4. While mixing, add acetaminophen, saccharin sodium, and sodium chloride.
5. Hold at 60°C to 65°C with continued moderate mixing until all are in solution.
6. Force cool to less than 30°C with slow mixing.
7. Blend flavor with alcohol, and add to tank with slow mixing.
8. Add purified water with mixing QS to make 1 L.
9. Mix well with moderate agitation until uniform.
10. Filter through an 8 µm Millipore membrane (or equivalent).

ACETAMINOPHEN EFFERVESCENT TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Acetaminophen (powder <300 μm)	500.00
500.00	2	Sodium bicarbonate	500.00
430.00	3	Tartaric acid (powder)	430.00
200.00	4	Dextrose	200.00
QS	5	Flavoring	QS
20.00	6	Kollidon® 30	20.00
–	7	Isopropanol	100.00 mL
60.00	8	PEG-6000 (powder)	60.00

MANUFACTURING DIRECTIONS

1. Granulate the mixture of items 1 to 5 with solution of items 6 and 7.
2. Pass through a 0.8 mm sieve, add item 8, and mix.
3. Press to tablets (average weight, 1700 mg; 16 mm diameter biplanar tablet).

ACETAMINOPHEN FAST-DISSOLVING TABLETS**MANUFACTURING DIRECTIONS**

1. To the vortex of a rapidly stirred vessel containing 2.85 kg of deionized water is added 300 g of croscarmellose sodium, forming slurry. This slurry is mixed for 10 minutes.
2. Concurrently, 5 kg of powdered acetaminophen is placed in the bowl of a mixer.
3. At the conclusion of the mixing time for the slurry of croscarmellose sodium, the slurry is added slowly to the acetaminophen in the mixer bowl, forming a granulation, which is then placed in trays and dried in a 70°C oven for 3 hours.
4. The dry granulation is then passed through a U.S. standard 14 mesh screen (1410 μm).
5. Dry granulation (4796 g) is then placed in a twin shell blender, and to it is added 1584 g of Avicel™ AC-815 (85% microcrystalline cellulose coprocessed with 15% of calcium, sodium alginate complex, and 1584 g of microcrystalline cellulose [Avicel™ PH-302]).
6. This is thoroughly blended for 10 to 15 minutes, after which 36.24 g of magnesium stearate is added and mixed for an additional 5 minutes.

7. Prior to being added to the blender, magnesium stearate had been passed through a U.S. standard 30 mesh screen.
8. The resulting blend is compressed into caplet-shaped tablets with average weight of 0.884 g and an average thickness of 7.869 mm (0.3098 in).
9. The hardness of these tablets averaged 11.98 kp. Friability of these tablets is measured at 0.433% after 10 minutes and 0.847% after 19 minutes.
10. The average disintegration time is 26 seconds in 10 mL of deionized water, forming a suspension with minimal shaking.

ACETAMINOPHEN, IBUPROFEN, AND ORPHENADRINE HYDROCHLORIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
250.00	1	Acetaminophen (powder <300 μm)	250.00
200.00	2	Ibuprofen	200.00
100.00	3	Orphenadrine hydrochloride	100.00
200.00	4	Ludipress®	200.00
5.00	5	Magnesium stearate	5.00
5.00	6	Aerosil® 200	5.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.5 mm sieve. Mix.
2. Press with high compression force.
3. Tablet weight is 761 mg for each 12 mm biplanar tablet.

ACETAMINOPHEN INSTANT GRANULES

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
166.66	1	Acetaminophen (fine powder)	166.66
426.64	2	Sucrose (fine powder)	426.64
300.00	3	Kollidon® CL-M	300.00
23.33	4	Aspartame	23.33
16.66	5	Orange flavor	16.66
16.66	6	Strawberry flavor	16.66
40.00	7	Kollidon® 30	40.00
250.00	8	Ethanol (96%)	250.00

MANUFACTURING DIRECTIONS

1. Granulate items 1 to 6 with solution made from items 7 and 8, and pass through a 0.8 mm sieve.
2. Fill 1.5 or 3.0 g in sachets (for 250 or 500 mg strength, respectively).
3. The free-flowing granules disperse well in cold water.
4. Suspend 1.5 or 3.0 g of the granules (=250 or 500 mg acetaminophen) in a glass of water.

ACETAMINOPHEN INSTANT GRANULES

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
192.30	1	Acetaminophen (fine powder)	192.30
500.00	2	Sorbitol (instant) (Merck)	500.00
192.30	3	Kollidon® CL-M	192.30
27.00	4	Aspartame	27.00
19.23	5	Orange flavor	19.23
19.23	6	Strawberry flavor	19.23
11.53	7	Sodium citrate	11.53
11.53	8	Citric acid	11.53
30.76	9	Kollidon® 90 F	30.76
192.30	10	Ethanol (96%)	192.30

MANUFACTURING DIRECTIONS

1. Granulate items 1 to 8 with solution made from items 9 and 10, and pass through a 0.8 mm sieve.
2. Fill 1.3 or 2.6 g in sachets (for 250 or 500 mg strength, respectively).
3. The free-flowing granules disperse well in cold water.
4. Suspend 1.2 or 2.6 g of the granules (=250 or 500 mg acetaminophen) in a glass of water.

ACETAMINOPHEN INSTANT GRANULES

Bill of Materials			
Scale (mg/sachet)	Item	Material Name	Qty/1000 Sachets (g)
500.00	1	Acetaminophen fine powder	500.00
1300.00	2	Sorbitol instant (Merck)	1300.00
500.00	3	Lutrol F 127	500.00
30.00	4	Citric acid (powder)	30.00
30.00	5	Sodium citrate	30.00
80.00	6	Kollidon® 90 F	80.00
500.00	7	Ethanol (96%)	500.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 5 in solution of item 6 in item 7.
2. Fill 2.44 g in sachets (=500 mg acetaminophen).
3. The free-flowing granules disperse well in cold water.
4. The taste of the suspension is only slightly bitter (2.44 g in a glass of water).

ACETAMINOPHEN MICROSPHERE TABLETS**MANUFACTURING DIRECTIONS**

1. Formulation: Acetaminophen (APAP) powder (melting point 169–170.5°C), 85%; carnauba wax, 7.5%; Pluronic F68, 7.5%.
2. Mill the Pluronic through a Fitz mill using a 40 mesh screen.
3. Blend all of the ingredients at 60 Hz slow speed with chopper for 10 minutes.
4. Subject the blend to liquiflash processing at 60 Hz and 37% nominal power using the 5 in V-groove heater head.
5. Sieve the collected microspheres.
6. Coat the fraction passing through a 40 mesh and retained on 120 mesh sieve.
7. Coat the microspheres selected in a fluid-bed coater for taste masking at a 30% coating level with a coating solution containing a 1:1 ethylcellulose/hydroxypropylcellulose blend in acetone:isopropyl alcohol solvent.
8. Prepare a preblend of 78.25% sucrose, 11.00% sorbitol, 10.00% xylitol, and 0.75% Tween (polysorbate) 80.
9. Process the floss preblend using the 5 in. crown head at a temperature of 250°C and rotational speed of 60 Hz (3600 rpm).
10. Chop the floss collected with 2% lactose (2% w/w of the floss) for 2 minutes at 100 rpm with the choppers on, and spray 200 proof ethanol (0.5% based on weight of the floss) on the chopped floss and mix.
11. Dry the floss at 45°C for 90 minutes with intermittent mixing.
12. Screen the dried floss through a 20 mesh screen.
13. Process APAP taste-masked microspheres (step 5), 47.97; floss (step 6), 48.88; grape flavor, 0.70; citric acid, 1.50; acesulfame potassium, 0.20; silicon dioxide, 0.25; and sodium stearyl fumarate, 0.50.
14. Blend the coated APAP microspheres with the sieved floss for 5 minutes in a mixer, followed by the addition of flavors, sweeteners, and citric acid for another 3 minutes.
15. Thereafter, add silicon dioxide and blend the mix for another 2 minutes. After the final addition, sodium stearyl fumarate, blend for an additional 2 minutes.

16. Tablet the blend using flat-faced bevel edge punches (tablet weights are 255 mg for 9-mm punch tooling, equivalent to 80 mg APAP, and 510 mg for 12-mm tooling, equivalent to 160 mg APAP dose).
17. The hardness values should range from 0.5 to 2.0 lb.

ACETAMINOPHEN, NOREPHEDRINE, AND PHENYLTOLOXAMINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
300.00	1	Acetaminophen (crystalline) (Merck)	300.00
25.00	2	Norephedrine hydrochloride (Knoll)	25.00
22.00	3	Phenyltoloxamine	22.00
200.00	4	Cornstarch	200.00
25.00	5	Kollidon® 30	25.00
–	6	Ethanol (96%)	QS
25.00	7	Kollidon® CL	25.00
5.00	8	Magnesium stearate	5.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 5 with solution of items 5 and 6.
2. Dry, pass through a 0.8 mm sieve, and add items 7 and 8.
3. Press with high compression force.
4. Tablet weight is 601 mg for 12 mm biplanar tablet.

ACETAMINOPHEN ORAL SUSPENSION

Bill of Materials			
Scale (mg/5 mL)	Item	Material Name	Qty/L (g)
250.00	1	Acetaminophen (micronized) (2% excess)	51.00
2500.00	2	Sucrose	500.00
5.00	3	Methylparaben	1.00
1.50	4	Propylparaben	0.30
0.30	5	Sodium citrate	0.06
35.00	6	Glycerin (glycerol)	7.00
400.00	7	Glycerin (glycerol)	80.00
2000.00	8	Sorbitol (70%)	400.00
10.00	9	Xanthan gum (Keltrol® F)	2.00
0.50	10	Dye	0.10
22.50	11	Flavor	4.50
3.50	12	Strawberry flavor	0.70
–	13	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

Note: Acetaminophen dispersion should be uniformly mixed. If acetaminophen dispersion is either added to hot syrup base or homogenized for a long time, flocculation may appear. While handling the syrup or mucilage or drug dispersion, the handling loss should not be more than 1%. If it exceeds 1%, a poor suspension may result.

1. Add 180 g of purified water to the mixer, and heat to 90°C.
2. Dissolve item 3 and item 4 while mixing.
3. Add and dissolve item 2 while mixing.
4. Cool down to approximately 50°C to 55°C.
5. Add and dissolve item 5 while mixing.
6. Filter the syrup through T-1500 filters washed with purified water.
7. Collect the syrup in a clean stainless steel tank.
8. Disperse item 9 in item 6 in a separate stainless steel container.
9. Add 40 g of hot purified water (90°C) at once while mixing.
10. Mix for 20 minutes to make a homogeneous smooth mucilage.
11. Mix item 7 in 10 g of purified water (25°C) in a separate stainless steel container.
12. Add item 1 while mixing with stirrer.
13. Mix for 25 minutes to make uniform suspension.
14. Add sugar syrup and mucilage to the mixer.
15. Rinse the container of mucilage with 15 g of purified water, and add the rinsings to the mixer.
16. Cool to 25°C while mixing.
17. Add item 1 dispersion to the mixer.
18. Rinse the container of dispersion with 15 g of purified water, and add rinsings to the mixer.
19. Check the suspension for uniformity of dispersion.
20. Mix for additional 5 minutes at 18 rpm and a vacuum of 0.5 bar, if required.
21. Add item 8 to the mixer, and mix for 10 minutes.
22. Dissolve item 10 in 7 g of purified water, and add to the mixer.
23. Disperse item 11 in 7 g of purified water, and add to the mixer.
24. Add item 12 to the mixer.
25. Add cold purified water (25°C) to bring the volume up to 1 L.
26. Homogenize for 5 minutes at low speed under a vacuum of 0.5 bar, 18 rpm, and temperature of 25°C.
27. Check the dispersion for uniformity.
28. Check the pH (limit: 5.7 ± 0.5 at 25°C). If required, adjust the pH with a 20% solution of citric acid or sodium citrate.
29. Transfer the suspension through a 630 µm sieve to the stainless steel storage tank after mixing for 5 minutes at 18 to 20 rpm at room temperature.

ACETAMINOPHEN, PHENYLPROPANOLAMINE, DEXTROMETHORPHAN, AND CHLORPHENIRAMINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
200.00	1	Acetaminophen	200.00
12.50	2	Phenylpropanolamine hydrochloride (10% excess)	13.75
10.00	3	Dextromethorphan hydrobromide (10% excess)	11.00
1.00	4	Chlorpheniramine maleate (10% excess)	1.10
64.65	5	Cellulose (microcrystalline) (Avicel™ PH101)	121.72
28.00	6	Sodium starch glycolate (pH 5.5–7.5)	28.00
17.00	7	Povidone (PVP K-29–32)	17.5
–	8	Distilled purified water	~80.0 mL
2.00	9	Magnesium stearate	2.00
125.00	10	Acetaminophen	125.00
50.00	11	Ascorbic acid; use item 12	–
56.25	12	Sodium ascorbate (special grade) (20% excess)	67.50
24.00	13	Sodium starch glycolate (pH 5.5–7.5)	24.00
15.00	14	Povidone (PVP K-29–32)	~ 15.00
–	15	Alcohol SD 3A (200 proof)	75.0 mL

MANUFACTURING DIRECTIONS

1. Dissolve chlorpheniramine and povidone (item 7) in the purified water.
2. Pass phenylpropanolamine, dextromethorphan, and an equal portion of Avicel™ (item 5) through a 790 µm screen to break up any agglomerates.
3. Blend the screened items in a suitable mixer for 5 minutes.
4. Load the acetaminophen (item 1), sodium starch glycolate (item 6), remaining Avicel™ (item 5), and blended items from previous step into a suitable planetary mixer.
5. Blend for 10 minutes.
6. Granulate the blend from the preceding solution.
7. Add the granulating solution in three equal portions, massing for 5 minutes after each addition.
8. Pass the wet mass through a 4.2 mm screen onto paper-lined trays.
9. Dry at 50°C until the granule loss on drying (LOD) is 1% to 1.5%.
10. Pass the dried granules through an oscillating granulator fitted with a 790 µm screen.
11. Load the dried granules into a suitable blender.

12. Pass the magnesium stearate through a 600 µm screen and add to the blender.
13. Blend for 5 minutes.
14. Compress to the following specifications: tablet weight 291 mg and tablet thickness 4.2 to 4.4 mm.

ACETAMINOPHEN, PROPOXYPHENAZONE, AND CAFFEINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
250.00	1	Acetaminophen powder	250.00
150.00	2	Propoxyphenazone (isopropyl antipyrine)	150.00
50.00	3	Anhydrous caffeine	50.00
120.00	4	Avicel™ PH102	120.00
5.00	5	Pharmacoat® 603	5.00
3.25	6	Magnesium stearate	3.25
9.75	7	Talcum	9.75
1.30	8	Silicic acid	1.30
7.00	9	Methocel™ E-15	7.00
32.50	10	Esmaspreng fine	32.50
21.20	11	Maize starch	21.20
–	12	Water purified	QS

MANUFACTURING DIRECTIONS

1. Place into a suitable vessel 5 g of Pharmacoat® and 74 g of purified water. Stir until homogeneous aqueous mucilage is obtained.
2. Mix in another vessel 250 g acetaminophen powder and 17.50 g Esmaspreng fine. Add the above granulating solution, and knead for approximately 10 minutes until an evenly moist mass of soft lumps is obtained.
3. Granulate by means of centrifugal granulator with 10 mm screen. Dry the moist granulate overnight on trays in drying oven at 45°C (RH: 20–30%).
4. Crush the dried cake through an oscillator with a 1.5 mm perforated plate.
5. In a suitable container, add 65 g deionized water and 7 g Methocel™.
6. Stir until homogeneous aqueous mucilage is obtained.
7. Mix into another vessel 150 g isopropyl antipyrine, 50 g caffeine, 15 g Esmaspreng fine, and 5 g maize starch.
8. Pass through a centrifugal granulator with 1 mm screen. Place mixture into another vessel, and knead for approximately 10 minutes until an evenly moist mass of small lumps is obtained.
9. Granulate through centrifugal granulator with 10 mm perforated screen.

10. Dry moist granulate overnight on trays in drying oven at 45°C (RH: 10–20%).
11. Crush the dried granules through oscillator with a 1.5 mm perforated plate. Store in airtight container.
12. Mix into a tumbling mixer 4.875 g talc, 1.625 g magnesium stearate, 0.65 kg silicic acid, and 60.00 g Avicel™ PH102.
13. Pass through a 0.5 mm round sieve, and load acetaminophen granulate and isopropyl antipyrine/caffeine granulate. Add premixture of talc into blender.
14. Mix the mixture well for 30 minutes (RH: 30–35%).
15. Store mix in airtight container.
16. Compress 650 mg tablet to 12.8 to 13.2 mm, hardness 6 to 20, disintegration time 5 minutes.

ACETAMINOPHEN, PSEUDOEPHEDRINE HYDROCHLORIDE, AND CHLORPHENIRAMINE HOT THERAPY SACHET

Bill of Materials			
Scale (mg/ sachet)	Item	Material Name	Qty/1000 Sachets (g)
650.00	1	Acetaminophen (micronized)	650.00
60.00	2	Pseudoephedrine hydrochloride	60.00
4.00	3	Chlorpheniramine maleate	4.00
1.20	4	Dispersed orange	1.20
18,081.10	5	Castor sugar	18,081.10
200.00	6	Aspartame	200.00
250.00	7	Maize starch (dried)	250.00
180.00	8	Citric acid	180.00
38.00	9	Sodium citrate	38.00
200.00	10	Sodium chloride	200.00
400.00	11	Blood orange flavor (dry)	400.00
QS	12	Purified water	QS

MANUFACTURING DIRECTIONS

1. See manufacturing directions for acetaminophen and pseudoephedrine hydrochloride hot therapy sachets.

ACETAMINOPHEN SUPPOSITORIES

Bill of Materials			
Scale (mg/ suppository)	Item	Material Name	Qty/1000 Suppositories (g)
80.00	1	Acetaminophen (micronized)	80.00
836.80	2	Hard fat (Suppocire AM)	836.80
3.20	3	Sorbitan monostearate (Crill-3)	3.20

MANUFACTURING DIRECTIONS

1. Fill weight is 920 mg per suppository. The molten suppository mass must be stirred throughout the storage period and during manufacturing and filling to avoid sedimentation of the active drug.
2. Load items 2 and 3 into the fat-melting vessel and heat to 50°C ± 3°C.
3. Transfer the molten mass to a mixer through filter sieves.
4. Set the temperature at 45°C ± 2°C.
5. Load item 1 into the mixer containing molten item 2.
6. Carefully mix the powder with molten item 2 for 20 minutes at 10 rpm, at a temperature of 45°C ± 2°C, and at a vacuum of 0.4 to 0.5 bar; then, homogenize for 10 minutes at low speed.
7. Continue mixing at 10 rpm.
8. Heat the storage vessel, and set the temperature at 45°C ± 2°C.
9. Transfer the molten mass from the mixer to the storage vessel.
10. Hold the mass at 45°C ± 2°C with continuous mixing at low speed.

ACETAMINOPHEN SUPPOSITORIES

Bill of Materials			
Scale (mg/ suppository)	Item	Material Name	Qty/1000 Suppositories (g)
125.00	1	Acetaminophen (micronized) (5% excess)	131.25
785.54	2	Hard fat (Suppocire AM)	785.54
3.21	3	Sorbitan monostearate (Crill-3)	3.21

MANUFACTURING DIRECTIONS

Fill weight is 920 mg per suppository. See manufacturing directions for acetaminophen suppositories.

ACETAMINOPHEN SUPPOSITORIES

Bill of Materials			
Scale (mg/ suppository)	Item	Material Name	Qty/1000 Suppositories (g)
250.00	1	Acetaminophen (micronized)	250.00
1140.00	2	Hard fat (Suppocire AM)	1140.00

MANUFACTURING DIRECTIONS

Fill weight is 1390 mg per suppository. See manufacturing directions for acetaminophen suppositories.

ACETAMINOPHEN SUPPOSITORIES

Bill of Materials			
Scale (mg/ suppository)	Item	Material Name	Qty/1000 Suppositories (g)
150.00	1	Acetaminophen (fine powder), excess	150.00
20.00	2	Aerosil® 200	20.00
1290.00	3	Lutrol E 1500	1290.00
554.00	4	Lutrol E 4000	554.00

MANUFACTURING DIRECTIONS

1. Melt the mixture of items 1 and 2 in a mixture of items 3 and 4.
2. Fill the molten mass in suppository molds.
3. Average weight is 2 g.

ACETAMINOPHEN SUPPOSITORIES

Bill of Materials			
Scale (mg/ suppository)	Item	Material Name	Qty/1000 Suppositories (g)
500.00	1	Acetaminophen (fine powder)	500.00
100.00	2	Lutrol E 400	100.00
600.00	3	Lutrol E 1500	600.00
800.00	4	Lutrol E 4000	800.00

MANUFACTURING DIRECTIONS

1. Fill weight is 2.09 g. Melt items 2 through 4, and add and dispense item 1.
2. Fill the molten mass in suppository molds.

ACETAMINOPHEN SUSPENSION

Bill of Materials			
Scale (mg/10 mL)	Item	Material Name	Qty/L (g)
500.00	1	Acetaminophen (powder)	50.00
50.00	2	Citric acid (powder)	5.00
50.00	3	Sodium citrate	5.00
500.00	4	Kollidon® CL-M	50.00
10.00	5	Orange flavor	1.00
3000.00	6	Dextrose	300.00
QS	7	Water	589.00

MANUFACTURING DIRECTIONS

1. Prepare the solution of dextrose in water, and add the other solid ingredients with stirring in the following sequence: citric acid, sodium citrate, orange flavor, Kollidon® CL-M, and acetaminophen.
2. A white, homogeneous suspension is obtained that is a practically tasteless, stable suspension showing almost no sedimentation over 24 hours and good redispersibility (easily homogenized by shaking two to three times).

ACETAMINOPHEN SYRUP

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
569.00	1	Sucrose (granulated sugar), NF	569.00
2.00	2	Sodium citrate (dihydrate powder), USP	2.00
1.00	3	Citric acid (anhydrous powder), USP	1.00
1.00	4	Saccharin sodium (powder), USP	1.00
1.00	5	Sodium chloride (powder), USP	1.00
204.00	6	Propylene glycol, USP	204.00
35.00	7	Acetaminophen, USP	35.00
77.11	8	Alcohol (ethanol, 190 proof), USP	77.112
0.12	9	Cherry flavor (artificial), N59456/A	0.12
0.12	10	FD&C Red No. 40	0.10
QS	11	Deionized purified water, USP	400.00
–	12	HyFlo filter aid	QS

MANUFACTURING DIRECTIONS

1. Add 300 mL of purified water to a jacketed stainless steel mixing tank. Start heating.
2. Add sugar with mixing.
3. Heat to 60°C to 65°C, and hold. Mix for complete solution.
4. Add, while mixing, sodium citrate, citric acid, saccharin sodium, and sodium chloride. Mix for complete solution.
5. Add propylene glycol with mixing.
6. Add acetaminophen powder with moderate mixing.
7. Continue mixing at 60°C to 65°C for complete solution.
8. Force cool to 25°C to 30°C with slow mixing.
9. Blend cherry flavor with approximately twice its volume of alcohol, and add with mixing.
10. Rinse the container with several portions of alcohol, and add. Mix until uniform.
11. Dissolve red dye in approximately 4 g of slightly warmed (50–60°C) purified water, and add with mixing.

12. Rinse the container twice with approximately 1.5 g purified water, and add. Mix until uniform.
13. Adjust volume to 1 L with purified water. Mix well.
14. Add a small amount of HyFlo filter aid to the mixing tank, and continue to mix slowly while filtering.
15. Filter through press until sparkling clear.
16. Use clarifying pad backed by lint-free filter paper.

ACETAMINOPHEN SYRUP

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
50.00	1	Acetaminophen (Merck)	50.00
50.00	2	Sorbitol (crystalline)	50.00
40.00	3	Cyclamate sodium	40.00
1.00	4	Strawberry flavor	1.00
200.00	5	Kollidon® 25	200.00
150.00	6	Glycerol	150.00
200.00	7	1, 2-Propylene glycol	200.00
310.00	8	Water	310.00

MANUFACTURING DIRECTIONS

1. First dissolve Kollidon® 25 and then the other solid components in the solvent mixture of glycerol, propylene glycol, and water.
2. The clear solution has a slightly bitter taste.
3. The solution remains clear for more than 1 week at 6°C and for more than 3 months at 25°C and 40°C.
4. The color of the solution changes only a little during 3 months at 25°C and 40°C.
5. To prevent discoloration during storage, 0.2% to 0.5% of cysteine could be added as antioxidant.

ACETAMINOPHEN SYRUP FOR CHILDREN

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
25.00	1	Acetaminophen (crystalline)	25.00
300.00	2	Kollidon® 25 or Kollidon® 30	300.00
60.00	3	Glycerol	600.00
40.00	4	Sodium cyclamate	40.00
QS	5	Orange flavor	<01.0
QS	6	Raspberry flavor	2.00
QS	7	Water	575.00

MANUFACTURING DIRECTIONS

1. Dissolve Kollidon® in water, add acetaminophen and cyclamate, heat to 50°C, and stir to obtain a clear solution.
2. Dissolve the flavors, and mix with glycerol.
3. The obtained syrup is a viscous, clear, sweet, and only slightly bitter liquid.

ACETAMINOPHEN TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Acetaminophen (fine powder)	500.00
44.15	2	Maize starch	44.15
0.84	3	Potassium sorbate	0.84
18.00	4	Povidone (PVP K-30)	18.00
4.00	5	Aerosil® 200	4.00
12.00	6	Gelatin (powder)	12.00
4.00	7	Glycerol	4.00
30.00	8	Cellulose (powder)	30.00
12.00	9	Primojel®	12.00
8.00	10	Stearic acid (fine powder)	8.00
2.00	11	Magnesium stearate	2.00
5.00	12	Talc (fine powder)	5.00
QS	13	Purified water	QS

MANUFACTURING DIRECTIONS

1. Binder solution: Prepare in several batches. Add items 3 to 5 with approximately 50% quantity of water, dissolve item 1 in water, add item 4, and dissolve at medium speed. Avoid foaming.
2. Add item 5, and mix for 3 minutes.
3. Dissolve item 6 in 70°C to 80°C purified water, and mix until clear. Avoid foaming.
4. Add item 7, and mix gently. Add to mixture from previous step.
5. Mix items 1 and 2 for 5 minutes.
6. Add binding solution, and mix at slow speed until granules form. Add extra water if necessary.
7. Dry in fluid-bed dryer at 55°C for 30 minutes. After 15 minutes, scrape granules to break up lumps to promote uniform drying. Dry to LOD 1% to 1.5%.
8. Grind through a 3 mm sieve and then through a 1 mm sieve. Load into double-cone blender.
9. Pass cellulose powder, Primojel®, and stearic acid through a 500 µm sieve; bag-mix magnesium stearate and fine talc powder, and pass through a 250 µm sieve; add portion of granules from the bulk to the bag, and mix for 1 minute.
10. Add both of these parts to the granules.
11. Compress 17.6 mm × 7.2 mm caplet punches to 10 to 14 kp hardness and 5.8 to 6.0 mm thickness.

ACETAMINOPHEN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Acetaminophen (crystalline)	500.00
137.00	2	Avicel™ PH102	137.00
35.00	3	Kollidon® VA 64	35.00
21.00	4	Kollidon® CL	21.00
3.00	5	Magnesium stearate	3.00
4.00	6	Aerosil® 200	4.00

MANUFACTURING DIRECTIONS

1. Pass the lubricant through a 200 mm sieve. Mix all other components.
2. Pass through 0.8 mm sieve, add the lubricant, and press with a high compression force of 25 to 30 kN.
3. Fill 699 mg.

ACETAMINOPHEN TABLETS

Bill of Materials			
Scale (g/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
500	1	Acetaminophen (crystalline)	500
150	2	Avicel™ PH102	150
20	3	Kollidon® VA 64	20
15	4	Kollidon® CL	15
15	5	PEG-6000 (powder)	15
2	6	Aerosil® 200	2

MANUFACTURING DIRECTIONS

1. Pass the lubricant through a 200 µm sieve. Mix all other components.
2. Pass through a 0.8 mm sieve, add the lubricant, and press with a high compression force of 25 to 30 kN.
3. Weight should be 703 mg.

ACETAMINOPHEN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Acetaminophen (powder)	500.00
30.00	2	Dicalcium phosphate	30.00
12.00	3	Kollidon® CL	12.00
20.00	4	Kollidon® VA 64	20.00
10.00	5	Kollidon® 90 F	10.00
—	6	Ethanol (96%)	70 mL (max.)
12.00	7	Kollidon® CL	12.00
10.00	8	Polyethylene glycol (powder)	10.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 4 with solution of item 5 and 6.
2. Dry, sieve, and mix with items 7 and 8.
3. Press with high compression force of 25 to 30 kN.
4. Tablet weight is 587 mg for an 11 mm biconvex tablet.

ACETAMINOPHEN TABLETS FOR CHILDREN

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
210.00	1	Acetaminophen (Merck)	210.00
168.00	2	Avicel™ PH101	168.00
13.00	3	Kollidon® VA 64	13.00
6.00	4	Kollidon® CL	6.00
2.00	5	Magnesium stearate	2.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with medium compression force.
2. Tablet weight is 401 mg for each 12 mm biplanar tablet.

ACETYLCYSTEINE SACHETS

Bill of Materials			
Scale (mg/ sachet)	Item	Material Name	Qty/1000 Sachets (g)
66.66	1	Acetylcysteine BP (200 mg/ sachet)	66.66
914.16	2	Sugar (18–60 mesh)	914.16
3.33	3	Saccharin sodium	3.33
0.66	4	Silicon dioxide (colloidal)	0.66
0.16	5	FD&C Yellow No. 6	0.16
QS	6	Mandarin flavor (e.g., Naarden)	~13.0 mL

MANUFACTURING DIRECTIONS

1. Load the acetylcysteine and half the amount of sugar and saccharin sodium into a suitable blender, and premix for 30 minutes.
2. Sift the premix through a 0.8 mm screen.
3. Load again into the blender.
4. Add the remaining amount of sugar and colloidal silicon dioxide, and blend until uniform (typically, this is achieved on the PK processor by heating the envelope to 40°C and mixing until the product cools to 30–35°C).
5. Dissolve the dye in 13 mL of distilled water.
6. Continue mixing the blended powders, and slowly add the solution from preceding step.
7. When addition of the solution is complete, continue massing until the granulation is evenly wetted and colored. If necessary, complete massing by adding additional quantities of distilled water (in approximately 1 mL increments).
8. Verify that massing is adequate, and note the total quantity of added water. Record the total quantity of water added. Do not overmass.
9. Spread the wet granules on trays, and dry at 50°C until LOD is NMT 1% (3 hours at 60°C at 5 mmHg).
10. Allow the granules to cool; then, sift on an oscillating granulator fitted with 1.18 mm aperture screen.
11. Load the granules from preceding step into a suitable blender, add the flavor, and blend until uniform (15 minutes), passing it through a 1.18 mm screen if necessary.
12. Fill into suitable approved sachets at a theoretical fill weight of 3 g per sachet.

ACETYLSALICYLIC ACID, ACETAMINOPHEN, AND CAFFEINE TABLETS (250 MG + 250 MG + 50 MG)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
250.00	1	Acetaminophen (Merck)	250.00
50.00	2	Caffeine powder	50.00
250.00	3	Acetylsalicylic acid	250.00
60.00	4	Kollidon® VA 64	60.00
20.00	5	Kollidon® CL	20.00
3.00	6	Aerosil® 200	3.00
4.00	7	Magnesium stearate	4.00

MANUFACTURING DIRECTIONS

1. The active ingredients and Kollidon® VA 64 are granulated in a roller compactor.
2. Pass the granules together with magnesium stearate, Aerosil® 200, and Kollidon® CL through an 800 µm sieve.
3. Blend for 10 minutes in a mixer.
4. Compress into tablets with a force of approximately 12 kN.

ACETYLSALICYLIC ACID + PARACETAMOL (=ACETAMINOPHEN) TABLETS (250 MG + 250 MG)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
250.00	1	Acetylsalicylic acid	250.00
250.00	2	Acetaminophen	250.00
60.00	3	Avicel™ PH101	60.00
15.00	4	Kollidon® VA 64	15.00
3.00	5	Macrogol 6000 powder	3.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with medium compression force.

ACETYLSALICYLIC ACID + VITAMIN C TABLETS (400 MG + 250 MG)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
400.00	1	Acetylsalicylic acid crystalline	400.00
250.00	2	Ascorbic acid	250.00
100.00	3	Ludipress®	100.00
20.00	4	Kollidon® CL	20.00
3.00	5	Macrolog 6000 powder	3.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with medium compression force.

ACETYLSALICYLIC ACID TABLETS (500 MG)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Acetylsalicylic acid crystalline	500.00
200.00	2	Avicel™ PH101	200.00
15.00	3	Kollidon® 30	15.00
25.00	4	Kollidon® CL	25.00
3.00	5	Magnesium stearate	3.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with low compression force.

ACETYLSALICYLIC ACID, ACETAMINOPHEN, AND CAFFEINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
250.00	1	Acetylsalicylic acid (crystalline)	250.00
250.00	2	Acetaminophen (crystalline)	250.00
50.00	3	Caffeine	50.00
50.00	4	Kollidon® 90 F	50.00
—	5	Isopropanol	QS
5.00	6	Magnesium stearate	5.00
16.00	7	Kollidon® CL	16.00

MANUFACTURING DIRECTIONS

1. Granulate items 1 to 3 with solution of items 4 and 5. Dry, and sieve through a 0.8 mm screen.
2. Add items 5 and 6, and press with low compression force (hardness 45 N). Each 12 mm biplanar tablet has an average weight of 670 mg.

ACETYLSALICYLIC ACID, ACETAMINOPHEN, AND CAFFEINE TABLETS (DIRECT COMPRESSION)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
400.00	1	Acetylsalicylic acid (crystalline)	400.00
100.00	2	Acetaminophen (crystalline)	100.00
30.00	3	Caffeine	30.00
100.00	4	Ludipress®	100.00
20.00	5	Kollidon® CL	20.00
30.00	6	PEG-6000 (powder)	30.00
5.00	7	Stearic acid	5.00

MANUFACTURING DIRECTIONS

1. Mix all components. Pass through a 0.8 mm sieve.
2. Press with compression force of 116 N. Each 12 mm biplanar tablet has an average weight of 683 mg.

ACETYLSALICYLIC ACID AND ACETAMINOPHEN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
250.00	1	Acetylsalicylic acid (crystalline)	250.00
250.00	2	Acetaminophen (crystalline)	250.00
60.00	3	Avicel™ PH101	60.00
15.00	4	Kollidon® 30 (or Kollidon® VA 64)	15.00
25.00	5	Kollidon® CL	25.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve. Mix.
2. Press with medium compression force.
3. Tablet weight is 605 mg for each 12 mm biplanar tablet.

ACETYLSALICYLIC ACID AND ACETAMINOPHEN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
250.00	1	Acetylsalicylic acid (40 mesh)	250.00
250.00	2	Acetaminophen (40 mesh)	250.00
15.00	3	Avicel™ PH102	15.00
7.20	4	Croscarmellose sodium (Ac-Di-Sol)	7.20
7.20	5	Stearic acid	7.20
4.00	6	Fumed silica	4.00

MANUFACTURING DIRECTIONS

1. Screen all ingredients through a 0.8 mm sieve.
2. Blend all ingredients in a V-blender, and mix for 10 minutes.
3. Compress to 670 mg tablet weight using appropriate tooling.

ACETYLSALICYLIC ACID AND ASCORBIC ACID TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
325.00	1	Acetylsalicylic acid (crystalline) (Merck)	325.00
250.00	2	Ascorbic acid (powder) (BASF)	250.00
120.00	3	Sorbitol (crystalline)	120.00
40.00	4	Avicel™ PH101	40.00
25.00	5	Kollidon® VA 64	25.00
20.00	6	Kollidon® CL	20.00
2.00	7	Magnesium stearate	2.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve. Mix.
2. Press with medium to high compression force (hardness 92 N). Each 12 mm biplanar tablet has an average weight of 790 mg.

ACETYLSALICYLIC ACID AND ASCORBIC ACID TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
325.00	1	Acetylsalicylic acid (crystalline) (Merck)	325.00
250.00	2	Ascorbic acid (powder) (BASF)	250.00
100.00	3	Avicel™ PH101	100.00
12.00	4	Kollidon® VA 64	12.00
30.00	5	Kollidon® CL	30.00
3.00	6	Magnesium stearate	3.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve. Mix.
2. Press with medium to high compression force (hardness 100 N). Each 12 mm biplanar tablet has an average weight of 726 mg.

ACETYLSALICYLIC ACID SUPPOSITORIES

Bill of Materials			
Scale (mg/ suppository)	Item	Material Name	Qty/1000 Suppositories (g)
100.00	1	Acetylsalicylic acid	100.00
400.00	2	Suppocire AM	400.00

MANUFACTURING DIRECTIONS

1. Heat item 2 to 50°C. Allow to cool to 40°C.
2. Add item 1 while stirring with a turbine mixer. Cool molds to -5°C to 0°C.
3. Continue mixing and cooling, and pour into molds at 35°C.
4. Remove suppositories from molds after 7 minutes.
5. Fill to appropriate weight for strength desired.

ACETYLSALICYLIC ACID TABLETS (BUFFERED)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
400.00	1	Acetylsalicylic acid (40 mesh)	400.00
40.00	2	Magnesium hydroxide	40.00
40.00	3	Aluminum hydroxide	40.00
135.00	4	Cellulose (microcrystalline) (Avicel™ PH101)	135.00
15.30	5	Stearic acid	15.30
15.30	6	Croscarmellose sodium (Ac-Di-Sol)	15.30
18.50	7	Hydroxy coatings	18.50

MANUFACTURING DIRECTIONS

1. Screen all ingredients except item 7 through a 40 mesh sieve.
2. Blend items 2 and 3 in a V-blender for 10 minutes.
3. Coat items 2 and 3 using Aquacoat® (FMC) aqueous polymer dispersion in a fluid-bed column using a 10% by weight formula.
4. Blend 50% of item 1 with items 4 and 5 for 10 minutes in a V-blender.
5. Add remaining item 1, and blend again for 10 minutes.
6. Blend item 7 with the mixture from the previous step for 10 minutes.
7. Add item 6, and blend for 7 minutes.
8. Compress 625 mg to the desired hardness using appropriate tooling.

ACETYLSALICYLIC ACID TABLETS (DIRECT COMPRESSION)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
400.00	1	Acetylsalicylic acid (crystalline) (Merck)	400.00
99.00	2	Ludipress®	99.00
1.00	3	Stearic acid	1.00
15.00	4	Kollidon® CL	15.00

MANUFACTURING DIRECTIONS

1. Mix all components. Pass through a 0.8 mm sieve.
2. Press with low compression force (hardness 90 N). Each 12 mm biplanar tablet has an average weight of 516 mg.

ACETYLSALICYLIC ACID TABLETS (DIRECT COMPRESSION)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
400.00	1	Acetylsalicylic acid (40 mesh)	400.00
55.60	2	Cellulose (microcrystalline) (Avicel™ PH101)	55.60
21.40	3	Starch (pregelatinized)	21.40
2.20	4	Stearic acid	2.20
10.00	5	Croscarmellose sodium (Ac-Di-Sol)	10.00
3.20	6	Fumed silica	3.20

MANUFACTURING DIRECTIONS

1. Screen approximately half of item 1 through a mill using 12 mesh screen with knives forward.
2. Preblend items 2 to 6 with 25% of item 1, and pass the mixture through the mill.
3. Pass the balance of item 1 through the mill.
4. Mix all the ingredients in a V-blender for 10 minutes, and compress using 13/32 in. tooling.
5. For enteric coating, coat with Aquateric (FMC) dispersion.

ACETYLSALICYLIC ACID TABLETS (DIRECT COMPRESSION)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
200.00	1	Avicel™ PH101	200.00
15.00	2	Kollidon® 30	15.00
25.00	3	Kollidon® CL	25.00
3.00	4	Magnesium stearate	3.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve. Mix.
2. Press with low compression force of (hardness 61 N). Each 12 mm biplanar tablet has an average weight of 707 mg.

ACNE COVER CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
37.00	1	Glyceryl stearate S/E	37.00
46.00	2	Mineral oil/Lanolin alcohol (liquid base CB3939)	46.00
9.00	3	Polawax GP2000	9.00
18.00	4	Stearic acid	18.00
QS	5	Deionized water	QS
36.00	6	Propylene glycol	36.00
2.00	7	Carboxymethyl cellulose (CMC-7HF)	2.00
9.00	8	Magnesium aluminum silicate (regular) (Veegum®)	9.00
9.00	9	Triethanolamine (99%)	9.00
120.00	10	Titanium dioxide	120.00
QS	11	Iron oxides	QS
50.00	12	Actives	50.00
QS	13	Perfume, preservative	QS

MANUFACTURING DIRECTIONS

1. Disperse CMC in propylene glycol and triethanolamine, and add warm water (60–65°C) while stirring until the gum is hydrated.
2. Add Veegum®, and stir until hydrated.
3. Heat oil phase to 60°C to 65°C.
4. Add water phase to oil phase while stirring.
5. Add pigments, and stir to cool, adding the actives at 30°C.
6. Homogenize using suitable equipment.
7. Fill. (Note that active ingredients may be added as required to this base formula.)

ACNE SCRUB

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
20.00	1	Magnesium aluminum silicate magnabrite HV	20.00
582.00	2	Water	582.00
100.00	3	Propylene glycol	100.00
150.00	4	Mineral oil and acetylated lanolin alcohol	150.00
30.00	5	Glyceryl stearate and PEG-100 stearate	30.00
14.00	6	Myristyl propionate	14.00
100.00	7	PEG-600	100.00
4.00	8	Eucalyptus oil	4.00
QS	9	Preservatives	QS

MANUFACTURING DIRECTIONS

1. Slowly sift item 1 into water, mixing until smooth.
2. Heat to 75°C.

3. Heat items 3 to 6 separately. Mix, and heat to 70°C.
4. Add this portion to item 1 dispersion, and mix well until smooth.
5. Add item 7 to mixture, and mix.
6. Finally, add items 8 and 9, and mix until cool.
7. *Note:* If using parabens, prepare a solution in a portion of water, and add before adding item 8 and after allowing parabens to cool to 50°C.

ACNE TREATMENT CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
20.00	1	Polychol 10 (Laneth-10)	20.00
5.00	2	Lanolin alcohols (Super Hartolan)	5.00
55.00	3	Cetyl alcohol C90	55.00
60.00	4	Polawax, NF	60.00
14.00	5	Sulfur	14.00
QS	6	Deionized water	QS
40.00	7	Veegum® (regular)	40.00
20.00	8	Propylene glycol	20.00
20.00	9	Resorcinol	20.00
QS	10	Perfume, preservative	QS

MANUFACTURING DIRECTIONS

1. Hydrate Veegum® in water.
2. Add rest of the water-phase ingredients, and heat to 70°C.
3. Heat oil phase to 70°C.
4. Disperse sulfur in the oil phase.
5. Add oil phase to water phase while stirring.
6. Stir to cool. Fill.

ALGINIC ACID + ALUMINUM HYDROXIDE + MAGNESIUM SILICATE TABLETS (500 MG+100 MG+25 MG)

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Alginic acid	500.00
100.00	2	Aluminum hydroxide dried gel (Giulini)	100.00
25.00	3	Magnesium trisilicate	25.00
170.00	4	Sodium bicarbonate	170.00
160.00	5	Sorbitol crystalline	160.00
627.00	6	Sucrose crystalline	627.00
900.00	7	Ludipress®	900.00
70.00	8	Kollidon® VA 64	70.00
50.00	9	Magnesium stearate	50.00
5.00	10	Vanillin	5.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with high compression force.

ALOE VERA GEL

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
4.00	1	Aloe vera extract (200-fold)	4.00
50.00	2	Propylene glycol	50.00
QS	3	Preservative	QS
736.00	4	Water	736.00
11.00	5	Cremophor RH 40	11.00
QS	6	Perfume	QS
200.00	7	Lutrol F 127	200.00

MANUFACTURING DIRECTIONS

1. Prepare solutions I (items 1–4) and II (items 5 and 6) separately, and add I into II.
2. Cool this mixture to <10°C (or heat to 70–80°C), and dissolve item 7.
3. Maintain the temperature until air bubbles escape.
4. Appearance is clear, viscosity is approximately 60 Pa, and pH is approximately 5.5.

ALPHA-BISABOLOL AQUEOUS MOUTHWASH SOLUTION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
2.00	1	Alpha-bisabolol, natural (BASF)	2.00
QS	2	Flavor	QS
25.00	3	Cremophor RH 40	25.00
50.00	4	Glycerol	50.00
1.00	5	Saccharin sodium	1.00
QS	6	Preservative	QS
922.00	7	Water	922.00

MANUFACTURING DIRECTIONS

1. Heat mixture of items 1 to 3 to approximately 60°C, and slowly add the warm solution of items 4 to 7 (60°C).
2. The clear, colorless liquid has a low viscosity.

ALPHA-BISABOLOL BUCCAL OR TOPICAL SOLUTION

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
1.20	1	Alpha-bisabolol (racemic) (BASF)	1.20
10.00	2	Cremophor RH 40	10.00
0.10	3	Butylhydroxytoluene (BHT)	0.10
QS	4	Preservative	QS
990.00	5	Water	990.00

MANUFACTURING DIRECTIONS

1. Heat mixture of items 1 to 3 to approximately 60°C, stir well, and slowly add the warm solution of items 4 in 5 to obtain a clear solution.

ALPHA-BISABOLOL ETHANOLIC MOUTHWASH SOLUTION

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
10.00	1	Alpha-bisabolol, racemic (BASF)	10.00
100.00	2	Flavor	100.00
60.00	3	Cremophor RH 40	60.00
10.00	4	Glycerol	10.00
2.00	5	Saccharin sodium	2.00
818.00	6	Ethanol (96%)	818.00

MANUFACTURING DIRECTIONS

1. Heat mixture of items 1 to 3 to approximately 60°C, and slowly add the warm solution of items 4 to 6.
2. The clear, colorless liquid can be diluted with water.

ALPHA-BISABOLOL MOUTHWASH SOLUTION

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
5.00	1	(–)Alpha-bisabolol, natural (BASF)	5.00
50.00	2	Lutrol F 127	50.00
QS	3	Flavor	QS
100.00	4	Propylene glycol (pharma)	100.00
300.00	5	Ethanol (96%)	300.00
545.00	6	Water	545.00

MANUFACTURING DIRECTIONS

1. Prepare solution of items 1 to 5, and slowly add the water.
2. The clear, colorless solution has pH 8.

ALUMINUM ACETYLSALICYLATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
250.00	1	Aluminum acetylsalicylate, excess	255.00
213.00	2	Mannitol	213.00
28.00	3	Cornstarch	28.00
10.00	4	Kollidon® 90 F	10.00
5.00	5	Lutrol E 6000	5.00
—	6	Isopropanol, QS	50.00 mL
23.00	7	Kollidon® CL	23.00
5.00	8	Magnesium stearate	5.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 3 with solution of items 4 to 6.
2. Dry, pass through a 0.8 mm sieve, and mix with items 7 and 8.
3. Compress with medium compression force. Each 12 mm biplanar tablet has an average weight of 540 mg.

ALUMINUM HYDROXIDE + MAGNESIUM SILICATE CHEWABLE TABLETS (120 MG+250 MG)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
120.00	1	Aluminum hydroxide dried gel (Giulini)	120.00
250.00	2	Magnesium trisilicate	250.00
232.00	3	Ludipress®	232.00
6.00	4	Aerosil® 200	6.00
6.00	5	Magnesium stearate	6.00
12.00	6	Cyclamate sodium	12.00
1.50	7	Menthol	1.50

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with a compression force of 20 kN at 640 mg.

ALUMINUM HYDROXIDE AND MAGNESIUM CARBONATE DRY SYRUP

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
200.00	1	Aluminum hydroxide dry gel (Giulini)	200.00
200.00	2	Basic magnesium carbonate	200.00
240.00	3	Kollidon® CL-M	240.00
211.50	4	Sorbitol (crystalline)	211.50
41.30	5	Orange flavor	41.30
82.60	6	Kollidon® 30	82.60
3.30	7	Coconut flavor	3.30
4.13	8	Banana flavor	4.13
4.13	9	Saccharin sodium	4.13
8.26	10	Water	8.26

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 5 with solution of items 6 to 10, pass through a sieve, and dry.
2. Shake 58 g of the granules with 100 mL of water.
3. Product remains homogeneous and without sedimentation for more than 24 hours.

ALUMINUM HYDROXIDE AND MAGNESIUM HYDROXIDE CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
200.00	1	Aluminum hydroxide (Rorer)	200.00
200.00	2	Magnesium hydroxide (Rorer)	200.00
100.00	3	Lactose monohydrate	100.00
30.00	4	Kollidon® VA 64	30.00
QS	5	Water	260.00 mL
315.00	6	Sucrose (crystalline)	315.00
100.00	7	Sorbitol (crystalline) (Merck)	100.00
60.00	8	PEG-6000 (powder)	60.00
12.00	9	Aerosil® 200	12.00
6.00	10	Talc	6.00
6.00	11	Magnesium stearate	6.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 5 with solution of items 4 to 5.
2. Dry and pass through a 0.8 mm sieve, add items 6 to 11, and press with high compression force (20 kN).
3. Each 16 mm biplanar tablet has an average weight of 1013 mg.

ALUMINUM HYDROXIDE AND MAGNESIUM HYDROXIDE CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
320.00	1	Aluminum hydroxide (dried gel)	320.00
320.00	2	Magnesium hydroxide powder	320.00
32.00	3	Sucrose	32.00
288.40	4	Mannitol	288.40
QS	5	Povidone (Plasdone®) (10% solution in equal parts water and alcohol)	QS
12.90	6	Glycerin	12.90
19.20	7	Magnesium stearate	19.20
6.40	8	Fumed silica	6.40
0.30	9	Oil of peppermint	0.30

MANUFACTURING DIRECTIONS

1. Mix items 1 to 4 in a suitable blender, add item 6 to item 5, and use this combination to moisten the mix of items 1 to 4.
2. Granulate by passing through a 20 mesh screen.
3. Add and thoroughly mix items 7 to 9, and compress using 0.5 in. flat-face, beveled-edge punches.

ALUMINUM HYDROXIDE AND MAGNESIUM HYDROXIDE ANTACID SUSPENSION

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
5.00	1	Purified bentonite (Veegum® HS)	5.00
2.00	2	Xanthan gum (Rhodigel)	2.00
401.00	3	Water	401.00
200.00	4	Sorbitol (70%)	200.00
360.00	5	Aluminum hydroxide gel	360.00
320.00	6	Magnesium hydroxide, USP	320.00
QS	7	Preservative, flavor	QS

MANUFACTURING DIRECTIONS

1. Slowly add a dry blend of item 1 and 2 to item 3, agitating with maximum available shear until a smooth and uniform mix is obtained.
2. Mix items 4 to 6 together in another vessel until uniform, and then add to previous mix.
3. Agitate until uniform.
4. Add item 7, and mix until uniform.

ALUMINUM HYDROXIDE AND MAGNESIUM HYDROXIDE ANTACID SUSPENSION

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
200.00	1	Magnesium aluminum silicate (Magnabrite S) (5% suspension)	200.00
2.00	2	Methylparaben	2.00
1.00	3	Propylparaben	1.00
0.50	4	Saccharin sodium	0.50
500.00	5	Aluminum hydroxide/Magnesium hydroxide fluid gel	500.00
3.00	6	Polysorbate 80	3.00
2.00	7	Flavor	2.00
291.50	8	Deionized water	291.50

MANUFACTURING DIRECTIONS

1. Add the parabens and saccharin to item 1 with stirring until dissolved (may heat to 80°C to dissolve).
2. Add item 5 with mixing.
3. Finally, add items 6 and 7. Mix well.

ALUMINUM HYDROXIDE AND MAGNESIUM HYDROXIDE SUSPENSION

Bill of Materials			
Scale (mg/ 5 mL)	Item	Material Name	Qty/L (g)
405.00	1	Aluminum hydroxide gel	290.00
100.00	2	Magnesium hydroxide paste (30%)	67.00
0.21	3	Ammonia solution (25%)	0.04
0.05	4	Ammonia solution (25%)	0.01
10.00	5	Methylparaben	2.00
0.25	6	Menthol	0.05
3.00	7	Propylparaben	0.60
1.00	8	Peppermint oil	0.20
50.00	9	Propylene glycol	10.00
1.25	10	Saccharin sodium	0.25
150.00	11	Sorbitol (70% solution)	30.00
4.50	12	Sodium hypochlorite (5%)	0.90
1.25	13	Sodium hypochlorite (5%)	0.25
15.00	14	Magnesium aluminum silicate (Veegum® HV)	3.00
QS	15	Purified water	QS to 1 L

Note: The quantity of the sodium hypochlorite solution should be adjusted according to the assay.

MANUFACTURING DIRECTIONS

1. Disperse item 14 in 60 g of hot purified water (70–80°C) in stainless steel vessel, using stirrer. Continue stirring for 30 minutes.
2. Transfer the dispersion into mixer (e.g., Krieger) vessel by vacuum, and mix for 30 minutes at 16/32 mixer speed.
3. Cool down to 30°C.
4. Add 200 g of hot purified water (70–80°C) to the mixer.
5. Mix and homogenize at 1420 rpm, mixer speed 16/32, and vacuum 0.5 bar for 30 minutes.
6. Cool down to 30°C.
7. Add 1 kg of purified water (70°C) to a suitable vessel, and heat to 85°C to 90°C for 1 hour.
8. Cool to 20°C to 25°C.
9. Mix items 13 and 4, and immediately add to purified water (20–25°C) in the storage vessel.
10. Mix for 2 minutes. Store in a previously cleaned storage vessel.
11. Load item 2 and 100 g of purified water (25–30°C) in a stainless steel mixing vessel with lid and stirrer.
12. Mix for 5 minutes at medium speed.
13. Transfer by vacuum into mixer.
14. Load 80 g of item 1 and 80 g of purified water (25–30°C) from preceding step in a stainless steel mixing vessel with lid and stirrer. Mix for 5 minutes at medium speed. Transfer by vacuum into mixer.
15. Load 50 g of item 1 and 50 g of purified water (25–30°C) from preceding step in a stainless steel mixing vessel with lid and stirrer.
16. Mix for 5 minutes at medium speed. Transfer by vacuum into mixer.
17. Transfer item 11 into mixer by vacuum.
18. Dissolve item 10 in 2 g of purified water (25–30°C) and transfer to mixer.
19. Mix and homogenize for 30 minutes at 1420 rpm under vacuum 0.5 bar.
20. Dissolve items 5 and 7 in item 9 (50–60°C) by stirring in stainless steel container in a water bath.
21. Dissolve items 6 and 8, and add to parabens/glycol solution. Mix well. Add to mixer.
22. Mix, and homogenize for 10 minutes under vacuum 0.5 bar.
23. Mix items 3 and 12 and 2 g of purified water, and immediately add to the mixer.
24. Mix for 10 minutes without vacuum.
25. Add cold purified water to bring the volume up to 1 L. Mix for 15 minutes.
26. Transfer the suspension through 630 µm sieve to the stainless steel storage tank. (Final pH is 7.5–8.0, and density is 1.04–1.06.)

ALUMINUM HYDROXIDE AND MAGNESIUM HYDROXIDE SUSPENSION

Bill of Materials			
Scale (mg/5 mL)	Item	Material Name	Qty/L (g)
200.00	1	Aluminum hydroxide gel	2004.00
80.00	2	Magnesium hydroxide paste (30%)	800.00
150.00	3	Sorbitol (70% solution)	30.00
10.00	4	Methyl paraben	2.00
1.00	5	Propyl paraben	0.20
2.00	6	Saccharin sodium	0.40
15.00	7	Magnesium aluminum silicate (Veegum® HV)	3.00
0.20	8	Ammonia solution (25%)	0.04
4.50	9	Sodium hypochlorite (5%)	0.90
100.00	10	Propylene glycol	20.00
0.75	11	Lemon mint flavor	0.15
QS	12	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

1. See manufacturing directions for aluminum hydroxide and magnesium hydroxide suspension.

ALUMINUM HYDROXIDE AND MAGNESIUM HYDROXIDE SUSPENSION

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
40.00	1	Aluminum hydroxide	40.00
40.00	2	Magnesium hydroxide	40.00
50.00 g	3	Cremophor RH 40	50.00
1.00	4	Silicon oil DC 200 (Serva)	1.00
100.00	5	Kollidon® CL-M	100.00
QS	6	Water	76.90

MANUFACTURING DIRECTIONS

1. Mix Cremophor RH 40 well with the silicon oil, add the water, and suspend the solid substances.

ALUMINUM HYDROXIDE AND MAGNESIUM HYDROXIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
405.00	1	Aluminum hydroxide gel (dried)	405.00
100.00	2	Magnesium hydroxide powder	100.00
108.00	3	Mannitol	108.00
38.80	4	Sorbitol powder	38.80
2.50	5	Saccharin sodium	2.50
16.70	6	Povidone (PVP K-30)	16.70
7.00	7	Magnesium stearate	7.00
2.00	8	Mint flavor (dry)	2.00
299.00	9	Purified water	299.00

MANUFACTURING DIRECTIONS

1. Dissolve items 4 and 5 in 59 g of purified water by using stirrer.
2. Add item 6 while mixing until clear solution is obtained.
3. Add items 1, 2, and 3 into mixer, and mix for 5 minutes using mixer and chopper at high speed.
4. Dilute concentrate-binding solution with 240 g of purified water.
5. Add binding solution at a rate of 9 to 11 g/min to the dry powders in mixer while mixing at low speed. Mix for 2 to 3 minutes. Scrape the sides, blade, and lid of the mixer. Mix and chop at low speed for an additional 2 to 3 minutes or until the granules stop flying around the chopper. Add extra-purified water, if required, and continue mixing until a satisfactory mass is obtained. Record extra quantity of purified water added.
6. Unload the wet mass into a clean Aeromatic bowl for drying. Avoid big lump formation, as this leads to nonuniform drying.
7. Dry the wet mass in an Aeromatic fluid-bed dryer at 60°C for 120 minutes. After 30 minutes of drying, scrape the semidried granules to break the lumps for uniform drying. Check the LOD (limit: NMT 5.5%).
8. Pass the dried granules through 1.5 mm sieve using granulator at medium speed. Collect in stainless steel drums. Set aside 7 to 9 g granules for later step.
9. Load the rest of the granules into blender. Pass items 8 and 7 through a sifter using a 250 µm sieve. Collect in a polyethylene bag.
10. Add approximately 7 to 9 g of granules, and mix gently.
11. Load into blender, and blend for 3 minutes.
12. Check temperature and humidity of the room before beginning compression (humidity limit: NMT 60%, temperature 25°C ± 1°C).
13. Compress the granules using a rotary tableting machine. Compress 680 mg tablets using 12.7 mm flat, beveled- edge punches.

ALUMINUM HYDROXIDE AND MAGNESIUM SILICATE CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
120.00	1	Aluminum hydroxide dried gel (Giulini)	120.00
250.00	2	Magnesium trisilicate	250.00
232.00	3	Ludipress®	232.00
6.00	4	Aerosil® 200	6.00
6.00	5	Magnesium stearate	6.00
12.00	6	Cyclamate sodium	12.00
1.50	7	Menthol	1.50

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with a compression force of 20 kN.
2. Because of the poor flowability of the powder, the tableting machine should be equipped with a special technical device to provide a continuous and homogeneous filling of the dies.
3. Each 16 mm biplanar tablet has an average weight of 640 mg.

ALUMINUM HYDROXIDE, MAGNESIUM CARBONATE (OR OXIDE), AND SIMETHICONE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
576.00	1	Sucrose	576.00
157.00	2	Aluminum hydroxide	157.00
160.00	3	Magnesium carbonate (or oxide)	160.00
97.00	4	Magnesium oxide	97.00
45.00	5	Kollidon® 90 F	45.00
22.00	6	Aerosil® 200	22.00
300.00	7	Simethicone suspension (30%)	300.00
9.00	8	Menthol	9.00
1.00	9	Saccharin sodium	1.00
49.00	10	Talc	49.00
13.00	11	Magnesium stearate	13.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 6 with the simethicone suspension, dry, sieve through a 0.8 mm screen, add items 8 to 11, and press with high compression force.
2. Tablet has an average weight of 1295 mg.

ALUMINUM HYDROXIDE, MAGNESIUM HYDROXIDE, AND SIMETHICONE SUSPENSION

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
27.00	1	Simethicone 30%	27.00
30.00	2	Cremophor RH 40	30.00
70.00	3	Water	70.00
80.00	4	Aluminum hydroxide dry gel (Giulini)	80.00
80.00	5	Magnesium hydroxide	80.00
90.00	6	Kollidon® CL-M	90.00
100.00	7	Sorbitol (crystalline)	100.00
4.00	8	Banana flavor	4.00
5.00	9	Coconut flavor	5.00
1.00	10	Saccharin sodium	1.00
QS	11	Water	QS to 1 L
QS	12	Citric acid (to adjust pH)	QS

MANUFACTURING DIRECTIONS

1. Mix Cremophor RH 40 with simethicone, and heat to approximately 50°C, stirring well.
2. Add warm water.
3. Dissolve the flavors and saccharin in water, and suspend aluminum hydroxide, magnesium hydroxide, and Kollidon® CL-M.
4. Add emulsion of items 1 to 3 to the stirred suspension of items 4 to 11, and adjust the pH to approximately 9 with item 12, if needed.

ALUMINUM HYDROXIDE, MAGNESIUM HYDROXIDE, AND SIMETHICONE SUSPENSION

Bill of Materials			
Scale (mg/5 mL)	Item	Material Name	Qty/L (g)
215.00	1	Aluminum hydroxide gel	435.00
80.00	2	Magnesium hydroxide paste (30%)	16.00
25.00	3	Simethicone emulsion (Simethicone Antifoam M30)	5.50
150.00	4	Sorbitol (70% solution)	30.00
0.20	5	Ammonia solution 25%	0.04
10.00	6	Methylparaben	2.00
1.00	7	Propylparaben	0.20
28.00	8	Methylcellulose 4000 (Methocel™ A4M)	5.60
2.00	9	Saccharin sodium	0.40
4.50	10	Sodium hypochlorite (5%)	0.90
1.00	11	Lemon mint flavor	0.20
QS	12	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

1. See manufacturing directions for aluminum and magnesium hydroxide suspension.

ALUMINUM HYDROXIDE, MAGNESIUM HYDROXIDE, AND SIMETHICONE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
200.00	1	Aluminum hydroxide gel (dried)	200.00
200.00	2	Magnesium hydroxide powder	200.00
200.00	3	Mannitol	200.00
45.00	4	Sorbitol powder	45.00
65.00	5	Dextrose (glucose) monohydrate	65.00
16.50	6	Povidone (PVP K-30)	16.50
2.50	7	Saccharin sodium	2.50
1.00	8	FD&C Yellow No.10 lake	1.00
2.50	9	Mint flavor (dry)	2.50
1.50	10	Lemon flavor (dry)	1.50
25.00	11	Simethicone GS granules	25.00
315.00	12	Dextrates (Emdex®)	315.00
1.00	13	Colloidal silicon dioxide (Aerosil® 200)	1.00
6.00	14	Magnesium stearate	6.00
–	15	Purified water	160.00

MANUFACTURING DIRECTIONS

1. Processing should be done at RH 50% ± 5% and temperature of 26°C ± 1°C.
2. Dissolve items 4, 5, and 7 in cold purified water (25–30°C) by using stirrer; then, add item 6 while mixing.
3. Add item 8, and disperse the color completely.
4. Check final weight; if required, adjust with purified water.
5. Load items 1, 2, and 3 into mixer, and mix for 5 minutes using mixer and chopper at high speed.
6. Add binding solution at a rate of 16 to 20 g/min to the dry powders in mixer while mixing at low speed. Mix for 2 to 3 minutes. Scrape the sides, blade, and lid of the mixer.
7. Mix and chop at low speed for an additional 2 to 3 minutes or until the granules stop flying around the chopper. Add extra-purified water, if required, and continue mixing until a satisfactory mass is obtained. Record extra quantity of purified water added.
8. Unload the wet mass into clean Aeromatic bowl for drying.
9. Avoid big lump formation, as this leads to nonuniform drying.
10. Dry the wet mass in an Aeromatic fluid-bed dryer at 60°C for 90 minutes.

11. After 30 minutes of drying, scrape the semidried granules to break up the lumps to promote uniform drying.
12. Pass the dried granules through a 1.5 mm sieve using a granulator at medium speed. Collect in stainless steel drums.
13. Load the granules into blender.
14. Add items 11 and 12 to stainless steel drum, and mix for 2 minutes using drum mixer; then, load into the blender, and mix along with the granules for 2 minutes.
15. Pass items 9, 10, 13, and 14 through sifter using 250 μ m sieve.
16. Load the sieved material into blender, and mix for 2 minutes. Unload into stainless steel drums.
17. Check temperature and humidity of the room before beginning compression.
18. Compress 1.2 g per tablet using 15.8 mm flat punch at RH 50% $\pm$ 5% at a temperature of 26°C $\pm$ 1°C.

ANALGESIC CLEAR GEL

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
25.00	1	Hydroxypropyl cellulose	25.00
QS	2	Deionized water	QS to 1 kg
400.00	3	Ethanol DEB 100	400.00
100.00	4	Menthol	100.00
150.00	5	Methyl salicylate	150.00
25.00	6	DEA-oleath-3-phosphate	25.00

MANUFACTURING DIRECTIONS

1. Hydrate hydroxypropyl cellulose in water at 60°C to 65°C.
2. Stir to cool.
3. Add ethanol.
4. Add remaining ingredients and stir until homogeneous.

ANALGESIC CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
130.00	1	Methyl salicylate	130.00
60.00	2	Menthol	60.00
20.00	3	Eucalyptus oil	20.00
5.00	4	Lanolin	5.00
1.00	5	Chloroxyleneol	1.00
150.00	6	Glyceryl stearate and PEG-100 stearate	150.00
73.00	7	Cetearyl alcohol	73.00
70.00	8	Glyceryl stearate	70.00
QS	9	Deionized water	QS to 1 kg
QS	10	Preservative, color	QS

MANUFACTURING DIRECTIONS

1. Heat oil and water phases separately to 70°C.
2. Add water phase to oil phase while stirring. Stir to cool.
3. Fill at 30°C.

ANALGESIC LOTION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
150.00	1	Methyl salicylate	150.00
70.00	2	Menthol	70.00
10.00	3	Lanolin oil	10.00
30.00	4	PEG-40 stearate	30.00
20.00	5	Glyceryl stearate	20.00
QS	6	Deionized water	QS
1.50	7	Carbopol® 980	1.50
10.00	8	Potassium hydroxide (10% aqueous solution)	10.00
QS	9	Preservative, color	QS

MANUFACTURING DIRECTIONS

1. Heat oil and water phases (except potassium hydroxide) separately to 65°C to 70°C.
2. Add water phase to oil phase while stirring.
3. Add potassium hydroxide solution to neutralize.
4. Stir to cool.
5. Fill at 30°C.

ANISE OIL SOLUTION

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
10.00	1	Anise oil	10.00
17.00	2	Cremophor RH 40	17.00
340.00	3	Ethanol	340.00
QS	4	Preservatives	QS
633.00	5	Water	633.00

MANUFACTURING DIRECTIONS

1. Mix the anise oil with Cremophor RH 40, heat to approximately 65°C, and stir strongly.
2. Slowly add the hot solution of items 3 to 5 to produce a clear or slightly opalescent, colorless liquid.

ANTAZOLINE AND XYLOMETAZOLINE EYE DROPS

Bill of Materials			
Scale (mg/100 mL)	Item	Material Name	Qty/L (g)
500.00 g	1	Antazoline sulfate	5.00
50.00 g	2	Xylometazoline hydrochloride	0.50
0.15	3	Hydroxypropylmethylcellulose (4000 cps)	1.50
0.10	4	Benzalkonium chloride; use benzalkonium chloride solution (17%) (7% excess)	0.63 mL
0.10	5	Edetate disodium	1.00
0.843	6	Sodium chloride	8.43
QS	7	Water purified	QS to 1 L

MANUFACTURING DIRECTIONS

Equipment used should be thoroughly cleaned and rinsed before proceeding. Use steam-jacketed, glass-lined, or stainless steel (No. 304 or better) tanks. The tank must be equipped with an agitator (preferably with speed control) and a cover to protect against air at all times during the manufacturing process, except when ingredients are being added or samples are being taken. Benzalkonium chloride markedly lowers the surface tension. During severe agitation or turbulent flow, substantial foaming will occur. This condition often exists in the processing equipment and in the overflow system of vacuum-filling machines. Benzalkonium chloride tends to concentrate in the foam. If the foam is not dissipated quickly, and if it is allowed to accumulate, a substantial excess of benzalkonium chloride may result near the surface of the liquid after the foam condenses; therefore, it is advisable to design the processing and filling systems in such a way as to minimize foaming and ensure rapid dissipation of any unavoidable foaming.

1. Fill mixing tank to 90% of final volume with purified water.
2. Heat water to 90°C, and while agitating, add and dissolve the hydroxypropylmethylcellulose by slowly sprinkling onto the surface of the water.
3. Methyl cellulose must be dispersed evenly over a period of time to ensure complete wetting and dispersion.
4. The agitation rate should be adjusted to avoid excessive foaming.
5. Allow 15 minutes for hydration of the hydroxypropylmethylcellulose before cooling.

6. Discontinue heating, and cool solution to approximately 40°C.
7. While agitating, add and dissolve antazoline sulfate, xylometazoline hydrochloride, benzalkonium chloride, edetate disodium, and sodium chloride.
8. Continue cooling to 25°C.
9. Turn off agitator, and QS to final volume. Mix well.
10. *Note:* Methylcellulose solutions filter at a slow rate. Recirculate the solution through filter assembly until clear.
11. Sterile filter, and fill.

ANTIACNE GEL

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
422.00	1	Witch hazel (distilled, 14% alcohol)	422.00
5.00	2	Salicylic acid	5.00
5.00	3	Aloe vera gel	5.00
10.00	4	Sorbitol	10.00
500.00	5	Polyglycerylmethacrylate	500.00
10.00	6	Propylene glycol	10.00
0.80	7	Methylparaben	0.80
0.20	8	Propylparaben	0.20

MANUFACTURING DIRECTIONS

1. Premix items 1 to 4.
2. Add item 5 with low-shear mixing until homogeneous.
3. Mix together items 6 to 8, and add them to the formulation.

ANTIFUNGAL FOOT POWDER

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
5.00	1	Dichlorobenzyl alcohol (Myacide SF)	5.00
5.00	2	Allantoin	5.00
200.00	3	Cornstarch	200.00
790.00	4	Talc	790.00

MANUFACTURING DIRECTIONS

1. Mix all ingredients using geometric dilution technique.

ANTISEPTIC CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
50.00	1	Polawax GP200	50.00
10.00	2	Lanolin	10.00
150.00	3	Mineral oil (70 cS)	150.00
70.00	4	Cetearyl alcohol	70.00
30.00	5	Dimethicone	30.00
QS	6	Deionized water	QS to 1 kg
5.00	7	Cetrimonium bromide	5.00
0.50	8	Chlorhexidine gluconate	0.50
QS	9	Perfume, preservative, color	QS

MANUFACTURING DIRECTIONS

1. Heat oil and water phases to 65°C.
2. Add water phase to oil phase while stirring.
3. Stir to cool.
4. Fill.

ANTISEPTIC LOTION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
30.00	1	Cetearyl alcohol and cetareth-20	30.00
50.00	2	Mineral oil (70 cS)	50.00
2.00	3	Lanolin alcohol	2.00
QS	4	Deionized water	QS to 1 kg
5.00	5	Cetrimonium bromide (as 40% cetrimide solution BP)	5.00
20.00	6	Glycerin	20.00
QS	7	Perfume, preservative, color	QS

MANUFACTURING DIRECTIONS

1. Heat oil and water phases separately to 70°C.
2. Add water phase to oil phase while stirring.
3. Stir to cool.
4. Fill at 30°C.

ANTISEPTIC LOTION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
30.00	1	Cetearyl alcohol and cetareth-20	30.00
45.00	2	Mineral oil (70 cS)	45.00
25.00	3	Stearyl alcohol	25.00
10.00	4	Lanolin	10.00
5.00	5	Polysorbate 60	5.00
15.00	6	Laneth-15	15.00
QS	7	Deionized water	QS to 1 kg
5.00	8	Cetrimonium bromide (as 40% cetrimide solution BP)	5.00
20.00	9	Glycerin	20.00
QS	10	Perfume, preservative, color	QS

MANUFACTURING DIRECTIONS

1. Heat oil and water phases separately to 70°C.
2. Add water phase to oil phase while stirring.
3. Stir to cool.
4. Fill at 30°C.

ANTISEPTIC WET WIPES

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
3.75	1	Cetrimonium bromide	3.75
0.15	2	Chlorhexidine gluconate	0.15
10.0–20.0	3	Polysorbate 20	10.0–20.0
10.0–20.0	4	Glycerin	10.0–20.0
QS	5	Deionized water	QS to 1 L
QS	6	Perfume	QS

MANUFACTURING DIRECTIONS

1. Preblend Polysorbate 20 and perfume.
2. Combine remaining components with stirring. Add perfume/Polysorbate 20 blend.
3. Stir until clear.
4. Package in wipes.

ASPARAGUS EXTRACT + PARSLEY EXTRACT TABLETS (200 MG+200 MG)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
200.00	1	Asparagus extract powder	200.00
200.00	2	Parsley extract powder	200.00
200.00	3	Sorbitol crystalline	200.00
20.00	4	Kollidon® VA 64	20.00
10.00	5	Kollidon® CL	10.00
4.00	6	Magnesium stearate	4.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve. Mix.
2. Press with low compression force at 636 mg.

ASPARTAME EFFERVESCENT TABLETS (20 MG)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
20.00	1	Aspartame	20.00
10.40	2	Sorbitol crystalline	10.40
14.30	3	Tartaric acid powder	14.30
18.70	4	Sodium carbonate	18.70
1.70	5	Kollidon® 25	1.70
1.10	6	PEG-6000 powder	1.10

MANUFACTURING DIRECTIONS

1. Mix and pass through a 0.5 mm sieve.
2. Press to tablets at 66 mg.

ASPARTAME GRANULES IN SACHETS

Bill of Materials			
Scale (mg/ sachet)	Item	Material Name	Qty/1000 Sachets (g)
30.00	1	Aspartame	30.00
2.00	2	Silicon dioxide (colloidal)	2.00
968.00	3	Cerelose powder N60 ^a	1052.00

^a Standard quantity of cerelose powder allows for LOD.

MANUFACTURING DIRECTIONS

1. Protect from moisture. Maintain RH 40% and temperature 25°C.

2. Oven dry cerelose powder at 50°C overnight until LOD is NMT 3% (3 hours, vacuum at 60°C).
3. Pass dried cerelose powder through 595 µm aperture screen in oscillating granulator.
4. Charge the following ingredients into suitable blender: aspartame, half of the amount of dried cerelose powder (milled), and colloidal silicon dioxide.
5. Add the balance of the dried cerelose powder (for a total amount of dried powder of 968 g/kg), and blend for 15 minutes.
6. Pass blended powders through an 840 µm screen using an oscillating granulator, and discharge into polyethylene-lined drums.
7. Fill weight is 1 g per sachet.

ASPARTAME POWDER IN SACHETS

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
47.50	1	Aspartame	47.50
2.50	2	Silicon dioxide (colloidal)	2.50
950.00	3	Mannitol granules	950.00

MANUFACTURING DIRECTIONS

1. Protect from humidity. Maintain RH 40% and temperature 25°C.
2. Pass mannitol granules and colloidal silicon dioxide through an 840 µm screen in oscillating granulator.
3. Charge the following ingredients into suitable blender: aspartame, half of the amount of mannitol granules, and colloidal silicon dioxide.
4. Add balance of mannitol granules, and blend for 15 minutes.
5. Pass blended powders through an 840 µm screen using an oscillating granulator, and discharge into polyethylene-lined drums.
6. Fill weight is 0.8 g per sachet.

ASPARTAME TABLETS (25 MG), DC

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
27.00	1	Aspartame	27.00
76.00	2	Ludipress®	76.00
12.00	3	Kollidon® CL	12.00
1.00	4	Magnesium stearate	1.00
3.00	5	Lutrol F68	3.00

MANUFACTURING DIRECTIONS

1. Mix all components, and pass through a 0.8 mm sieve.
2. Press to tablets with low compression force at 120 mg.

ASPARTAME TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
20.00	1	Aspartame	20.00
4.00	2	Cellulose (microcrystalline) (Avicel™ PH101), NF	4.00
4.00	3	Sodium starch glycolate (pH 5.5–7.5), NF International	4.00
0.50	4	Silicon dioxide (colloidal)	0.50
0.50	5	Povidone (PVP K-29–32), USP	0.50
14.00	6	Anhydrous alcohol (isopropyl, refined) USP	~14.00
34.00	7	Lactose (granulated)	34.00
4.00	8	Leucine, USP	4.00
3.00	9	Sodium benzoate (powder), NF	3.00

MANUFACTURING DIRECTIONS

1. Charge aspartame, cellulose microcrystalline, sodium starch glycolate, silicon dioxide, and povidone in a suitable mixer.
2. Blend for 20 minutes or until uniform.
3. While mixing, slowly add isopropyl alcohol to blended powders until a suitable granulating mass is obtained. Avoid overwetting.
4. Pass wet mass through a 2.38 mm screen on an oscillating granulator, and spread onto paper-lined trays.
5. Oven dry at 45°C to 50°C until LOD is NMT 1.2%.
6. Pass dried granulation through an 840 µm screen on an oscillating granulator.
7. Load dried granulation into a suitable mixer.
8. Add granulated lactose, leucine, and sodium benzoate, and blend for approximately 10 minutes.
9. Discharge into polyethylene-lined drums.
10. Compress tablets in a low-humidity area not to exceed 40% RH at 23°C.
11. Compress, using 7/32 in. concave punches, to the following specifications: weight of 10 tablets is 0.7 g; thickness of a tablet is 2.9 to 3.3 mm.

ASPARTAME TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
25	1	Aspartame	25
25	2	Dibasic calcium phosphate	25
3	3	Kollidon® VA 64	3
10	4	Water	10
3	5	Kollidon® CL	3
3	6	PEG-6000 (powder)	3

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 3 with items 4 and 5.
2. Pass through a 0.8 mm sieve. Mix with item 6.
3. Press to tablets 60 mg in weight with a 5 mm biplanar shape.

ASPARTAME TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
25.00	1	Aspartame	25.00
76.00	2	Ludipress®	76.00
12.00	3	Kollidon® CL	12.00
1.00	4	Magnesium stearate	1.00
3.00	5	Lutrol F 68	3.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press to tablets with low compression force.
2. Each 8 mm biplanar tablet has an average weight of 120 mg.

ASPARTAME TABLETS, EFFERVESCENT

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
20.00	1	Aspartame	20.00
10.40	2	Sorbitol (crystalline)	10.40
14.30	3	Tartaric acid (powder)	14.30
18.70	4	Sodium bicarbonate	18.70
1.70	5	Kollidon® 25	1.70
1.10	6	PEG-6000 (powder)	1.10

MANUFACTURING DIRECTIONS

1. Mix, pass through a 0.5 mm sieve, and press to tablets.
2. Each 6 mm biplanar tablet has an average weight of 66 mg.

ASPIRIN, ACETAMINOPHEN, AND CAFFEINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
225.00	1	Aspirin (40 mesh)	225.00
250.00	2	Acetaminophen (20 mesh)	250.00
30.00	3	Caffeine (granular)	30.00
100.00	4	Cellulose (microcrystalline) (Avicel™ PH102)	100.00
45.00	5	Anhydrous lactose	45.00
10.00	6	Croscarmellose sodium (Ac-Di-Sol)	10.00
5.00	7	Fumed silica	5.00
10.00	8	Stearic acid	10.00

MANUFACTURING DIRECTIONS

1. Mix items 1 to 6 in a suitable blender.
2. Pass the mixture through a mill using a 12 mesh screen with knives forward.
3. Add items 7 and 8, and blend the milled mixture for 20 minutes in a V-blender.
4. Compress to tablet weight of 675 mg.

ASPIRIN, ACETAMINOPHEN, CAFFEINE, AND SALICYLAMIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
200.00	1	Aspirin (40 mesh)	200.00
100.00	2	Salicylamide	100.00
100.00	3	Acetaminophen (40 mesh)	100.00
60.00	4	Caffeine (Granular)	60.00
150.00	5	Cellulose (microcrystalline) (Avicel™ PH101)	150.00
13.00	6	Stearic acid, USP	13.00
3.00	7	Fumed silica	3.00

MANUFACTURING DIRECTIONS

1. Screen all ingredients through a 20 mesh sieve.

2. Blend all the ingredients in a V-blender for 20 minutes.
3. Compress 615 mg tablets using 5/8 in. tooling.

ASPIRIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
325.00	1	Aspirin	325.00
25.52	2	Starch 1500®	25.52
21.33	3	Microcrystalline cellulose (50 µm)	21.33
6.33	4	Powdered cellulose	6.33

MANUFACTURING DIRECTIONS

1. Blend in a twin-shell blender.
2. Compress 378.00 mg tablets.

ASPIRIN-COATED CRYSTALS**FORMULATION**

Aqueous-based polymeric coating solution: Hydroxypropyl-methylcellulose (HPMC E5), 6.0%; propylene glycol, 1.0%; FD&C Red No. 3, 0.01%; and distilled water, QS to 100.

MANUFACTURING DIRECTIONS

1. A standard coating pan and an air suspension 6 in. column are used to coat aspirin crystals of 100 to 200 mesh using top-spray, bottom-spray, and tangential spray fluid-bed coating processes.
2. Aspirin crystal load is placed in the product container.
3. The crystals are fluidized in an expansion chamber.
4. The spray nozzle is located low in the expansion chamber so that liquid is applied when the crystals are moving at a higher velocity.
5. This serves to minimize surface wetting and to inhibit agglomeration.
6. A filter is used to separate entrained crystals from the exiting process air stream.
7. The pump is calibrated with coating solution prior to start-up of the coating process.
8. The turbine is activated, and the process air is heated to 55°C.
9. The spray and shake cycle is started and run continually until the coating solution is completely depleted.
10. The coated aspirin crystal bed is dried for 10 minutes, and the product is cooled to 35°C.
11. The product is removed, weighed, and passed through a 20 mesh screen to remove any agglomerates.

12. Tablets are prepared containing five components: 50% by weight aspirin crystals (100–200 mesh) coated previously with 3% to 6% polyvinylpyrrolidone (PVP); 25% calcium carbonate buffer, 5% to 15% hydroxypropylmethylcellulose (K100LV) as the gel-forming hydrophilic matrix material; 14.5% to 19.5% microcrystalline cellulose (Avicel™ PH101) as the excipient/binder; and 0.5% stearic acid as the hydrophobic lubricant.
13. The components of the tablet formulation are weighed and mixed.
14. 650 mg samples are compressed using 1/2 in. punches.

ATTAPULGITE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
475.00	1	Attapulgit (regular)	475.00
275.00	2	Attapulgit (colloidal)	275.00
12.00	3	PVP K 30	12.00
7.00	4	Ac-Di-Sol	7.00
15.00	5	Kollidon® CL	15.00
30.00	6	Sucrose	30.00
50.00	7	Klucel® EF	50.00
40.00	8	Sucrose	40.00
35.00	9	Ac-Di-Sol	35.00
25.00	10	Kollidon® CL	25.00
14.00	11	Talc (fine powder)	14.00
5.00	12	Pectin	5.00
7.00	13	Glyceryl behenate	7.00
5.00	14	Aerosil® 200	5.00
5.00	15	Magnesium stearate	5.00
—	16	Purified water	32.00
—	17	Ethanol (95%)	23.00

MANUFACTURING DIRECTIONS

Use face mask, hand gloves, and clean uniform. Avoid dust and inhalation of powder.

1. Dissolve sucrose (item 6) in purified water by using an appropriate stirrer at slow speed in a stainless steel container.
2. Dissolve Klucel® EF in the ethanol by using an appropriate stirrer at slow speed in stainless steel container.
3. Mix the two steps in a stainless steel drum by using an appropriate stirrer at slow speed.

4. Take item 8 (sucrose), and pass through a Fitz mill using sieve No. 24250 (impact forward, high speed). Collect in a stainless steel drum.
5. Add items 1 to 5, and sift the material through a 500 µm sieve using a Russell sifter.
6. Mix for 3 minutes.
7. Add the binding solution prepared earlier at a speed of 6 to 8 kg/min to the dry powder in an appropriate mixer at slow speed. After addition, scrape sides and blades; then, mix and chop further for 1 minute at slow speed. Check for satisfactory wet mass. Add additional purified water, if required, to obtain satisfactory wet mass.
8. Spread the granules onto stainless steel trays to a thickness of one-fourth of the tray thickness, and load the trays on the trolley.
9. Load the trolleys into the oven, and dry the granules at 55°C for 16 hours.
10. After 4 hours of drying, stir the granules on the trays, and change the position of the trays for uniform drying.
11. Check the LOD of dried granules (limit: 2.5–3.5%).
12. The LOD should be strictly maintained; otherwise, tablet hardness and friability are affected. If required, dry further to obtain the desired LOD.
13. Grind the dried granules using first a 2.5 mm sieve and then a 1.25 mm sieve.
14. Load the ground material into a double-cone blender.
15. Sift items 9, 10, 12, and 14 through a 500 µm sieve, and add mixture to the double-cone blender.
16. Mix for 5 minutes.
17. Sift items 11, 13, and 15 through a 250 µm sieve, and collect in a polyethylene bag.
18. Add approximately 2 to 3 kg bulk granules from earlier step, mix, and add to the double-cone blender.
19. Mix for 1 minute.
20. Compress the granules using an 18 mm × 8 mm oblong, capsule-shaped, parallel, concave plain punch for a 1 g tablet weight of hardness 12 to 18 kp.
21. Coat the tablets using one of the HPMC coating solutions (see Appendix).

AZULENE SOLUTION (1%)

MANUFACTURING DIRECTIONS

1. Mix 1 g azulene with 3 g Cremophor RH 40, and heat to approximately 60°C.
2. Slowly add water (60°C) to 100 mL, and cool to room temperature.

BABY CREAM, BENZALKONIUM CHLORIDE AND ZINC OXIDE

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
0.002 mL	1	Benzalkonium chloride solution	2.30 mL
85.00 mg	2	Zinc oxide (powder)	85.00
100.00 mg	3	Polawax (emulsifying, nonionic wax)	100.00
16.00 mg	4	Alcohol cetostearyl	16.00
4.00 mg	5	Lanolin (acetylated/anhydrous, regular)	4.00
80.00 mg	6	Glycerin (96%)	80.00
10.00 mg	7	Oil (neutral, vegetable triglycerides mixture; Miglyol®)	10.00
0.50 mg	8	Propylparaben (Aseptoform™ P)	0.50
1.00 mg	9	Methylparaben (Aseptoform™ M)	1.00
0.80 mL	10	Purified water	QS to 800.00 mL
0.24 mg	11	Perfume (Diabolo 110.388/B)	0.24

MANUFACTURING DIRECTIONS

Avoid mixing air into emulsion. Emulsify under vacuum to minimize air entrapment. Use jacketed tank with vacuum with high-speed agitator (adjustable, slow-speed, anchor type with Teflon sweep blades).

1. If necessary, mill zinc oxide in a Fitz mill or similar device (impact forward, maximum speed), fitted with a 250 µm screen.
2. Repeat three times.
3. Heat 800 mL of water to 75°C in a steam-jacketed mixing tank, and dissolve methylparaben.
4. Maintain temperature at 75°C.
5. Disperse milled zinc oxide in solution of previous step.
6. Maintain temperature at 75°C.
7. Dissolve benzalkonium chloride and glycerin in solution, and maintain temperature at 75°C.
8. In a separate steam-jacketed tank, add Polawax, cetostearyl alcohol, acetylated lanolin, oil, and propylparaben. Carefully melt at 70°C.
9. Adjust the turbomixer of the steam-jacketed tank containing the aqueous phase to maximum speed, keeping the temperature at 75°C.
10. Slowly add the oil phase to the aqueous phase.
11. Generate as much vacuum as possible, and maintain it for the rest of the process.

12. Circulate cold water to allow a slow temperature decrease (down to 60°C).
13. Stop the turbomixer, and set the anchor-type agitator at minimum speed until 40°C to 45°C is reached.
14. The temperature decrease must be very slow.
15. Break the vacuum, and add perfume to cream with anchor-type agitator set at slow speed.
16. Continue to mix until the perfume is completely dispersed.

BABY LOTION

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
50.00	1	Alcohol (ethanol; natural cosmetic grade)	50.00
50.00	2	Propylene glycol	50.00
0.80	3	Ethoxylated nonyl phenol	0.80
0.005	4	FD&C Red dye No. 40	5.70 mg
0.41	5	FD&C Blue dye No. 1	0.41
0.70	6	FD&C Yellow dye No. 5	0.70
0.40	7	Perfume essence (Nelandia)	0.40
QS	8	Hydrochloric acid (reagent-grade bottles)	~0.01
QS	9	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

Use 316 or more resistant-grade stainless steel tank.

1. Charge approximately 800 mL of purified water in main mixing tank.
2. Add alcohol and propylene glycol, and mix for 5 minutes.
3. Separately dissolve each dye in sufficient water to obtain 0.5% dye solutions.
4. Add color solutions to main tank, and mix.
5. Rinse containers with small portions of purified water, and add rinsings.
6. Dissolve perfume essence in ethoxylated nonyl phenol.
7. Add solution from previous step to main tank, and mix for 5 minutes.
8. Determine pH of solution, and adjust if necessary with 5% hydrochloric acid solution.
9. Mix well. pH should be 5.7 to 5.9.
10. QS to 1 L with purified water.

BABY SHAMPOO

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
250.00	1	Sodium alkyl ether sulfate/sulfonate	250.00
30.00	2	Monatonic CAB surfactant	30.00
30.00	3	Cocamide DEA surfactant (Synotol CN 90)	30.00
1.00	4	Methylparaben	1.00
0.52	5	Anhydrous citric acid	0.52
0.003	6	FD&C Yellow dye No. 6	3.50 mg
0.01	7	FD&C Yellow dye No. 5	15.00 mg
4.00	8	Ethoxylated nonyl phenol	4.00
3.00	9	Perfume I	3.00
1.00	10	Perfume II	1.00
8.50	11	Sodium chloride	8.50
QS	12	Purified water	QS to 1 kg

MANUFACTURING DIRECTIONS

Use 315 or more resistant-grade stainless steel tank.

1. Add approximately 270 g of purified water to the main mixing tank.
2. With slow agitation, add cocamide DEA surfactant.
3. Add and dissolve methylparaben, and mix for approximately 10 minutes.
4. Add the following ingredients to tank: sodium alkyl sulfate/sodium alkyl ether sulfate/sulfonate, monatonic CAB surfactant, and approximately 280 g of purified water.
5. Mix for 15 minutes until complete solution is obtained.
6. With constant stirring, slowly add citric acid (10% solution) until a pH of 6.9 to 7.1 is maintained constantly for 5 minutes after the last addition of the citric acid solution.
7. Separately dissolve FD&C Yellow No. 5 and 6 (if used) in sufficient purified water.
8. Add dye solution from preceding step to main tank, and mix.
9. Rinse containers with a small portion of purified water, and add rinsings.
10. Separately mix ethoxylated nonyl phenol with perfumes (perfume available from Firmenich; Plainsboro, NJ), and add to main mixing tank.
11. Rinse container with purified water, and add rinsings.
12. Mix until completely dissolved.
13. Slowly add in small portions sodium chloride to adjust the viscosity to between 1500 and 3500 cps.
14. Mix for 15 minutes.
15. If necessary, QS to 1 kg with purified water.

BARIUM SULFATE ORAL SUSPENSION (23%)**FORMULATION**

Barium sulfate, 100.0 g; Kollidon® 90 F, 5.0 g; carboxymethyl cellulose sodium, 0.4 g; sodium bisulfite, <0.5 g; preservatives, QS; water, 320.0 g.

MANUFACTURING DIRECTIONS

1. Dissolve the preservatives and the carboxymethyl cellulose sodium in the hot water.
2. Add Kollidon® 90 F and sodium bisulfite.
3. In the obtained clear solution, suspend barium sulfate.

BASIC CREAM FOR VARIOUS ACTIVE INGREDIENTS

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
70.00	1	Cetylstearyl alcohol	70.00
15.00	2	Cremophor A 6	15.00
15.00	3	Cremophor A 25	15.00
120.00	4	Liquid paraffin	120.00
2.00	5	Paraben(s)	2.00
680.00	6	Water	680.00
80.00	7	Propylene glycol	80.00
1.00–20.00	8	Active ingredient	1.00–20.00

MANUFACTURING DIRECTIONS

1. Separately heat a mixture of items 1 to 5 and the water to approximately 80 °C.
2. Add the water to the obtained solution with rigorous stirring.
3. Heat items 7 and 8 until the active ingredient is dissolved, mix with aqueous solution, and continue to stir during cooling to room temperature.
4. This white basic cream can be readily used for active ingredients soluble in 1, 2-propylene glycol.

BENZALKONIUM CHLORIDE CONTRACEPTIVE GEL

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
50.00	1	PEG-6, PEG-32, and glycol stearate (Tefose® 63)	50.00
30.00	2	Apricot kernel oil PEG-6 esters (Labrafil® M 1944 CS)	30.00
816.00	3	Deionized water	816.00
80.00	4	Hydroxyethylcellulose	80.00
24.00	5	Benzalkonium chloride (50 wt% in water)	24.00

MANUFACTURING DIRECTIONS

1. Mix items 3 and 4 at room temperature.
2. Heat to 75°C, and add items 1 and 2 while stirring.
3. Cool with gentle stirring to 30°C; then, add item 5 and stir.

BENZOYL PEROXIDE AND ALPHA-BISABOLOL GEL

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
2.00	1	Alpha-Bisabolol, natural (BASF)	2.00
60.00	2	Propylene glycol	60.00
100.00	3	Triethanolamine	100.00
30.00	4	Cremophor RH 40	30.00
30.00	5	Kollidon® 30	30.00
408.00	6	Water	408.00
10.00	7	Carbopol® 940	10.00
400.00	8	Water	400.00
50.00	9	Benzoyl peroxide	50.00

MANUFACTURING DIRECTIONS

1. Prepare suspension of items 7 and 8. Let swell for 1 hour.
2. Add this suspension to the well-stirred solution of items 1 to 5.
3. Add item 9 to produce a colorless, transparent gel.

BENZOYL PEROXIDE ANTIACNE CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
460.50	1	Deionized water	460.50
5.00	2	Carbomer 940	5.00
10.00	3	Hydroxypropylmethylcellulose (HPMC, medium viscosity)	10.00
137.50	4	Deionized water	137.50
70.00	5	Purified bentonite (Polargel®, NF)	70.00
2.00	6	Methylparaben	2.00
1.00	7	Propylparaben	1.00
20.00	8	Glyceryl stearate	20.00
60.00	9	Propylene glycol	60.00
20.00	10	PEG-600	20.00
20.00	11	Myristyl propionate	20.00
50.00	12	Dimethicone	50.00
70.00	13	Purified bentonite (Polargel, NF)	70.00
10.00	14	Titanium dioxide	10.00
100.00	15	Benzoyl peroxide (70%)	100.00

MANUFACTURING DIRECTIONS

1. Sift Carbomer 940 into vortex in water. When completely dispersed, sift in the HPMC.
2. Add parabens with stirring, and heat to at least 80°C until dissolved.
3. Add glyceryl stearate.
4. Blend in propylene glycol and items 10 to 13 in order, and mix well.
5. After addition of the Polargel®, allow 15 minutes of mixing to complete hydration.
6. Blend propylene glycol portion into the first part.
7. Add benzoyl peroxide and titanium dioxide to the mixture, and mill.

BENZOYL PEROXIDE ANTIACNE GEL

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
2.50	1	Acrylates/C10-30 alkyl acrylate cross-polymer (Permulen TR1)	2.50
4.00	2	Carbopol 980	4.00
QS	3	Deionized water	QS to 1 kg
40.00	4	Isopropyl myristate	40.00
10.00	5	Cetyl alcohol	10.00
20.00	6	Glyceryl stearate	20.00
50.00	7	Sodium hydroxide (0.5 M)	50.00
15.00	8	Deionized water	15.00
50.00	9	Benzoyl peroxide	50.00
50.00	10	PEG-600	50.00
QS	11	Perfume, preservative	QS

MANUFACTURING DIRECTIONS

1. Hydrate Carbopol and permulen in warm water at 60°C.
2. When fully hydrated, heat to 70°C.
3. Heat oil phase to 70°C.
4. Add water phase to oil phase while stirring.
5. Add sodium hydroxide, and continue stirring.
6. Combine benzoyl peroxide, PEG-600, and deionized water, and add to the emulsion.
7. Homogenize at 35°C with caution, using suitable equipment.

BENZOYL PEROXIDE ANTIACNE LOTION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
40.00	1	Purified bentonite (Polargel®, NF)	40.00
10.00	2	Hydroxypropylmethylcellulose (HPMC)	10.00
522.20	3	Water	522.20
190.00	4	Water	190.00
2.00	5	Methylparaben	2.00
2.00	6	Propylparaben	2.00
20.00	7	Glyceryl stearate	20.00
60.00	8	Propylene glycol	60.00
20.00	9	Myristyl propionate	20.00
5.00	10	Dimethicone	5.00
QS	11	Iron oxides	QS
10.00	12	Titanium dioxide	10.00
100.00	13	Benzoyl peroxide (77%)	100.00

MANUFACTURING DIRECTIONS

1. Sift the Polargel® into water with rapid mixing.
2. Allow to hydrate for 15 minutes.
3. Pass HPMC through a coarse sieve, add to the Polargel® solution, and mix until all lumps are removed.
4. Add parabens to the water with stirring, and heat to 90°C to dissolve the parabens.
5. Add items 4 to 10, and mix well; then, add these to the HPMC mixture.
6. Mix well again.
7. Finally, add items 11 to 13, and mix.

BENZOYL PEROXIDE ANTIACNE MICROEMULSION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
470.00	1	Ethoxydiglycol (Transcutol®)	470.00
250.00	2	PEG-8 caprylic/Capric glycerides (Labrasol®)	250.00
150.00	3	Dipelargonate propylene glycol (DPPG)	150.00
80.00	4	Benzoyl peroxide	80.00
50.00	5	Propylene glycol laurate (Lauroglycol®)	50.00

MANUFACTURING DIRECTIONS

1. Mix items 1 to 3.
2. Dissolve item 4 in this mixture with mixing for 1.5 to 2.0 hours.
3. Add item 5 to mixture, and mix until uniform emulsion is obtained.

BENZYL BENZOATE SOLUTION

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
100.00	1	Benzyl benzoate	100.00
220.00	2	Cremophor RH 40	220.00
410.00	3	Ethanol (96%)	410.00
270.00	4	Water	270.00

MANUFACTURING DIRECTIONS

1. Heat the mixture of benzyl benzoate and Cremophor RH 40 to approximately 60°C.
2. Stir strongly, and slowly add the water.
3. Finally, add the ethanol to produce a clear, colorless liquid.

BERBERINE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
5.00	1	Berberine sulfate, with excess	5.70
54.10	2	Lactose monohydrate	54.10
54.10	3	Ludipress®	54.10
1.20	4	Magnesium stearate	1.20

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with low compression force.
2. Each 6 mm biplanar tablet has an average weight of 115 mg.

BETA-CAROTENE + VITAMIN C + VITAMIN E CHEWABLE TABLETS (10 MG + 500 MG + 250 MG)**FORMULATION**

Beta-carotene dry powder 10%, 100 g; ascorbic acid, crystalline (BASF), 250 g; sodium ascorbate, crystalline, 280 g; vitamin E acetate dry powder SD, 50, 500 g; (BASF) sorbitol, crystalline, 600 g; Ludipress®, 500 g; fructose, 350 g; polyethylene glycol 6000, powder, 50 g.

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a sieve, and press with high compression force at 2600 mg.

BETA-CAROTENE + VITAMIN C + VITAMIN E EFFERVESCENT TABLETS (12 MG + 150 MG + 25 MG)

FORMULATION

Lucarotene dry powder 10% CWD G/Y (BASF), 120 g; ascorbic acid, crystalline (BASF), 150 g; dry vitamin E acetate 50% DC (BASF), 50 g; Ludipress® LCE [1], 705 g; Kollidon® VA64, 50 g; citric acid, anhydrous, 450 g; sodium bicarbonate, 320 g; polyethylene glycol 6000, powder, 75\g; orange flavor (Dragoco), 50\g; aspartame (Searle), 30\g.

MANUFACTURING DIRECTIONS

1. Mix all components. Pass through a sieve.
2. Press with high compression force at a maximum of 30% of relative atmospheric humidity at 2.045 mg.

BETA-CAROTENE + VITAMIN C + VITAMIN E TABLETS (7 MG + 60 MG + 25 MG)

FORMULATION

Betavit® dry powder 10% (BASF), 75 g; ascorbic acid, powder (BASF), 60 g; vitamin E acetate dry powder 50%, 50 g; sorbitol, crystalline, 240 g; Kollidon® CL, 30 g; magnesium stearate, 5 g.

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with low compression force at 497 mg.

BETA-CAROTENE + VITAMIN C + VITAMIN E TABLETS (12 MG + 250 MG + 125 MG)

FORMULATION

Beta-carotene dry powder 10%, 125 g; ascorbic acid, crystalline (BASF), 125 g; sodium ascorbate, crystalline (BASF), 141 g; vitamin E acetate dry powder SD 50, 250 g; (BASF) Ludipress® or sorbitol, crystalline, 119 g; polyethylene glycol 6000, powder, 5 g; orange flavor (FDO), 15 g; sodium cyclamate, 10 g.

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a sieve, and press with medium compression force at 790 mg.

BETA-CAROTENE EFFERVESCENT TABLETS (7 MG)

FORMULATION

Lucarotin® dry powder 10% CWD (BASF), 70 g; Ludipress®, 113 g; citric acid, anhydrous, 200 g; sodium bicarbonate, 120 g; sodium carbonate, 12 g; sodium cyclamate, 20 g; aspartame, 15 g; orange flavor, 20 g; polyethylene glycol 6000, powder, 30 g.

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with medium or high compression force at maximum 30% of relative atmospheric humidity.

BETA-CAROTENE EFFERVESCENT TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
7.00	1	Beta-carotene; use Lucarotin® CWD (dry powder, 10%) (BASF)	70.00
113.00	2	Ludipress®	113.00
200.00	3	Anhydrous citric acid	200.00
120.00	4	Sodium bicarbonate	120.00
12.00	5	Sodium carbonate	12.00
20.00	6	Sodium cyclamate	20.00
15.00	7	Aspartame	15.00
20.00	8	Orange flavor	20.00
30.00	9	PEG-6000 (powder)	30.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve. Mix.
2. Press with medium or high compression force at maximum RH 30%.
3. Use 12 mm biplanar punches for 602 mg tablets.

BETA-CAROTENE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
15.00	1	Beta-carotene (dry powder, 10% with excess)	160.00
240.00	2	Ludipress®	240.00
175.00	3	Dicalcium phosphate, granulated with 5% Kollidon® 30	175.00
6.00	4	Kollidon® CL	6.00
2.00	5	Magnesium stearate	2.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with medium compression force.
2. Compress 400 mg in 12 mm biplanar punches.

BETA-CAROTENE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Quantity/1000 Tablets (g)
15.00	1	Beta-carotene (dry powder, 10%)	150.00
175.00	2	Dicalcium phosphate, granulated with 5% Kollidon® 30	175.00
100.00	3	Avicel™ PH101	100.00
5.00	4	Kollidon® CL	5.00
2.50	5	Aerosil® 200	2.50
20.00	6	Talc	20.00
2.50	7	Calcium arachinate	2.50

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with a medium compression force.
2. Compress 502 mg in 12 mm biplanar punches.

BETA-CAROTENE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
20.00	1	Beta-carotene (dry powder, 10%)	220.00
250.00	2	Avicel™ PH101	250.00
20.00	3	Kollidon® CL	20.00
2.00	4	Aerosil® 200	2.00

MANUFACTURING DIRECTIONS

1. Mix all components, and press with a low compression force.
2. Compress 518 mg in 12 mm biplanar punches.

BETA-CAROTENE, VITAMIN C, AND VITAMIN E CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
10.00	1	Beta-carotene (dry powder, 10%)	100.00
250.00	2	Ascorbic acid (crystalline) (BASF)	250.00
280.00	3	Sodium ascorbate (crystalline)	280.00
500.00	4	Vitamin E acetate (dry powder, SD 50)	500.00
600.00	5	Sorbitol (crystalline)	600.00
500.00	6	Ludipress®	500.00
350.00	7	Fructose	350.00
50.00	8	PEG-6000 (powder)	50.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a sieve, and press with high compression force.
2. Each 20 mm biplanar tablet has an average weight of 2.6 g.

BETA-CAROTENE, VITAMIN C, AND VITAMIN E TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
12.00	1	Beta-carotene (dry powder, 10% with excess)	125.00
125.00	2	Ascorbic acid (crystalline) (BASF)	125.00
141.00	3	Sodium ascorbate (crystalline) (BASF)	141.00
250.00	4	Vitamin E acetate (dry powder, SD 50)	250.00
119.00	5	Ludipress® or sorbitol (crystalline)	119.00
5.00	6	PEG-6000 (powder)	5.00
15.00	7	Orange flavor (FDO)	15.00
10.00	8	Sodium cyclamate	10.00

MANUFACTURING DIRECTIONS

1. Mix all components. Pass through a sieve.
2. Press with medium compression force.
3. Compress 790 mg into 12 mm biplanar tablets.

BETA-CAROTENE, VITAMIN C, AND VITAMIN E TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
6.00	1	Beta-carotene; use Betavit (dry powder, 10% with excess) (BASF)	65.00
100.00	2	Ascorbic acid (powder) (BASF)	100.00
60.00	3	Vitamin E acetate (dry powder, 50%)	60.00
369.00	4	Ludipress®	369.00
6.00	5	Magnesium stearate	6.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve. Mix.
2. Press with medium or high compression force.
3. Compress 599 mg into 12 mm biplanar tablets.

BETA-CAROTENE, VITAMIN C, AND VITAMIN E TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
6.00	1	Beta-carotene; use Betavit (dry powder, 10% with excess) (BASF)	65.00
100.00	2	Ascorbic acid (powder) (BASF)	100.00
60.00	3	Vitamin E acetate (dry powder, 50%)	60.00
233.00	4	Sorbitol (crystalline) (Merck)	233.00
30.00	5	Kollidon® VA 64	30.00
8.00	6	Kollidon® CL	8.00
4.00	7	Magnesium stearate	4.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve. Mix.
2. Press with medium or high compression force.
3. Compress 502 mg into 12 mm biplanar tablets.

BETA-CAROTENE, VITAMIN C, AND VITAMIN E TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
7.00	1	Beta-carotene; use Betavit (dry powder, 10% with excess) (BASF)	75.00
60.00	2	Ascorbic acid (powder) (BASF)	60.00
50.00	3	Vitamin E acetate (dry powder, 50%)	50.00
240.00	4	Sorbitol (crystalline)	240.00
30.00	5	Kollidon® CL	30.00
5.00	6	Magnesium stearate	5.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve. Mix.
2. Press with low compression force.
3. A colorant pigment should be added to obtain a homogeneous appearance of tablets.
4. Use 12 mm biplanar punches for 497 mg tablets.

BETAMETHASONE AND NEOMYCIN GEL CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Quantity/ kg (g)
1.30	1	Betamethasone valerate	0.13
6.50	2	Neomycin sulfate	0.65
150.00	3	Lutrol E 400	15.00
100.00	4	Miglyol® 812	10.00
200.00	5	Lutrol F 127	20.00
QS	6	Water	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Dissolve betamethasone valerate in a mixture of Lutrol E 400 and Miglyol® 812.
2. Dissolve Lutrol F127 and neomycin sulfate in water at 5°C to 10°C.
3. Mix both solutions.
4. Maintain cool temperature until the air bubbles disappear. A milky white, soft gel cream is obtained.

BETAMETHASONE CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Quantity/ kg (g)
70.00	1	Cetylstearyl alcohol	70.00
15.00	2	Cremophor A 6	15.00
15.00	3	Cremophor A 25	15.00
12.00	4	Liquid paraffin	12.00
2.00	5	Paraben(s)	2.00
697.00	6	Water	697.00
80.00	7	Propylene glycol	80.00
1.00	8	Betamethasone	1.00

MANUFACTURING DIRECTIONS

1. Heat the mixture of items 1 to 5 and item 6 separately to approximately 80°C.
2. Add together with rigorous stirring.
3. Heat items 7 and 8 until the active ingredient is dissolved.
4. Mix with the previous mixture, and continue to stir to cool to room temperature to produce white cream.

BETAMETHASONE GEL

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
1.00	1	Betamethasone valerate	1.00
100.00	2	Ethanol (96%)	100.00
200.00	3	Propylene glycol	200.00
220.00	4	Lutrol F 127	220.00
QS	5	Water QS	470.00

MANUFACTURING DIRECTIONS

1. Prepare a solution of items 1 to 3 at room temperature and a solution of items 4 and 5 at approximately 6°C (or >70 °C).
2. Mix both solutions.
3. Maintain the temperature until the air bubbles disappear.
4. A certain amount of propylene glycol could be substituted by water. The obtained gel is clear and colorless.

BETAMETHASONE VALERATE CREAM

Bill of Materials			
Scale (g/100 g)	Item	Material Name	Qty/kg (g)
0.10	1	Betamethasone valerate (34% excess)	1.34
2.00	2	Poloxyl 20 cetostearyl ether (Cetomacrogol 1000)	20.00
8.00	3	Cetostearyl alcohol	80.00
0.10	4	Methylparaben	1.00
0.034	5	Propylparaben	0.34
0.10	6	Chlorocresol	1.00
6.00	7	Mineral oil (liquid paraffin)	60.00
0.29	8	Monobasic sodium phosphate	2.90
17.80	9	Petrolatum (soft white paraffin)	178.00
66.00	10	Purified water	660.00

MANUFACTURING DIRECTIONS

1. Heat item 10 to 90°C in mixer.
2. Dissolve items 4 and 5 (parabens) to a clear solution by stirring.
3. Dissolve 3 g of item 2 in the parabens solution while stirring.
4. Dissolve items 6 and 8 in the parabens solution while stirring.
5. Set the mixer at a temperature of 65°C to 70°C and speed at 8 rpm. Use manual mode.
6. Load 17 g of items 2, 3, and 9 and 45 g of item 7 in a fat-melting vessel.

7. Heat to 70°C to 75°C while stirring. Maintain temperature at 65°C to 7°C.
8. Mix item 1 in 10 g of item 7 in a stainless steel container.
9. Homogenize for 10 minutes to make a smooth slurry.
10. Check the temperature of the aqueous phase in the mixer (should be 65–70°C).
11. Check the temperature of the fatty phase in the fat-melting vessel (should be 65–70 °C).
12. Set the mixer speed at 8 rpm and vacuum at 0.4 to 0.6 bar.
13. Transfer the fatty phase to the aqueous phase in mixer vessel through filter under vacuum while mixing.
14. Start the homogenizer at high speed. Homogenize for 10 minutes.
15. Check and record the pH of cream (limit 4.5–5.2 at 30°C).
16. Cool the temperature to 50°C while mixing. Release the vacuum.
17. Take out 400 g of the cream into the stainless steel vessel, and set aside.
18. Add slurry from earlier step to the remaining cream base in mixer.
19. Rinse the container of slurry using 5 g of item 7, and transfer the rinsings to the mixer.
20. Homogenize for 10 minutes at high speed (mixer speed 8 rpm).
21. Load 400 g cream from preceding step to the mixer.
22. Set the mixer in manual mode at 8 rpm and a vacuum of 0.4 to 0.6 bar.
23. Homogenize at high speed with recirculation, temperature 25°C. Homogenize for 10 minutes with recirculation, stop the homogenizer, and continue mixing to produce a white, homogeneous cream of pH 4.5 to 5.2 at 30°C.

BETAMETHASONE VALERATE OINTMENT

Bill of Materials			
Scale (g/100 g)	Item	Material Name	Qty/kg (g)
0.10	1	Betamethasone; use betamethasone valerate	1.30
84.87	2	Petrolatum (soft white paraffin)	848.70
15.00	3	Mineral oil (liquid paraffin)	150.00

MANUFACTURING DIRECTIONS

1. Melt item 2 in a fat-melting vessel at 75°C while mixing (do not overheat item 2). Maintain temperature of the molten mass in the melting vessel at 60°C to 65°C.

2. Start the steam on the mixer vessel, and set the temperature at 60°C.
3. Transfer 160 g of the molten mass at 60°C to the mixer vessel.
4. Retain the rest of the quantity in the fat-melting vessel.
5. Start mixing in the mixer vessel at medium speed with a vacuum between 0.4 and 0.6 bar until obtaining actual temperature of 40°C to 45°C. Maintain the temperature of mixer vessel at 40°C to 45°C.
6. Add item 1 in 80 g of item 3, and homogenize for 3 minutes using a homogenizer.
7. Keep the slurry aside.
8. Rinse the homogenizer and container with 70 g of item 3.
9. Transfer item 1 slurry from step 7 and the rinsings from the previous step to the mixer vessel.
10. Start mixing under a vacuum of 0.4 to 0.6 bar for 15 minutes.
11. The temperature should be maintained at 40°C to 45°C.
12. Slowly transfer the rest of the quantity of molten mass (temperature 60°C) into mixer vessel. Continue mixing for 5 minutes after each addition.
13. At the end of addition, mix an additional 10 minutes under a vacuum of 0.4 to 0.6 bar.
14. Homogenize for 5 minutes at high speed under a vacuum of 0.4 to 0.6 bar.
15. Cool the ointment to 30°C to 35°C with stirring under a vacuum of 0.4 to 0.6 bar.

BISACODYL DELAYED-RELEASE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
05.00	1	Bisacodyl	5.00
20.00	2	Cellulose (microcrystalline) (Avicel™ PH102)	20.00
45.27	3	Lactose (spray dried) ^a	45.27
04.00	4	Maize starch (dried) ^b	4.00
00.73	5	Magnesium stearate	0.73

^a Particle size distribution: minimum: 98%, 250 µm, 30% to 60%, 100 µm; maximum: 15%, 45 µm.

^b LOD NMT 4.5%, when dried at 120°C for 4 hours.

MANUFACTURING DIRECTIONS

Handle bisacodyl carefully; it can cause itching if it comes into contact with skin. Overmixing of lubricants reduces the hardness. Check the temperature and RH of the room before beginning processing. Limit RH to 50% to 60% and temperature to 27°C to 30°C.

1. Mix items 1 and 2 in a stainless steel drum for 2 to 3 minutes.
2. Pass the mixed powder through a 500 µm sieve using sifter.
3. Collect in stainless steel drum.
4. Pass item 3 through a 500 µm sieve using sifter.
5. Collect in stainless steel drum.
6. Load the sieved material into the drum mixer, and mix for 5 minutes.
7. Mix items 4 and 5 in a polyethylene bag for 1 minute.
8. Pass the mix through a 250 µm sieve.
9. Collect in a polyethylene bag.
10. Add 3 to 5 g powder to it, and mix for 1 minute.
11. Add this mixture, and mix for 1 minute in a drum blender.
12. Check the moisture content (limit: 1.0–1.5%).
13. Compress the granules using a rotary tableting machine; 6 mm biconvex tablets have an average weight of 750 mg and hardness of 4 to 5 kp.
14. Apply enteric coating.

BISACODYL SUPPOSITORIES

Bill of Materials			
Scale (mg/ suppository)	Item	Material Name	Qty/1000 Suppositories (g)
5.00	1	Bisacodyl (micronized) (2% excess) ^a	5.10
447.50	2	Hard fat (Witepsol E 76)	447.50
447.50	3	Hard fat (Witepsol W 45)	447.50

^a 100% particles should be less than 70 µm; fill weight is 1800 mg per suppository.

MANUFACTURING DIRECTIONS

The molten suppository mass must be kept stirred throughout the storage period and during manufacturing and filling to avoid sedimentation of the active drug. The active ingredient causes skin irritation, which vanishes after some time without aftereffects. Avoid dust formation during processing. In particular, protect eyes and mucous membranes.

1. Load items 2 and 3 into the fat-melting vessel, and heat to 50°C ± 3°C.
2. Transfer the molten mass to a mixer through a 0.8 mm sieve.
3. Set the temperature at 40°C ± 2°C.
4. Load item 1 to the mixer containing molten mass. Carefully mix the powder with the molten mass.
5. Set the mixer at a temperature of 40°C ± 2°C and speed of 10 rpm (manual mode), and mix for 20 minutes.

- Set the mixer at a temperature of $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$, speed of 10 rpm (manual mode), and vacuum of 0.6 bar.
- Homogenize at low speed while mixing for 10 minutes. Homogenize at high speed while mixing for 3 minutes.
- Continue mixing of the mass under vacuum in mixer.
- Heat the storage vessel, and set the temperature at $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$.
- Transfer the molten mass from the mixer to the storage vessel.
- Hold the mass at $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$, continuously mixing at low speed.
- Fill weight is 900 mg per suppository. Use a fill weight of 1.8 g for 10 mg suppositories.

BISMUTH CARBONATE SUSPENSION

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
266.66	1	Light kaolin	266.66
8.30	2	Pectin	8.30
6.70	3	Bismuth carbonate	6.70
9.40	4	Cellulose (microcrystalline; Avicel™ RC-591)	9.40
1.40	5	Methylparaben	1.40
0.20	6	Saccharin sodium	0.20
0.40	7	Aspartame	0.40
40.00 mL	8	Sorbitol	40.00 mL
5.00 mL	9	Ethanol	5.00 mL
QS	10	Deionized water	QS to 1 L

MANUFACTURING DIRECTIONS

- Dissolve item 2 in hot water.
- Disperse item 1 in 75 mL of item 10 at room temperature.
- With constant agitation, add item 3, and continue stirring.
- Mix, and cool to room temperature.
- Disperse item 4 in item 10, and add it to the batch.
- Dissolve item 2 in item 1 dispersion, and add to the batch.
- Dissolve items 6 and 7 in water, and add to the batch.
- Add flavor, color, and water to volume.
- Pass through homogenizer or colloid mill if necessary.

BISMUTH SUBSALICYLATE AND CALCIUM CARBONATE TABLET

FORMULATION

Bismuth subsalicylate, 262.5 mg; microcrystalline cellulose NF, 213.3 mg; calcium carbonate, 67.5 mg; mannitol, 67.5 mg;

sodium starch glycolate, 40.5 mg; polyvinyl pyrrolidone, 13.5 mg; magnesium stearate, 5.4 mg; polysorbate 80, 3.4 mg; silica, 0.7 mg; dye, 0.7 mg; total, 675.0 mg.

MANUFACTURING DIRECTIONS

- The ingredients are added to a mixer or granulator in the following order: part of microcrystalline cellulose, calcium carbonate, part of sodium starch glycolate, Polysorbate 80, dye, and bismuth subsalicylate.
- After the addition of the bismuth subsalicylate and mixing at high shear, the mixture is dried at 86°C to less than 2% moisture.
- Additional powders (microcrystalline cellulose, sodium starch glycolate, mannitol, and polyvinylpyrrolidone) are added, and granules are formed by spraying water (approximately 10% by weight of the composition) onto the mixture under high shear.
- After additional drying to less than 3% moisture, silica (glidant) and magnesium stearate (lubricant) are added and mixed for approximately 1 minute.
- Caplets are then formed on a rotary tablet press.

BISMUTH SUBSALICYLATE SUSPENSION

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
15.00	1	Magnesium aluminum silicate (Magnabrite K)	15.00
1.50	2	Methyl cellulose	1.50
910.00	3	Deionized water	910.00
0.50	4	Saccharin sodium	0.50
30.00	5	Bismuth subsalicylate	30.00
4.00	6	Salicylic acid	4.00
10.00	7	Sodium salicylate	10.00
29.00	8	Ethanol	29.00
QS	9	Preservatives	QS
QS	10	Colorings	QS

MANUFACTURING DIRECTIONS

- Dry blend items 1 and 2, and slowly add them to item 3, agitating until smooth.
- Add items 4 to 7 to this dispersion, gradually mixing well each time.
- Finally, add items 8 to 10 to smooth mix.

BISMUTH SUBSALICYLATE SWALLOW TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
262.50	1	Bismuth subsalicylate	262.50
213.30	2	Microcrystalline cellulose	213.30
67.50	3	Calcium carbonate	67.50
67.50	4	Mannitol	67.50
40.50	5	Sodium starch glycolate	40.50
13.50	6	Polyvinylpyrrolidone (PVP)	13.50
5.40	7	Magnesium stearate	5.40
3.40	8	Polysorbate 80	3.40
0.70	9	Silica	0.70
0.70	10	Dye	0.70

MANUFACTURING DIRECTIONS

1. Mix the ingredients in a mixer in the following order: part of microcrystalline cellulose, calcium carbonate, part of sodium starch glycolate, Polysorbate 80, dye, and bismuth subsalicylate.
2. After the addition of bismuth subsalicylate and mixing at high shear, the mixture is dried at 86°C to less than 2% moisture.
3. Additional powders (microcrystalline cellulose, sodium starch glycolate, mannitol, and PVP) are added, and granules are formed by spraying water (approximately 10% by weight of the composition) onto the mixture under high shear.
4. After additional drying to less than 3% moisture, silica (glidant) and magnesium stearate (lubricant) are added and mixed for approximately 1 minute.
5. Caplets are then formed on a rotary tablet press.

BLEACHING AND ANTIMICROBIAL DENTIFRICE**MANUFACTURING DIRECTIONS**

1. Weight percentage: hydrogen peroxide (50%), 10.00; carbamide peroxide, 14.00; sodium fluoride, 0.38; Pecogel S-2120 (VP/dimethacolyacrylate is an inclusion complex polymer to retard the solubility of emulsified bleaching actives. It is obtained from Phoenix Chemical, Inc.), 0.50; hydroxyethyl cellulose, 0.50; triethanolamine, 0.30.
2. Water, purified, 10.00; glycerin, 10.75; tetrafluoroethylene (Teflon), 50.58; sodium lauryl sulfate, 1.25; sodium saccharin, 0.18; sodium citrate, 0.20; citric acid, 0.20; triclosan, 0.06; flavor, 1.10.

BRAN-SUCROSE-GELATIN-CALCIUM CARBONATE TABLET**MANUFACTURING DIRECTIONS**

1. Prepare gelatin-sucrose syrup by placing the following ingredients in a mixing kettle equipped with a heater and agitator: distilled water, 24,000 g; gelatin, 3000 g; sucrose granular, 31,995 g.
2. Heat the mixture to approximately 65.5°C with agitation until solution is affected and then slowly stir the gelatin-sucrose syrup and hold at a temperature of approximately 65.5°C until needed.
3. Commminute wheat bran in a Schutz-O'Neill Airswept Pulverizer to provide a particle size whereby a minimum of 94% passes through a U.S. standard No. 20 mesh screen and a maximum of 60% passes through a U.S. standard No. 80 mesh screen.)The required amount of bran for the batch is calculated by the formula: $44,250 \text{ g} \times 100 / (100\% \text{ moisture in bran})$.
4. After pulverizing, transfer the bran to a heavy-duty double-sigma arm mixer and mix with 1500 g of calcium carbonate, and rapidly add the previously prepared gelatin-sucrose syrup thereto with stirring.
5. When the bran appears to be damp, stir the mixture for a 30 minute period and then stop.
6. Add powdered sucrose (16,600 g) and agitate the mixture for an additional 2 to 5 minutes.
7. Discharge the wet mix through an Ambrette screw extruder and spread the extrudate on drying trays and dry in an oven at 107.2°C to 3% moisture content.
8. Granulate the dried extrudate employing a Fitz mill (2A plate) and then press into 1 g tablets by a conventional tableting machine.

BRAN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
250.00	1	Bran wheat (milled <1 mm)	250.00
200.00	2	Ludipress®	200.00
5.00	3	Kollidon® 30	5.00
4.00	4	Aerosil® 200	4.00
4.00	5	Magnesium stearate	4.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a sieve, and press with medium compression force.
2. If the bran is not milled, the hardness of the tablet is higher, but the content uniformity is lower.
3. Compress 477 mg tablets using 12 mm punches.

BREAST CARE CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Quantity/ kg (g)
20.00	1	Polysorbate 60	20.00
70.00	2	Cetyl alcohol	70.00
60.00	3	Mineral oil (70 cS)	60.00
40.00	4	Glyceryl stearate	40.00
QS	5	Deionized water	QS
QS	6	Preservative	QS

MANUFACTURING DIRECTIONS

1. Heat oil and water phases separately at 65°C to 70°C.
2. Add water phase to oil phase while stirring.
3. Stir to cool.
4. Fill at 20°C.
5. Only food-grade materials should be used.

BROMHEXINE HYDROCHLORIDE SYRUP

Bill of Materials			
Scale (mg/5 mL)	Item	Material Name	Qty/L (g)
4.00	1	Bromhexine HCl	0.80
1000.00	2	Glycerin (glycerol)	200.00
10.00	3	Benzoic acid	2.00
1.70	4	All fruits flavor	0.34
5.00	5	Tartaric acid	1.00
151.58	6	Alcohol (ethanol, 95%)	30.31
2857.00	7	Sorbitol (70% solution)	571.40
10.00	8	Sodium carboxymethyl cellulose (sodium CMC)	2.00
0.72	9	Sodium hydroxide pellets	0.14
QS	10	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Add 250 g of item 10 to the manufacturing vessel, and heat to 65°C to 70°C.
2. Add 20 g of item 2 in a separate stainless steel container, and mix item 8 using an Ekato stirrer, carefully avoiding lump formation.
3. Transfer the slurry to the manufacturing vessel, and continue mixing to make a clear mucilage. Avoid air entrapment.

4. Cool to 30°C while mixing at slow speed. Transfer the mucilage to container.
5. Load 100 g of item 2 to the manufacturing vessel.
6. Add item 6 in a separate stainless steel container, and dissolve item 3 using stirrer.
7. Add 60 g of item 2 to the container while mixing at slow speed.
8. Add and dissolve item 1 to the container while mixing at slow speed. Avoid splashing of the solution. Be sure bromhexine is dissolved completely.
9. Add item 4 to the container, and mix well.
10. Transfer the solution to the manufacturing vessel while mixing at high speed.
11. Rinse the container with 20 g of item 2, and transfer the rinsings to the manufacturing vessel while mixing.
12. Rinse the container with 20 g of item 10, and transfer the rinsing to the manufacturing vessel while mixing.
13. Add 15 g of item 10 in a separate stainless steel container.
14. Dissolve item 5 using a stirrer, and transfer it to the manufacturing vessel while mixing. Check for clarity of the solution in the manufacturing vessel. The solution must be clear without any undissolved particles of the drug.
15. Add item 7 to the manufacturing vessel while mixing at high speed.
16. Transfer the cooled mucilage of item 8 to the manufacturing vessel used in the preceding step while mixing at slow speed.
17. Check and record the pH of the solution (limit: 3.3–3.6).
18. Dissolve item 9 in 5 g of cooled item 10 (30°C) in a separate stainless steel container.
19. Adjust the pH of the syrup in the manufacturing vessel using the sodium hydroxide solution.
20. Add sodium hydroxide solution, small portions at a time. Mix well, and check the pH after every addition. Adjust the pH to 3.5 (limit: 3.3–3.6).
21. Bring the volume up to 1 L with item 10, and finally, mix for 15 to 20 minutes at high speed.
22. Check and record the pH (limit: 3.3–3.6).
23. Filter the syrup at 1.5 bar.
24. Recirculate.

BROMHEXINE HYDROCHLORIDE SYRUP (ALCOHOL FREE)

Bill of Materials			
Scale (mg/5 mL)	Item	Material Name	Qty/L (g)
4.00	1	Bromhexine HCl	0.80
1000.00	2	Glycerin (glycerol)	200.00
12.00	3	Sodium benzoate	2.40
1.70	4	All fruit flavors	0.34
17.00	5	Tartaric acid	3.40
2250.00	6	Sorbitol (70% solution)	450.00
10.00	7	Sodium carboxymethyl cellulose (sodium CMC)	2.00
QS	8	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Add 240 g of item 8 (25°C) to the manufacturing vessel.
2. Add item 5, and mix for 20 minutes at high speed.
3. Load 180 g of item 2 into the manufacturing vessel, and mix for 3 minutes.
4. Add item 1 to the manufacturing vessel, and mix for 30 minutes at high speed.
5. Add 20 g of item 2 in a suitable vessel, and levigate item 7 using stirrer, carefully avoiding lump formation.
6. Add 40 g of item 8 (70°C) to the stainless steel container while mixing to make a clear mucilage. Mix for 15 minutes. Avoid air entrapment.
7. Cool down to 25°C to 30°C while mixing at slow speed.
8. Transfer the mucilage to the manufacturing vessel.
9. Rinse the vessel with 10 g of item 8, and transfer to the manufacturing vessel.
10. Mix at slow speed for 20 minutes.
11. Transfer item 6 to the manufacturing vessel while mixing. Mix at low speed for 5 minutes.
12. Add 20 g of item 8 (25°C) in a separate stainless steel container, and dissolve item 3 using an Ekato stirrer until a clear solution is obtained.
13. Transfer this solution to the manufacturing vessel, and mix at low speed for 3 minutes.
14. Add item 4 to the manufacturing vessel, and mix at low speed for 3 minutes.
15. Record the pH of the solution (limit: 3.3–3.7). Adjust the pH of the solution with a 10% solution of sodium hydroxide, if required.
16. Make the volume up to 1 L with item 8 (25°C), and finally, mix for 15 to 20 minutes at high speed.

17. Filter the syrup at 1.5 bar.
18. Recirculate.

BROMHEXINE HYDROCHLORIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
8.00	1	Bromhexine HCl	8.00
78.00	2	Lactose monohydrate	78.00
30.40	3	Cornstarch	30.40
3.00	4	Gelatin (powder)	3.00
QS	5	Purified water	12.00
0.60	6	Magnesium stearate	0.60

MANUFACTURING DIRECTIONS

The binding solution is susceptible to microbiological growth; hence, prepare the solution directly before the granulation process. Protect bromhexine HCl from light.

1. Make slurry in a separate container by dissolving item 4 in hot item 5 (70–80°C).
2. Mix for 10 minutes using stirrer at medium speed.
3. Pass items 1, 2, and 3 through a 630 µm sieve using a sifter.
4. Charge the sieved material into the mixer.
5. Mix, using mixer and chopper, for 5 minutes at high speed. Add binding solution to the dry powders in the mixer while mixing at low speed.
6. After the addition is complete, mix for an additional 4 minutes at low speed or until a satisfactory mass is obtained.
7. Spread the wet granules onto the trays.
8. Load the trolleys into the drying oven.
9. Dry the granules at 60°C for 10 hours.
10. Turn the granules after 4 hours of drying in order to obtain uniform drying.
11. Transfer the dried granules in stainless steel drums.
12. Check moisture content (limit: NMT 2%).
13. Pass the dried granules through first a 1.5 mm and then a 1.0 mm sieve using a granulator. Collect in stainless steel drums.
14. Load the granules into the blender.
15. Pass item 6 through a 250 µm sieve using a sifter, and add to the granules in blender. Blend for 2 minutes.
16. Compress the granules using a rotary tableting machine.
17. Use a 7 mm flat, beveled-edge punch to compress 1.2 g per tablet at a hardness of NLT 3 kp.

BURN CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
120.00	1	Glyceryl stearate SE (Monthybase)	120.00
80.00	2	Myristate octyldodecyl (MOD)	80.00
20.00	3	Apricot kernel oil PEG-6 esters (Labrafil® M 1944 CS)	20.00
0.50	4	Sodium methylparaben	0.50
0.50	5	Sodium propylparaben	0.50
0.50	6	Sorbic acid	0.50
767.50	7	Deionized water	767.50
10.00	8	Avocado oil	10.00
1.00	9	Fragrance	1.00

MANUFACTURING DIRECTIONS

1. Mix and heat items 1 to 7 to 75°C.
2. Cool slowly with stirring.
3. At 30°C, add item 8 and then item 9.

BURN CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
15.00	1	Magnesium aluminum silicate (Veegum®)	15.00
568.00	2	Deionized water	568.00
30.00	3	Propylene glycol	30.00
2.00	4	Dimethicone emulsion	2.00
100.00	5	Mineral oil, light	100.00
170.00	6	Acetylated lanolin alcohol	170.00
50.00	7	Benzocaine, USP	50.00
30.00	8	C18–C36 acid	30.00
120.00	9	Glyceryl stearate and PEG-100 stearate	120.00
5.00	10	Polysorbate 60	5.00
QS	11	Preservatives	QS

MANUFACTURING DIRECTIONS

1. Slowly add item 1 to water, agitating with extensive shear force until smooth.
2. Add items 3 and 4, and heat to 75°C to 80°C.
3. Mix and heat items 5 to 11, keeping item 7 suspended, to 75°C to 80°C. Mix the two parts while cooling. Pour and fill at 40°C.

CAFFEINE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
150.00	1	Caffeine powder	150.00
36.00	2	Cellulose (microcrystalline) (Avicel™ PH102)	36.00
46.00	3	Anhydrous lactose	46.00
48.50	4	Di-Pac granular	48.50
3.00	5	Croscarmellose sodium (Ac-Di-Sol SD-711)	3.00
1.50	6	Fumed silica	1.50
0.75	7	Stearic acid	0.75
0.75	8	Magnesium stearate	0.75
1.20	9	Flavor	1.20

MANUFACTURING DIRECTIONS

1. Screen items 1,7, and 8 separately through a 40 mesh sieve.
2. Blend items 1 to 6 and 9 in a V-blender, and mix for 3 minutes.
3. Add item 8 to the blender, and mix for another 5 minutes.
4. Compress, using 7 kg pressure and 3/8 in. flat, beveled-edge punches to produce tablets with an average weight of 311 mg.

CALAMINE CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
80.00	1	Polawax GP200	80.00
10.00	2	Polysorbate 60	10.00
50.00	3	Caprylic/Capric triglyceride	50.00
QS	4	Deionized water	QS to 1 kg
100.00	5	Witch hazel distillate	100.00
50.00	6	Glycerin	50.00
20.00	7	Zinc oxide	20.00
20.00	8	Calamine	20.00
QS	9	Preservative, color	QS

MANUFACTURING DIRECTIONS

1. Heat oil and water phases separately to 65°C to 70°C.
2. Add water phase to oil phase while stirring.
3. Add zinc oxide and calamine under high shear.
4. Stir to cool.

CALAMINE CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Quantity/ kg (g)
20.00	1	Cellulose (microcrystalline) (Avicel™ RC-591)	20.00
100.00	2	Glycerin	100.00
1.80	3	Methylparaben	1.80
0.20	4	Propylparaben	0.20
100.00	5	Glyceryl stearate and PEG-100 stearate	100.00
25.00	6	Cetyl alcohol	25.00
50.00	7	Zinc oxide	50.00
50.00	8	Calamine	50.00
653.00	9	Distilled water	653.00

MANUFACTURING DIRECTIONS

1. Mix item 2 with item 9, 5 and 6 and heat to 75°C.
2. Add items 3 and 4. Mix until dissolved using a shearing mixer.
3. Maintain temperature at 75°C, and gradually add item 1. Continue mixing at 75°C for 15 minutes or until item 1 is homogeneously dispersed. Mix well.
4. When temperature drops to 60°C to 65°C, gradually add items 7 and 8. Mix well until powders are homogeneously dispersed.
5. Pass through homogenizer if necessary. Adjust theoretical weight with warm distilled water, and continue mixing until the cream congeals.

CALAMINE LOTION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
78.30	1	Calamine	78.30
78.30	2	Zinc oxide	78.30
19.60	3	Glycerin	19.60
230.80	4	Deionized water	230.80
558.00	5	Calcium hydroxide solution	558.00
34.40	6	Purified bentonite (Polargel®, NF)	34.40
0.60	7	Carboxymethyl cellulose	0.60

MANUFACTURING DIRECTIONS

1. Prepare a saturated solution of item 5 by putting 3 g of item 5 in 1000 mL of purified water. Mix vigorously for 1 hour.
2. Decant the clear, supernatant liquid for use in the formula.

3. Add the balance of water.
4. Add items 6 and 7 to this solution with rapid mixing. Continue mixing for 15 minutes.
5. In a separate vessel, blend items 1 and 2.
6. Add item 3, and mix until uniform.
7. Begin adding the aqueous solution with mixing until it is blended into a lotion.

CALCIUM AND VITAMIN D TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Anhydrous calcium phosphate (dibasic)	500.00
133 IU	2	Vitamin D (as vitamin D3) (3.33 µg/tablet)	3.33 mg
15.00	3	Starch (pregelatinized, NF)	15.00
55.00	4	Cellulose (microcrystalline, NF)	55.00
6.00	5	Magnesium stearate, NF	6.00
5.00	6	Talc (powder), USP	5.00
12.00	7	Wax (hydrogenated vegetable oil) (Sterotex K)	12.00
15.50	8	Sodium starch glycolate, NF	15.50

MANUFACTURING DIRECTIONS

1. Pass one-half of dibasic calcium phosphate through a mesh screen into a blender.
2. Premix by hand the pregelatinized starch with vitamin D₃ beadlets in a suitable container, and sift through a mesh screen into the blender.
3. Charge the microcrystalline cellulose and the remaining calcium phosphate through a mesh screen into the blender.
4. Mix for 20 minutes.
5. Discharge approximately one-third of the granulation into polyethylene-lined drums.
6. Mix the magnesium stearate, talc, hydrogenated vegetable oil wax, and sodium starch glycolate.
7. Mill through a No. 40 mesh screen into the blender.
8. Return granulation from previous step to the blender. Blend together.
9. Compress.

CALCIUM CARBONATE AND GLYCINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
400.00	1	Calcium carbonate (precipitated)	400.00
200.00	2	Glycine (aminoacetic acid)	200.00
QS	3	Starch	QS
6.50	4	Mineral oil (light)	6.50
QS	5	Purified water	QS

MANUFACTURING DIRECTIONS

1. Add starch to a planetary mixer, and add 10 times the quantity of purified water.
2. Heat to boil with constant stirring until a thick, translucent white paste is formed. Use this paste in granulation.
3. Charge calcium carbonate and glycine in a sigma-blade or a planetary mixer and mix for 10 minutes.
4. Granulate this powder with the starch paste until a suitable mass is obtained.
5. Force the wet mass through a No.12 mesh screen onto dryer trays.
6. Dry in an air-forced oven at 54.4°C to 60°C or in a fluid-bed dryer.
7. Pass the dried granules through a No.12 mesh screen and then through a No.18 mesh screen.
8. Pass the granules through a 30 mesh screen, remove the portion passing through the screen, and regranulate.
9. Charge the particles retained on 30 mesh screen in a tumble mixer, add mineral oil, and mix for 8 minutes.
10. Compress 640 mg tablets using 7/16 in. punches.

CALCIUM CARBONATE AND VITAMIN D TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
600.00	1	Calcium (elemental); use calcium carbonate (90%) for direct compression	1665.00
0.235	2	Vitamin D ₃ (200 IU); use vitamin D ₃ beadlets	0.282
4.16	3	Magnesium stearate	4.16
83.25	4	Sodium starch glycolate	83.25

MANUFACTURING DIRECTIONS

1. Make a premix of vitamin D₃ successively in three portions of calcium carbonate (total amount

equivalent to approximately 3% of total calcium carbonate) using geometric dilution.

2. Mix for 10 minutes each time (total: 30 minutes).
3. Add the premix to the sodium starch glycolate. Mix for 10 minutes.
4. Set the blend aside, protected from light, until the next step.
5. Pass the magnesium stearate through a 420 µm aperture screen, if required, and blend it with another portion of calcium carbonate (approximately 10% of total calcium carbonate).
6. Mix for 5 minutes. Set aside.
7. Add the blended material to the balance of the calcium carbonate. Mix for 10 minutes.
8. Add the premix to blend from step 7. Mix for 5 minutes.
9. Compress on specially shaped 0.8100 in. × 0.3700 in. ovaloid bisected punches with a monogram on one side.
10. Theoretical weight of 10 tablets = 17.527g.
11. Coat using one of the HPMC formulae (see Appendix).

CALCIUM CARBONATE CHEWABLE TABLETS

MANUFACTURING DIRECTIONS

1. Granulated calcium carbonate (93.3% calcium carbonate, 6.3% glucose, and 0.4% gelatin), 42.87%; magnesium stearate, 2.50%; colored speckles, 0.75%; flavorants, 0.78%; MPD (31-menthoxy propane 1,2-diol), 0.07%; WS-3 (N-ethyl-*P*-menthane-3-carboxamide), 0.05%; aspartame, 0.198%; sodium saccharin, 0.102%; mannitol, QS.
2. Dry blend the ingredients in a mixer until homogeneous and then direct compress in a tableting machine to approximately 8.5 Strong Cobb units of hardness to produce chewable antacid tablets each weighing 1.25 g (500 mg calcium carbonate per tablet).
3. These tablets may also be prepared by utilizing granulated calcium carbonate, which is a 50/50 coblend of calcium carbonate/mannitol.

CALCIUM CARBONATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Calcium carbonate (precipitated)	500.00
65.00	2	Kollidon® 30	65.00
97.00	3	Water	97.00
32.00	4	Kollidon® CL	32.00
53.00	5	Ludipress®	53.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 and 2 with the water (item 3).
2. Pass through a 0.8 mm sieve, mix the dry granules with items 4 and 5, and press with low compression force.
3. Fill 656 mg in 12 mm planar punches.

CALCIUM CHEWABLE TABLETS (200 MG CA)**FORMULATION**

Calcium gluconate (Merck), 845.0 g; calcium citrate (Merck), 500.0 g; Ludipress® LCE, 297.5 g; citric acid anhydrous, fine granular, 100.0 g; polyethylene glycol 6000, powder, 80.0 g; orange flavor (Dragoco), 30.0 g; Aerosil® 200, 17.0 g; aspartame, potassium (Searle), 5.0 g.

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with high compression force at 2417 mg.

CALCIUM D-PANTOTHENATE CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
600.00	1	Calcium D-pantothenate (BASF), with excess	610.00
150.00	2	Sorbitol (crystalline)	150.00
140.00	3	Avicel™ PH101	140.00
30.00	4	Kollidon® CL	30.00
50.00	5	PEG-6000 (powder)	50.00
QS	6	Flavors	QS

Note: Kollidon® CL may be omitted and the tablet weight adjusted.

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with low compression force.
2. Compress 987 mg tablets in 12 mm biplanar punches.

CALCIUM D-PANTOTHENATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Quantity/1000 Tablets (g)
100.00	1	Calcium D-pantothenate (BASF)	100.00
150.00	2	Ludipress®	150.00
10.00	3	Kollidon®	10.00
3.00	4	Magnesium stearate	3.00

MANUFACTURING DIRECTIONS

1. Mix all components. Pass through a 0.8 mm sieve.
2. Press into 252 mg tablets using medium compression force and biplanar 8 mm punches.

CALCIUM D-PANTOTHENATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
280.00	1	Calcium D-pantothenate (BASF), with excess	285.00
50.00	2	Avicel™ PH101	50.00
150.00	3	Dibasic calcium phosphate	150.00
20.00	4	Kollidon® CL	20.00
3.00	5	Stearic acid	3.00
3.00	6	Magnesium stearate	3.00

MANUFACTURING DIRECTIONS

1. Mix all components. Pass through a 0.8 mm sieve.
2. Press into 518 mg tablets using medium compression force and 12 mm biplanar punches.

CALCIUM EFFERVESCENT TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
634.00	1	Calcium lactate	634.00
610.00	2	Calcium gluconate	610.00
185.21	3	Calcium carbonate	185.21
400.00	4	Sodium bicarbonate	400.00
468.25	5	Tartaric acid	468.25
46.25	6	Povidone (Kollidon® 30)	46.25
11.75	7	Povidone (Kollidon® 30)	11.75
QS	8	Isopropyl or ethyl alcohol (96%)	QS
97.50	9	Crospovidone (Kollidon® CL)	97.50
46.25	10	PEG-6000	46.25
QS	11	Flavor	QS

MANUFACTURING DIRECTIONS

1. Granulate items 1 to 6 in a solution of items 7 and 8.
2. Dry, sieve, and mix well with items 9 to 11.
3. Compress at low pressure to form 2.5 g tablets, 20 mm in diameter.

CALCIUM GLUCONATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Quantity/1000 Tablets (g)
350.00	1	Calcium gluconate (powder), with excess	360.00
117.00	2	Lactose monohydrate	117.00
11.00	3	Kollidon® 30	11.00
QS	4	Isopropanol	90.00
25.00	5	Kollidon® CL	25.00
2.00	6	Magnesium stearate	2.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 3 with item 4.
2. Dry, pass through a 0.8 mm sieve, and mix with items 5 and 6.
3. Press into 500 mg tablets using high compression force and 12 mm biplanar punches.

CALCIUM GLYCEROPHOSPHATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Calcium glycerophosphate	500.00
117.50	2	Cornstarch	117.50
15.00	3	Kollidon® 90 F	15.00
60.00	4	Water	60.00
15.00	5	Kollidon® CL	15.00
2.50	6	Magnesium stearate	2.50

MANUFACTURING DIRECTIONS

1. Granulate items 1 to 3 with item 4, dry, sieve, and mix with items 5 and 6.
2. Press into 650 mg tablets using medium to high compression force and 12 mm biplanar punches.

CALCIUM GLYCEROPHOSPHATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Calcium glycerophosphate	200.00
297.50	2	Ludipress®	297.50
2.50	3	Magnesium stearate	2.50
QS	4	Aerosil® 200	QS

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, and mix.
2. Press into 470 mg tablets using high compression force and 12 mm biplanar punches.

CALCIUM GLYCEROPHOSPHATE TABLETS (200 MG)

FORMULATION

Calcium glycerophosphate, 200.0 g; Ludipress®, 297.5 g; magnesium stearate, 2.5 g; Aerosil® 200, QS.

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with high compression force at 470 mg.

CALCIUM IODIDE AND ASCORBIC ACID SYRUP

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
311.60	1	Glucose liquid (corn syrup)	311.60
53.90	2	Glycerin (96%)	53.90
30.00	3	Anhydrous calcium iodide; use calcium iodide solution 27% w/w	111.11
1.00	4	Ascorbic acid (white powder)	1.00
485.30	5	Sucrose (granulated sugar)	485.30
0.80	6	Saccharin sodium (powder) ^a	0.80
8.00	7	Sodium cyclamate (XIII powder)	8.00
1.31	8	Honey artificial flavor, AU-73	1.31
0.33	9	Floral mint artificial flavor	0.33
51.53	10	Alcohol (ethanol, 190 proof)	51.53
0.60	11	Isoproterenol sulfate (powder)	0.60
0.05	12	FD&C Yellow dye No. 5	0.05
0.25	13	Caramel (acid proof)	0.25
QS	14	Water purified	~344.0 mL

^a Use 1.2 g of saccharin to replace cyclamate; adjust balance with sucrose.

MANUFACTURING DIRECTIONS

Isoproterenol is toxic; wear a dust mask, and avoid contact. The product is sensitive to oxidation. Manufacture under N₂ protection, and protect product from light and heat; all water must be boiled, cooled, and gassed with nitrogen.

1. Load glucose and glycerin into a suitable mixing tank.
2. Add 187 mL purified water to tank with mixing.
3. Begin bubbling N₂ protection for the balance of the process.

- Add and dissolve saccharin sodium and sodium cyclamate, if used, with mixing.
- Add calcium iodide to the tank with good mixing.
- Add and dissolve ascorbic acid and sugar.
- Dissolve the flavors in alcohol, and add with mixing to the main batch.
- Dissolve isoproterenol in 10 to 13 mL of water, and add with mixing to the main batch.
- Dissolve dye in 3.5 mL purified water, and add solution to tank with mixing. (*Note:* Dye may be deleted.) Add caramel with mixing to main batch.
- Move N₂ source from the bottom to the top of the tank.
- Turn off mixer.
- Allow to stand overnight under N₂ protection to let entrapped gases escape.
- QS to 1 L. Mix for 1 hour.
- Filter and circulate product through a suitable filter press until sparkling clear.

CALCIUM PHOSPHATE TABLETS FOR CATS AND DOGS (DIRECT COMPRESSION)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
400.00	1	Dicalcium phosphate	400.00
100.00	2	Wheaten flour	100.00
1.00	3	Citric acid crystalline	1.00
272.00	4	Lactose monohydrate	272.00
QS	5	Flavors	QS
20.00	6	Kollidon® 90 F	20.00
4.00	7	Magnesium stearate	4.00

MANUFACTURING DIRECTIONS

- Pass all components through a 0.8 mm sieve. Mix.
- Press with medium to high compression force (20 kN).
- Compress into 800 mg tablets using 12 mm biplanar punches.

CALCIUM PHOSPHATE TABLETS FOR CATS AND DOGS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
400.00	1	Dicalcium phosphate	400.00
100.00	2	Wheaten flour	100.00
1.00	3	Citric acid crystalline	1.00
262.00	4	Lactose monohydrate	262.00
QS	5	Flavors	QS
30.00	6	Kollidon® 30 F	30.00
150.00	7	Water	150.00 mL
4.00	8	Magnesium stearate	4.00

MANUFACTURING DIRECTIONS

- Granulate items 1 to 6 in item 7, dry, add item 8, and pass through a 0.8 mm sieve.
- Compress 800 mg tablets using 12 mm biplanar punches.

CARBAMIDE PEROXIDE CHEWING GUM

FORMULATION

Gum base, 26.25 g; calcium carbonate, 3.75 g; sorbitol, 28.05 g; mannitol, 7.50 g; maltitol, 21.62 g; glycerin, 1.00 g; flavorant, 3.15 g; gum arabic, 1.16 g; titanium dioxide, 0.17 g; wax candelilla, 0.03 g; sodium stearate/sodium palmitate, 50% each, 3.00 g; tripolyphosphate sweetener, 0.82 g; Imwitor 370, 1.00 g; carbamide peroxide, 3.00 g.

MANUFACTURING DIRECTIONS

- Heat the gum base to sufficiently soften the base without adversely affecting the physical and chemical make-up of the base.
- Add the molten gum base and the filler to a mixing kettle.
- Last, add the sugar alcohols, glycerin, flavor, high-intensity sweetener, and stain-removing agent carbamide peroxide with mixing to obtain a homogeneous mixture.
- Discharge the mixture from the mixing kettle and rolled and score into the desired piece size by conventional techniques.

CARBAMIDE PEROXIDE AND HYDROGEN PEROXIDE BLEACHING ORAL DENTIFRICE

MANUFACTURING DIRECTIONS

- Gel composition as weight percent contains sodium fluoride, 0.32 (0.14 w/v fluoride ion); Carbopol 974 P-NF, 1.25; sorbitol (70% solution), 10.00; glycerin, 10.00; carbamide peroxide, 14.00; sodium lauryl sulfate, 1.50; sodium saccharin, 0.20; flavor, 1.25; FD&C Yellow No. 5, 0.15; FD&C Red No. 40, 0.05; water purified, 29.60.
- Paste composition in weight percent contains sodium fluoride, 0.32; hydrogen peroxide (50% solution), 10.00; Carbopol 943, 0.51; sorbitol (70% solution), 5.18; glycerin, 5.18; sodium lauryl sulfate, 1.50; sodium saccharin, 0.20; flavor, 1.25; polytetrafluoroethylene (Teflon), 52.00; water, purified, 29.86.
- Neutralize both phases (steps 1 and 2) to a pH of approximately 5.5 and 6.5 with freshly prepared 10% sodium hydroxide. The ratio of the stripe composition to the main composition should be approximately 15:100.
- This hydrogen peroxide/carbamide peroxide blend composition is effective and stable when used topically for bleaching tooth surfaces.

- When extruded from the tube container, the gel composition will be in the form of one or more stripes enclosed in the periphery of the toothpaste surrounded by the paste composition.
- The gel and the paste composition must be of sufficiently heavy viscosities to prevent migration (bleeding) of the colored gel into the white paste composition.

CARBINOXAMINE MALEATE, PHENYLPROPANOLAMINE, AND ACETAMINOPHEN SUSTAINED-RELEASE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
5.00	1	Carbinoxamine maleate	5.00
75.00	2	Phenylpropanolamine hydrochloride	75.00
50.00	3	Acetaminophen	50.00
143.35	4	Sucrose and maize starch microgranules	143.35
6.34	5	Polyvidone (PVP)	6.34
0.01	6	Dye	0.01
0.075	7	Dye	0.075
0.025	8	Dye	0.025
23.99	9	Talc	23.99

MANUFACTURING DIRECTIONS

This product requires separate preparation of microgranules for each active ingredient. This preparation requires a coating pan equipped with air suction and hot air heating system, mixer, automatic airless pump with a spray gun, vibrating sieve, and capsule-filling machine with triple-feed microgranular system.

- Place the neutral microgranules in the coating pan. Prepare a 20% solution of PVP.
- Maintain the temperature of microgranules at $20^{\circ}\text{C} \pm 2^{\circ}\text{C}$.
- Using the pump, apply the solution of PVP; then, project the active ingredient onto the microgranules with a plastic scoop until they are dry.
- Repeat these operations until all the active ingredients have been incorporated.
- Sieve the microgranules with a 1.11 mm sieve.
- Dry the microgranules at $30^{\circ}\text{C} \pm 5^{\circ}\text{C}$ for 3 hours.
- Prepare a 40% solution of shellac in alcohol and the required quantity of talc.
- Apply the shellac solution, maintaining a microgranule temperature of $20^{\circ}\text{C} \pm 2^{\circ}\text{C}$, and add the talc simultaneously.
- Sieve the microgranules through a 1.18 mm sieve.

- Dry the microgranules at 18°C to 23°C for 8 hours. Store until used.
- Test for dissolution, and rework if necessary.

CARBONYL IRON, COPPER SULFATE, AND MANGANESE SULFATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
24.00	1	Carbonyl iron (BASF)	24.00
0.16	2	Copper sulfate	0.16
3.50	3	Manganese sulfate	3.50
100.00	4	Ludipress®	100.00
2.00	5	Magnesium stearate	2.00

MANUFACTURING DIRECTIONS

- Pass all components through a 0.5 mm sieve. Mix.
- Press into 131 mg tablets using medium compression force and 8 mm biplanar punches.

CARNITINE AND COENZYME Q SOLUTION

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
1.00	1	Coenzyme Q 10	1.00
1.00	2	Lutrol E 400	1.00
4.00	3	Cremophor RH 40	4.00
QS	4	Preservative	QS
QS	5	Water	QS to 1 L
40.00	6	Carnitine	40.00

MANUFACTURING DIRECTIONS

- Heat the mixture of items 1 to 5 to 60°C . Stir well.
- Cool to room temperature, and add and dissolve item 6.

CETIRIZINE HYDROCHLORIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Quantity/1000 Tablets (g)
15.00	1	Cetirizine hydrochloride	15.00
3.00	2	PVP	3.00
1.50	3	Silicon dioxide	1.50
135.00	4	Lactose	135.00
1.50	5	Glyceryl behenate	1.50
QS	6	Water	QS

MANUFACTURING DIRECTIONS

1. Place cetirizine and lactose in a fluidized-bed apparatus.
2. Spray an aqueous PVP solution (in 85 g of water) to get granules.
3. Dry the granules thus obtained and pass through a sieve (1 mm mesh), and weigh, add, and blend glyceryl behenate in a drum mixer.
4. Press the resulting mixture into 156 mg tablets.
5. Coat these tablet cores with the following formulation: ethyl cellulose, 10 g; hydroxypropyl cellulose, 10 g; stearic acid, 2 g; alcohol, 188 g.
6. First dissolve ethyl cellulose, povidone, and stearic acid in denatured alcohol (188 g).
7. Spray the coating solution is then sprayed onto the tablet cores in a coating pan.

CETRIMIDE ANTISEPTIC CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
50.00	1	Cetearyl alcohol and cetrimonium bromide	50.00
75.00	2	White petroleum jelly	75.00
60.00	3	Mineral oil (70 cS)	60.00
QS	4	Deionized water	QS to 1 kg
QS	5	Perfume, preservative, color	QS

MANUFACTURING DIRECTIONS

1. Heat oil and water phases separately to 60°C to 65°C.
2. Add the water phase to the oil phase while stirring.
3. Stir to cool.

CETILPYRIDINIUM LOZENGES (2.5 MG)**FORMULATION**

Cetylpyridinium chloride (Merck), 2.5 g; Ludipress® LCE, 370.0 g; polyethylene glycol 6000, powder, 20.0 g; menthol, crystalline, 6.0 g; aspartame, potassium (Searle), 1.5 g.

MANUFACTURING DIRECTIONS

1. Mix all components. Pass through a 0.8 mm sieve.
2. Press with low compression force at 402 mg.

CHARCOAL TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
250.00	1	Activated charcoal	250.00
150.00	2	Bolus alba (Merck)	150.00
28.00	3	Kollidon® 25	28.00
38.00	4	Acacia gum	38.00
QS	5	Water + isopropanol (10 + 3)	575.00 mL
15.00	6	Cremophor EL	15.00
QS	7	Isopropanol	300.00 mL

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 4 with item 5, and pass through a 1 mm sieve.
2. Dry until a relative powder humidity of 90% is reached.
3. Add solution of items 6 and 7, and pass again through a 0.8 mm sieve.
4. Dry the granules, and press into 481 mg tablets using low compression force and 12 mm planar punches.
5. Dry the obtained tablets.

CHLOPHEDIANOL, IPECAC, EPHEDRINE, AMMONIUM CHLORIDE, CARBINOXAMINE, AND BALSAM TOLU SYRUP

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
0.001 mL	1	Ipecac fluid extract	1.00 mL
5.00	2	Chlophedianol hydrochloride	5.00
1.32	3	Ephedrine hydrochloride (powder)	1.32
8.80	4	Ammonium chloride (reagent-grade granules)	8.80
0.80	5	Carbinoxamine maleate	0.80
0.90	6	Methylparaben	0.90
0.10	7	Propylparaben	0.10
6.25	8	Balsam of tolu (eq. aqueous extract)	6.25
2.66	9	Saccharin sodium (dihydrate powder)	2.66
319.22	10	Sucrose (granulated sugar)	319.22
238.33	11	Glucose liquid (corn syrup)	238.33
83.93	12	Sorbitol solution (calculate as 70% sorbitol crystals)	83.93
40.00	13	Alcohol	40.00
166.67	14	FD&C Red dye (Amaranth E123)	166.67 mg
0.80	15	Raspberry flavor	0.80
100.00	16	Propylene glycol	100.00
QS	17	HyFlo filter aid	0.50
QS	18	Water purified	~450.00 mL

MANUFACTURING DIRECTIONS

1. Place balsam of tolu and 25 mL of water in a steam bath.
2. Raise the temperature, stirring continuously in order to mix water with the balsam.
3. Boil for half an hour, and allow to decant while cooling.
4. Discard extracted balsam of tolu.
5. Filter the supernatant liquid through filter paper, and store apart.
6. Place 150 mL water in a jacketed mixing tank, and heat to boiling.
7. Add and dissolve parabens with mixing.
8. Add and dissolve sugar with constant mixing.
9. Heat to 70°C to 75°C.
10. Once sugar is dissolved, add glucose, sorbitol, and saccharin sodium. Mix well until dissolved.
11. Dissolve ammonium chloride in 28 mL water.
12. Add to mixing tank.
13. Add extract balsam of tolu from first step with mixing. Mix well, and cool to 25°C to 30° C.
14. Add and dissolve ephedrine and carbinoxamine in 20 mL water, and add to mixing tank. Mix well.
15. Add and dissolve chlorphedianol in 50 g of propylene glycol, and add to mixing tank.
16. Add balance of propylene glycol to mixing tank.
17. Add and dissolve ipecac fluid extract and raspberry flavor in alcohol.
18. Add to mixing tank.
19. Dissolve dye in 5 mL water, and add to tank with continuous mixing.
20. Rinse container with 5 mL of water, and add rinsings.
21. Adjust to volume with purified water.
22. Add HyFlo filter aid to syrup, and mix well.
23. Recirculate through filter press or equivalent until sparkling clear.

CHLORHEXIDINE GEL

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
20.00	1	Chlorhexidine diacetate	20.00
300.00	2	1,2-Propylene glycol (pharma)	300.00
220.00	3	Lutrol F 127	220.00
460.00	4	Water	460.00

MANUFACTURING DIRECTIONS

1. Dissolve chlorhexidine diacetate in propylene glycol at >70°C.
2. Stir well, and slowly add Lutrol F 127 and water.
3. Maintain the temperature until the air bubbles escape.
4. A clear, colorless gel is obtained.

CHLORHEXIDINE LOZENGES

Bill of Materials			
Scale (mg/lozenge)	Item	Material Name	Qty/1000 lozenges (g)
5.00	1	Chlorhexidine	5.00
150.00	2	Sorbitol (crystalline)	150.00
5.00	3	Kollidon® VA 64	5.00
5.00	4	Menthol (crystalline)	5.00
5.00	5	Eucalyptol (crystalline)	5.00
1.00	6	Aspartame, potassium	1.00
0.10	7	Saccharin sodium	0.10
2.00	8	Aerosil® 200	2.00
1.00	9	Magnesium stearate	1.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with medium compression force.
2. Compress into 175 mg lozenge using 8 mm biplanar punches.

CHLORPHENIRAMINE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
4.00	1	Chlorpheniramine maleate	4.00
75.00	2	Starch 1500	75.00
65.62	3	Microcrystalline cellulose (50 µm)	65.62
2.96	4	Stearic acid	2.96
1.11	5	Fumed silica	1.11
0.37	6	Magnesium stearate	0.37

MANUFACTURING DIRECTIONS

1. Blend half of the Starch 1500 with the fumed silica and chlorpheniramine for 5 minutes.
2. Pass this mixture through a 40 mesh screen, and return to blender.
3. Add the remaining Starch 1500 to the material in step 1, and blend for 5 additional minutes.
4. Add the microcrystalline cellulose and stearic acid to the material from step 2, and blend for an additional 10 minutes.
5. Add the magnesium stearate to the material from step 3, and blend for an additional 5 minutes.

CHLORPHENIRAMINE MALEATE SYRUP

Bill of Materials			
Scale (mg/5 mL)	Item	Material Name	Qty/L (g)
2.00	1	Chlorpheniramine maleate	0.40
3000.00	2	Sucrose	600.00
4.50	3	Methylparaben	0.90
1.50	4	Propylparaben	0.30
1.00	5	Citric acid (monohydrate)	0.20
2.40	6	Sodium citrate	0.48
2.00	7	Green banana flavor	0.40
—	8	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Add 500 g of purified water to the manufacturing vessel, and heat to 95°C to 98°C.
2. Add items 3 and 4 while mixing to dissolve at high speed.
3. Mix for 5 minutes.
4. Add item 2 while mixing at slow speed.
5. Maintain a temperature of 95°C to 98°C.
6. Mix for 1 hour at high speed.
7. Cool down to 30°C while mixing at slow speed.
8. Dissolve items 5 and 6 in 20 g of cooled purified water (25°C).
9. Transfer the solution to the manufacturing vessel while mixing at high speed.
10. Mix for 2 minutes.
11. Add 8 g of cold purified water (25–30°C) in a separate container, and dissolve item 1 by using stirrer.
12. Mix for 10 minutes, and transfer to the manufacturing vessel.
13. Rinse the container with 2 g of cooled purified water (25°C), and transfer the rinsings to the manufacturing vessel while mixing at high speed.
14. Add item 7 to the manufacturing vessel while mixing.
15. Mix for 10 minutes at high speed.
16. Bring the volume up to 1 L with purified water, and finally, mix for 15 to 20 minutes at high speed.
17. Check and record the pH (limit: 5.0–5.2 at 25°C).
18. If required, adjust pH with 10% citric acid or 10% sodium citrate solution.
19. Filter the syrup at 1.5 bar.
20. Bubble the syrup with nitrogen gas.

CHLORPHENIRAMINE AND PSEUDOEPHEDRINE CHEWABLE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
3.35	1	Chlorpheniramine maleate	3.35
100.00	2	Pseudoephedrine hydrochloride	100.00
396.65	3	Cab-o-Sil M5	396.65
200.00	4	Water	200.00

MANUFACTURING DIRECTIONS

1. Chlorpheniramine maleate and pseudoephedrine hydrochloride are mixed in the water until thoroughly dissolved.
2. Cab-o-Sil M5 (silicon dioxide) is poured into a planetary mixer, to which the dissolved drug solution is added and mixed at slow speed.
3. This is continued for 5 minutes until the solution and Cabo-Sil are completely mixed.
4. The mixture is dried in a forced hot air oven for 5 hours to an LOD of less than 2%.
5. Magnesium stearate is then added as a lubricant, and tartaric acid is added as an acidulant.
6. The excipients are then thoroughly mixed, and the entire composition is compressed into 1 g tablets, each one possessing a potency of 4 mg chlorpheniramine maleate and 120 mg pseudoephedrine hydrochloride.

CHLORPHENIRAMINE, PSEUDOEPHEDRINE, AND DEXTROMETHORPHAN CHEWABLE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
8.00	1	Chlorpheniramine maleate	8.00
120.00	2	Pseudoephedrine hydrochloride	120.00
60.00	3	Dextromethorphan hydrobromide	60.00
812.00	4	Cab-o-Sil M5	812.00
200.00	5	Water	200.00

MANUFACTURING DIRECTIONS

1. Chlorpheniramine maleate, dextromethorphan HBr, and pseudoephedrine hydrochloride are mixed in the water until thoroughly dissolved.
2. Cab-o-Sil M5 (silicon dioxide) is poured into a planetary mixer, to which the dissolved drug solution is added and mixed at slow speed.

3. This is continued for 5 minutes until the solution and Cab-o-Sil are completely mixed.
4. The entire composition is dried in a forced hot air oven for 7 hours at 50°C.
5. The composition is dried to an LOD of 1.25%.
6. The dried material is then screened through a No. 30 U.S. standard mesh screen.
7. The excipients are added as mentioned before, and the blend is compressed into 1 g tablets, each one possessing a potency of 4 mg chlorpheniramine maleate, 60 mg pseudoephedrine hydrochloride, and 30 mg dextromethorphan HBr.

CHYMOTRYPSIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
27.00	1	Chymotrypsin, with excess	27.50
71.50	2	Ludipress®	71.50
1.00	3	Magnesium stearate	1.00

MANUFACTURING DIRECTIONS

1. Mix all components. Pass through a 0.8 mm screen.
2. Press with low compression force.
3. Compress into 100 mg tablets using 8 mm biplanar punches.

CIMETIDINE TABLETS (200 MG)

FORMULATION

Cimetidine, 200 g; Ludipress®, 295 g; magnesium stearate, 5 g.

MANUFACTURING DIRECTIONS

1. Pass the mixture through a 0.8 mm screen.
2. Press with low compression force at 510 mg at low humidity (30%).

CIMETIDINE CHEWABLE TABLETS

MANUFACTURING DIRECTIONS

1. Cimetidine premix granules: cimetidine, 200 mg; Eudragit E100, 20 mg; antacid (Al/Mg) granules sorbitol, direct compression grade, 590 mg; lactose, direct compression grade spray dried, 325 mg; lactose crystalline, 325 mg; dried aluminum hydroxide gel, 250 mg; magnesium hydroxide, 200 mg; croscarmellose sodium type A, 30 mg; magnesium stearate, 15 mg; total, 1735 mg.

2. Tableting mix for compression: cimetidine, 220 mg; premix granules antacid (Al/Mg), 1735 mg; granules microcrystalline cellulose (Avicel™ PH102), 200 mg; aspartame, 10 mg; aniseed, 20 mg; butterscotch, 20 mg; magnesium stearate, 15.0 mg; total, 2220 mg.
3. Add a 40% (w/w) solution of the Eudragit E100 in methylene chloride with mixing to the cimetidine and blend until granules are formed.
4. Dry the resulting granules and then sieve through a 16 mesh screen.
5. Sieve aluminum hydroxide, magnesium hydroxide, and other ingredients for the antacid granules through a 12 mesh (1.4 mm) screen and mix together.
6. Compress the resulting mix on a rotary tablet press, and mill the resulting compacts using a 12 mesh screen.
7. Place cimetidine granules, antacid granules, and extragranular excipients into a cone blender and mix thoroughly.
8. Discharge the resulting mix from the blender and compress on a suitable rotary tablet press fitted with the appropriate punches.

CITRATE EFFERVESCENT POWDER

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/kg (g)
0.50	1	Oil lemon terpeneless	0.50
10.00	2	Lemon flavor (natural microseal)	10.00
QS	3	Alcohol dehydrated (absolute, doubly rectified)	6.50
440.33	4	Sodium bicarbonate	440.33
0.35	5	Saccharin sodium	0.35
157.50	6	Anhydrous sodium citrate	157.50
178.82	7	Anhydrous citric acid (powder)	178.82
222.50	8	Acid tartaric	222.50

MANUFACTURING DIRECTIONS

1. All processing should be done in controlled humidity at a maximum RH of 40% at 25°C.
2. Sodium citrate and citric acid are anhydrous.
3. Dissolve lemon oil in dehydrated alcohol with stirring in a suitable container (delete this step if using powdered lemon flavor).
4. Sift sodium bicarbonate, if necessary, through a 595 µm screen.
5. Load into a suitable mixer and mix for 10 minutes.
6. Very slowly add solution from first step to the mixer while mixing. Continue mixing for at least 10 minutes and up to a total of 30 minutes, depending on equipment.
7. Screen the massed granulation mixture through a 595 µm screen and divide approximately in half.

- Premix saccharin sodium into sodium citrate (and lemon powder, if used), and sift through a 595 μm screen or mill fitted with a 595 μm screen (knives forward, medium speed).
- Sift both citric acid and tartaric acid separately through a 595 μm screen, or mill separately using a comminuting mill with a 595 μm aperture (knives forward, medium speed).
- Load materials into a suitable blender, preferably in the following order: milled tartaric acid, milled citric acid, half of granulation mixture, milled saccharin sodium, sodium citrate, and remaining granulation mixture.
- Blend for 20 minutes, and pack into double plastic bags inside fiber drums.
- Provide silica gel protection to maintain low humidity in drums.
- If blended material is lumpy, pass through a 1.2 mm screen before bagging.

CROSPVIDONE EFFERVESCENT TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
1000.00	1	Crospovidone (micronized)	1000.00
150.00	2	Citric acid	150.00
25.00	3	Aerosil® 200	25.00
100.00	4	Sucrose (crystalline)	100.00
1.00	5	Saccharin sodium	1.00
QS	6	Water	QS
5.00	7	Magnesium stearate	5.00
125.00	8	Sodium bicarbonate	125.00
65.00	9	Flavor mixture	65.00

MANUFACTURING DIRECTIONS

- Granulate mixture of items 1 to 5 with item 6, dry, and pass through a sieve.
- Mix the dry granules with items 7 to 9, and press with medium compression force.
- The dosage may be increased to 2000 mg crospovidone by increasing the tablet weight to 3200 mg.
- Compress 1590 mg tablets using 20 mm diameter biplanar punches.

CROSPVIDONE ORAL SUSPENSION (2000 MG/10 ML)

FORMULATION

Kollidon® CL-M, 20.0 g; sorbitol, crystalline, 10.0 g; Kollidon® 90F, 2.0 g; preservatives, QS; flavor, QS; water, 100 mL.

MANUFACTURING DIRECTIONS

- Dissolve sorbitol, Kollidon® 90F, preservatives and flavors in the water. Add Kollidon® CL-M, and homogenize by shaking.

CROSPVIDONE WATER-DISPERSIBLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
1000.00	1	Crospovidone M (BASF)	1000.00
50.00	2	Aerosil® 200	50.00
250.00	3	Sucrose (crystalline)	250.00
5.00	4	Saccharin sodium	5.00
2.00–3.00	5	Flavors	2.00–3.00
380.00	6	Water	380.00
5.00	7	Magnesium stearate	5.00

MANUFACTURING DIRECTIONS

- Granulate mixture of items 1 to 5 with item 6, dry, and pass through a sieve.
- Mix the dry granules with item 7 and press with low compression force.
- The dosage may be increased to 2000 mg crospovidone by increasing the tablet weight to 2600 mg.
- Compress 1280 mg tablets using 20 mm biplanar punches.

CYANOCOBALAMIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
50.00 μg	1	Cyanocobalamin; use gelatin-coated cyanocobalamin (0.1%)	50.00
150.00	2	Ludipress®	150.00
1.50	3	Magnesium stearate	1.50
2.00	4	Sicovit Quinoline lake, yellow	2.00
3.00	5	Sicovit Yellow lake, orange	3.00

MANUFACTURING DIRECTIONS

- Prepare a premix of item 1 and 2 and add to items 3 to 5.
- Pass through a 0.5 mm sieve and press with low compression force.
- Compress into 209 mg tablets using 8 mm biplanar punches.

DEXPANTHENOL GEL CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
50.00	1	Dexpantenol (BASF)	50.00
100.00	2	Liquid paraffin	100.00
150.00	3	Lutrol E 400	150.00
180.00	4	Lutrol F 127	180.00
QS	5	Water	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Dissolve dexpantenol and Lutrol E 400 in water, add liquid paraffin, and stir, heating to 60°C to 70°C.
2. Slowly add Lutrol F 127, and stir until dissolved.
3. Cool to room temperature, stirring continuously until the air bubbles disappear.

DEXTROMETHORPHAN, PSEUDOEPHEDRINE, AND CHLORPHENIRAMINE MALEATE SYRUP

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
2.00	1	Dextromethorphan hydrobromide	2.00
4.00	2	D-Pseudoephedrine hydrochloride	4.00
0.40	3	Chlorpheniramine maleate	0.40
25.00	4	Sorbitol syrup	25.00
0.20	5	Saccharin sodium	0.20
3.00	6	Hydroxyethyl cellulose (Natrosol™)	3.00
2.50	7	Sodium benzoate	2.50
1.05	8	Banana flavor	1.05
1.10	9	Custard flavor	1.10
1.20	10	Trisodium citrate dihydrate (powder)	1.20
QS	11	Deionized water	QS to 1 L

MANUFACTURING DIRECTIONS

1. In a suitable stainless steel vessel, combine sorbitol syrup, hydroxyethyl cellulose, and deionized water. Mix well.
2. Add sodium benzoate and stir again for 5 minutes.
3. After obtaining a clear solution, stir the hydroxyethyl cellulose suspension, rinse the container with deionized water, and transfer the rinsings to the vessel.
4. Heat the vessel to 40°C to 50°C and stir the mix for 1 hour.
5. After 1 hour, a clear gel without lumps is obtained.
6. Dilute the gel with sorbitol syrup, and cool to 30°C.
7. In a separate vessel, add deionized water, and heat while stirring to 50°C.
8. After this temperature is reached, dissolve, in this order, dextromethorphan hydrobromide,

chlorpheniramine maleate, and pseudoephedrine hydrochloride and saccharin sodium.

9. Cool the solution to 25°C.
10. In a suitable stainless steel container, add deionized water, and while stirring, dissolve trisodium citrate under 0.6 bar vacuum and high speed.
11. Transfer the active substance solution to the syrup vehicle.
12. Rinse the vessel twice with deionized water.
13. Add while stirring (low) the custard and banana flavors.
14. Mix for 10 minutes.
15. Then, while stirring, add the solution from the preceding step. Keep stirring for 15 minutes at moderate speed.
16. Stop stirring, and check pH (limit: 5.9–6.2). Adjust with 10% trisodium citrate solution. After each addition, where necessary, stir for 5 minutes before recording pH again.
17. Finally, make up the volume with deionized water, and stir once more for 15 minutes under vacuum (0.6 bar) at moderate speed.
18. Stop stirring, and remove vacuum. Check final volume once more.
19. Filter the clear syrup under compressed air pressure, first through a filter of 330 µm and then through a 20 µm filter of propylene type.

DIHYDROXYALUMINUM SODIUM CARBONATE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
31.00	1	Dihydroxyaluminum sodium carbonate (Giulini A 265)	31.00
61.50	2	Sugar	61.50
2.00	3	Magnesium stearate	2.00
15.00	4	Starch	15.00
QS	5	Flavor, sweetener	0.50

MANUFACTURING DIRECTIONS

1. Blend to mix and compress 110 mg in 6 mm punch.

DIMENHYDRINATE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
50.00	1	Dimenhydrinate	50.00
245.00	2	Ludipress®	245.00
5.00	3	Magnesium stearate	5.00

MANUFACTURING DIRECTIONS

1. Mix all components, sieve, and press with low compression force.
2. Compress into 300 mg tablets using 8 mm biplanar punches.

DIMENHYDRINATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
50.00	1	Dimenhydrinate	50.00
50.00	2	Cellulose (microcrystalline) (Avicel™ PH101)	50.00
125.00	3	Lactose	125.00
2.29	4	Croscarmellose sodium (Ac-Di- Sol, SD-711)	2.29
1.00	5	Fumed silicon dioxide	1.00
0.50	6	Stearic acid	0.50
0.50	7	Magnesium stearate	0.50

MANUFACTURING DIRECTIONS

1. Screen items 1,5, and 6 separately through a 40 mesh sieve.
2. Blend items 1, 2, 4, and 5 in a V-blender for 3 minutes.
3. Add item 3 in the blender and mix for 17 minutes.
4. Add item 6, and blend for 3 minutes.
5. Add item 7 to the blender and mix for 5 minutes.
6. Compress using 3/8 in. flat, beveled-edge punches to a hardness of 6 kp and average tablet weight of 228 mg.

DIMENHYDRINATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Dimenhydrinate	100.00
40.00	2	Lactose monohydrate	40.00
40.00	3	Cornstarch	40.00
6.00	4	Kollidon® 90 F	6.00
30.00	5	Isopropanol	30.00
14.00	6	Kollidon® CL	14.00
16.00	7	Talc	16.00
2.00	8	Aerosil® 200	2.00
2.00	9	Calcium arachinate	2.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 4 with item 5, dry, pass through a 0.8 mm sieve, mix with items 6 to 9, and press with low compression force.
2. Compress into 210 mg tablets using 9 mm biconvex punches.

DIMENHYDRINATE TABLETS (50 MG), DC**FORMULATION**

Dimenhydrinate, 50.0 g; Aerosil® 200, 4.0 g; Ludipress®, 140.0 g; Kollidon® CL, 2.0 g; magnesium stearate, 1.5 g.

MANUFACTURING DIRECTIONS

1. Mix dimenhydrinate with Aerosil® 200, add the other components, and sieve.
2. Press with low compression force at 202 mg.

**DIPHENHYDRAMINE AND
PSEUDOEPHEDRINE CHEWABLE TABLETS**

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
25.00	1	Diphenhydramine hydrochloride	25.00
60.00	2	Pseudoephedrine hydrochloride	60.00
415.00	3	Cab-o-Sil	415.00
200.00	4	Water	200.00

1. Mix diphenhydramine hydrochloride and pseudoephedrine hydrochloride in the water until thoroughly dissolved.
2. Pour Cab-o-Sil M5 (silicon dioxide) into a planetary mixer, to which add the dissolved drug solution and mix at slow speed.
3. Continued for 5 minutes until the solution and Cab-o-Sil are completely mixed.
4. Dry the entire composition in a forced hot air oven for 7 hours at 50° C.
5. Dry the composition to LOD 1%.
6. Screen the dried material through a No. 30 U.S. standard mesh screen and compress to give average weight of 1 g containing 50 mg diphenhydramine hydrochloride and 120 mg pseudoephedrine hydrochloride.

DIPHENHYDRAMINE HYDROCHLORIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
25.00	1	Diphenhydramine hydrochloride	25.00
150.00	2	Calcium phosphate (dibasic)	150.00
20.00	3	Starch (StaRX 1500)	20.00
QS	4	PVP	QS
QS	5	Alcohol, USP	QS
75.00	6	Stearic acid (fine powder)	75.00
25.00	7	Cellulose (microcrystalline)	25.00
QS	8	Purified water, USP	QS

MANUFACTURING DIRECTIONS

1. In a planetary mixer, place diphenhydramine hydrochloride, calcium phosphate dibasic, and starch.
2. Mix for 5 to 10 minutes.
3. In a separate mixer, charge PVP, alcohol, and water in the ratio 1:50:40.
4. Moisten this mixture with solution from the previous step to granulate.
5. Record the volume used.
6. Pass the wet mass through a No. 14 mesh screen on dryer trays.
7. Dry the granulation at 48.8°C to 54.4°C, or use a fluid-bed dryer.
8. Pass the dried granules through a No. 20 mesh screen.
9. Charge dried granules to twin-shell blender and add stearic acid (previously passed through No. 30 mesh screen) and microcrystalline cellulose.
10. Mix for 5 to 7 minutes.
11. Compress to 300 mg tablets using a rotary press with 5/16 in. standard concave punches.

ECONAZOLE NITRATE AND BENZOYL PEROXIDE ANTIACNE CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
200.00	1	PEG-6 and PEG-32 and glyceryl stearate (Tefose® 63)	200.00
30.00	2	Mineral oil	30.00
30.00	3	Apricot kernel oil PEG-6 esters (Labrafil® M 1944)	30.00
0.50	4	Sorbic acid	0.50
0.50	5	Sodium methylparaben	0.50
724.00	6	Deionized water	724.00
5.00	7	Benzoyl peroxide	5.00
10.00	8	Econazole nitrate	10.00

MANUFACTURING DIRECTIONS

1. Mix and heat items 1 to 6 together, and bring temperature to 75°C.
2. Allow to cool while stirring.
3. Add items 7 and 8 at 30°C, and mix well until uniform.

ECONAZOLE NITRATE AND BENZOYL PEROXIDE ANTIACNE LOTION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
50.00	1	PEG-6 stearate, cetech-20, and steareth-20 (Tefose® 2000)	50.00
30.00	2	Mineral oil	30.00
20.00	3	Cetyl alcohol	20.00
0.70	4	Sodium methylparaben	0.70
0.30	5	Sorbic acid	0.30
884.00	6	Deionized water	884.00
5.00	7	Benzoyl peroxide	5.00
10.00	8	Econazole nitrate	10.00

MANUFACTURING DIRECTIONS

1. Mix and heat items 1 to 3 together, and bring temperature to 75°C.
2. Allow to cool while stirring.
3. Mix items 4 to 6 and add to previous step while stirring.
4. Cool with stirring.
5. Add items 7 and 8 at 30°C while stirring.

EUCALYPTOL SOLUTION

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
80.00	1	Eucalyptol	80.00
40.00	2	Cremophor RH 40	40.00
QS	3	Preservative	QS
QS	4	Water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Mix eucalyptol and cremophor at 65°C, stir well, and slowly add the warm solution of item 3 to produce a clear or slightly opalescent, colorless liquid.

EUCALYPTOL SOLUTION (8%)**FORMULATION**

1. Eucalyptol, 8.0 g; Cremophor RH 40 [1], 4.0 g.
2. Preservative, QS; Water, 100 mL.

MANUFACTURING DIRECTIONS

1. Mix eucalyptol and Cremophor at 65°C, stir well, and slowly add the warm solution 2.

EUCALYPTUS AND MINT EMULSION

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
427.50	1	Distilled water	427.50
375.00	2	Eucalyptamint	375.00
70.00	3	Sodium stearyl lactylate (Patronic® SSL)	70.00
35.00	4	PEG-20 hydrogenated lanolin (Supersat ANS4)	35.00
17.50	5	Ritasynt IP	17.50
80.00	6	Cetearyl alcohol, polysorbate 60, PEG-15 stearate, and steareth-20 (Ritachol 1000)	80.00

MANUFACTURING DIRECTIONS

1. Heat item 1 to 71°C.
2. Combine rest of the ingredients in another container, and heat to 71°C.
3. Slowly add water at 71°C, and mix for 1 hour.
4. Cool the mixture to 35°C to 45°C, and fill.

EUCALYPTUS AND MINT OINTMENT

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
160.00	1	Menthol	160.00
40.00	2	Eucalyptus	40.00
800.00	3	Anhydrous lanolin, USP	800.00

MANUFACTURING DIRECTIONS

1. Mix lanolin until melted (approximately at 50°C), add remaining ingredients, and mix for 1 hour.
2. Fill hot.

FERROUS FUMARATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
200.00	1	Ferrous fumarate	200.00
295.00	2	Ludipress®	295.00
5.00	3	Magnesium stearate	5.00

MANUFACTURING DIRECTIONS

1. Mix all components. Pass through a 0.8 mm sieve.
2. Press with low compression force.
3. Compress into 509 mg tablets using 12 mm biplanar punches.

**FERROUS SULFATE, MANGANESE SULFATE,
AND COPPER SULFATE TABLETS**

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
65.00	1	Anhydrous ferrous sulfate	65.00
3.50	2	Manganese sulfate	3.50
0.16	3	Copper sulfate	0.16
70.00	4	Ludipress®	70.00
10.00	5	Kollidon® 30	10.00
2.00	6	Magnesium stearate	2.00
3.00	7	Aerosil® 200	3.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.5 mm sieve, mix, and press with high compression force.
2. Compress into 149 mg tablets using 8 mm biplanar punches.

FERROUS SULFATE ORAL SOLUTION

Bill of Materials			
Scale (mg/5 mL)	Item	Material Name	Quantity/ L (g)
75.00	1	Ferrous sulfate ^a	125.00
294.00	2	Sucrose	490.00
147.00	3	Maltitol solution (Lycasin® 80/55)	245.00
0.30	4	Citric acid (monohydrate)	0.50
0.90	5	Citric acid (monohydrate)	1.50
0.06	6	FD&C Yellow No. 6 (sunset yellow FCF)	1.00
3.12	7	Guarana flavor 12144-33	5.20
0.33	8	Potassium sorbate	0.55
0.30	9	Saccharin sodium	0.50
—	10	Purified water	QS to 1 L

^a Equivalent to 15 mg iron (Fe).

MANUFACTURING DIRECTIONS

1. Bubble nitrogen throughout the process.
2. Check and record pH of the purified water (limit: 5.0–6.5).
3. Collect 166.67 g of purified water in mixer.
4. Heat to 90°C to 95°C for 10 minutes.
5. Add item 8. Stir to dissolve to a clear solution.
6. Add item 2. Stir to dissolve to a clear solution.
7. Add item 3. Stir for 10 minutes, and cool to 30°C to 35°C.
8. Dissolve item 4 in 10 g of purified water (30–35°C), and add to first step.
9. Dissolve item 9 in 10 g of purified water (30–35°C), and add to first step.
10. Dissolve item 5 in 273.33 g of purified water (30–35°C).
11. Then, add item 1 to the clear solution, and dissolve slowly without aeration.
12. Add to mixer.
13. Dissolve item 6 in 10 g of purified water (25–30°C), and add to first step.
14. Add item 7 to first step.
15. Mix at low speed for 10 minutes.
16. Bring volume up to 1 L with purified water.
17. Check and record pH (target: 2.20, limit: 1.95–5.15).
18. Filter the drops with recirculation.
19. Transfer the filtered drops to a storage vessel under an N₂ blanket.
20. Use the nitrogen blanket in the tank throughout the storage and filling period.

FERROUS SULFATE ORAL SYRUP

Bill of Materials			
Scale (mg/5 mL)	Item	Material Name	Qty/L (g)
200.00	1	Ferrous sulfate ^a	40.00
3350.00	2	Sucrose	670.00
750.00	3	Maltitol solution (Lycasin® 80/55)	150.00
4.16	4	Citric acid (monohydrate)	833.20
8.33	5	Citric acid (monohydrate)	1.66
0.50	6	Color	0.10
15.50	7	Flavor	3.10
—	8	Purified water	QS to 1 L

^a Equivalent to 40 mg elemental iron.

MANUFACTURING DIRECTIONS

1. Bubble nitrogen throughout the process.
2. Heat 300 g of purified water to 95°C.
3. Add item 2 while stirring at low speed.
4. Dissolve to clear solution by stirring at 95°C.
5. Add item 3.
6. Stir at low speed, and cool to 25°C to 30°C.
7. Dissolve item 4 in 17 g of item 8, and add to the first step.
8. Dissolve item 5 in 180 g of purified water in a separate stainless steel container.
9. Then, add item 1 to the clear solution, and dissolve slowly without aeration.
10. Add to first step.
11. Dissolve item 6 in 16 g of purified water, and add to the first step.
12. Add item 7 to the first step.
13. Mix at low speed for 10 minutes.
14. Bring volume up to 1 L with purified water.
15. Check and record pH (limit: 2–5).
16. Filter the syrup at 1.5 bar.
17. Recirculate approximately 100 to 150 mL of syrup.
18. Use a nitrogen blanket in the tank throughout the storage period.

FERROUS SULFATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
200.00	1	Anhydrous ferrous sulfate, with excess	203.00
185.00	2	Ludipress®	185.00
15.00	3	Kollidon® VA 64	15.00
4.00	4	Magnesium stearate	4.00
4.00	5	Talc	4.00
3.00	6	Aerosil® 200	3.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press to tablets with medium compression force.
2. Compress into 413 mg tablets using 8 mm biplanar punches.

FIR NEEDLE OIL SOLUTION

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
30.00	1	Fir needle oil (Frey & Lau)	30.00
50.00	2	Camphora	50.00
60.00	3	Cremophor RH 40	60.00
403.00	4	Ethanol (96%)	403.00
457.00	5	Water	457.00

MANUFACTURING DIRECTIONS

1. Mix the active ingredients with Cremophor RH 40, and heat to 50°C to 60°C.
2. Add the ethanol to the well-stirred solution; then, slowly add the warm water to produce a clear or slightly opalescent liquid.
3. The amount of Cremophor RH 40 required depends on the type of fir needle oil.

FOLIC ACID TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
5.00	1	Folic acid ^a	5.24
12.00	2	Maize starch (dried) ^b	12.00
5.26	3	Cellulose (microcrystalline) (Avicel™ PH102)	5.26
20.00	4	Cellulose (microcrystalline) (Avicel™ PH102)	20.00
1.50	5	Colloidal silicon dioxide (Aerosil® 200)	1.50
66.00	6	Lactose (spray-dried) ^c	66.00
2.50	7	Talc (fine powder)	2.50
2.50	8	Stearic acid (fine powder)	2.50

^a Extra folic acid is added (0.08 mg/tablet) to compensate water (water NMT 8.0%).

^b LOD: NMT 4.5% when dried at 120°C for 4 hours.

^c Meets the USP NF, except particle size distribution, as follows: minimum 98%, 250 µm; 30% to 60%, 100 µm; maximum 15%, 45 µm.

MANUFACTURING DIRECTIONS

1. Folic acid must be protected from exposure to direct light.
2. Sift items 1, 2, and 3 through a Fitz mill (impact forward, high speed), and collect in a stainless steel drum.
3. Load the material into a blender, and mix for 3 minutes.
4. Sift items 4 to 8 through a 500 µm sieve using a sifter, and collect in a stainless steel drum.
5. Load this sieved material into a blender.
6. Mix for 5 minutes.
7. Unload the lubricated powder into a stainless steel drum. Check for small lumps or globules in the powder mix.
8. If required, pass the entire mass through a 500 µm sieve using a sifter, and mix for 1 minute in a blender.
9. Compress into 1.15 g tablets (hardness: 3–7 kp) using 7 mm round flat punches.
10. For 1 mg tablets, compensate with lactose, and compress as in step 9.

FOLIC ACID TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
5.00	1	Folic acid	5.00
195.00	2	Ludipress®	195.00
1.50	3	Magnesium stearate	1.50

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press into tablets using medium compression force.
If the content uniformity does not meet the requirements, prepare a premix of the active ingredient with a small part of the Ludipress® or with lactose monohydrate before mixing with the other components of the formulation.
2. Compress into 213 mg tablets using 8 mm biplanar punches.

FOOT BATH

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
200.00	1	Polysorbate 20	200.00
2.50	2	Menthol	2.50
10.00	3	Alpha-bisabolol	10.00
20.00	4	Disodium undecylenamido MEA-sulfosuccinate	20.00
20.00	5	Perfume (menthol compatible)	20.00
QS	6	Deionized water	QS to 1 L
QS	7	Preservative, color	QS

MANUFACTURING DIRECTIONS

1. Predissolve menthol, alpha-bisabolol, and perfume in Polysorbate 20.
2. Add mixture to the water phase while stirring.
3. Stir until homogeneous, and then fill.

FOOT FRESHENER CREAM

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/L (g)
30.00	1	Alcohol and ceteareth-20 (Cosmowax® EM5483)	30.00
30.00	2	Isopropyl myristate (Crodamol® IPM)	30.00
5.00	3	Cetyl esters (Crodamol® SS)	5.00
20.00	4	Oleyl alcohol	20.00
5.00	5	Propylene glycol	5.00
5.00	6	Carbopol 980	5.00
QS	7	Deionized water	QS to 1 L
300.00	8	Ethanol (DEB100)	300.00
2.00	9	Triclosan (Irgasan® DP300)	2.00
0.50	10	Menthol	0.50
4.00	11	Triethanolamine 99 (to give pH 6–7)	~4.00

MANUFACTURING DIRECTIONS

1. Preblend ethanol, irgasan, and menthol, and warm to 50°C.
2. Heat water and oil phases separately to 70°C.
3. Add the water phase to the oil phase while stirring.
4. Stir to cool, adding the preblend at 60°C. Adjust pH.

FOOT MOUSSE

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
300.00	1	Ethanol (DEB100)	300.00
1.00	2	Menthol	1.00
QS	3	Deionized water	QS
20.00	4	Undecyleneamide DEA and diethanolamine	20.00
5.00	5	Cetrimonium bromide	5.00
10.00	6	PEG-75 and water	10.00
QS	7	Perfume, preservative, color	QS

MANUFACTURING DIRECTIONS

1. Dissolve menthol in ethanol.
2. Add remaining ingredients.
3. Pack into mechanical mousse applicator, such as the Kunststoff AG Supermatic foamer system, Airspray International BV jet foamers, or Calmar foamers.

GARLIC EXTRACT + THYME EXTRACT + VITAMIN C (300 MG + 25 MG + 100 MG)

FORMULATION

Garlic extract, granulated (Aflopa), 300 g; thyme extract, 25 mg; powder (Aflopa), 25 g; ascorbic acid, crystalline (BASF), 100 g; Kollidon® CL, 14 g; Ludipress®, 268 g; magnesium stearate, 7 g.

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press to tablets with medium compression force at 714 mg.

GARLIC TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
95.00	1	Calcium phosphate, dibasic	95.00
94.00	2	Lactose monohydrate	94.00
9.00	3	Kollidon® 30	9.00
25.00	4	Water	25.00
100.00	5	Dried garlic powder	100.00
2.00	6	Magnesium stearate	2.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 and 2 with solution of items 3 and 4, pass through a 0.8 mm sieve, add items 5 and 6, and press with low compression force.
2. Compress 312 mg using 9 mm biconvex punches.

GINKGO EXTRACT TABLETS (40 MG)**FORMULATION**

Ginkgo biloba extract, dry powder, 240 g; Aerosil® (Biogen) 200, 1 g; Kollidon® CL, 4 g; Ludipress®, 203 g; magnesium stearate, 2 g.

MANUFACTURING DIRECTIONS

1. Mix the ginkgo extract with Aerosil 200, add the other components, pass through a 0.8 mm sieve, and press to tablets with low compression force at 254 mg.

GLYCERIN SUPPOSITORIES

Bill of Materials			
Scale (mg/ suppository)	Item	Material Name	Qty/1000 Suppositories (g)
1800.00	1	Glycerin (glycerol)	1800.00
0178.00	2	Sodium stearate	178.00
0099.00	3	Purified water	99.00

MANUFACTURING DIRECTIONS

1. The suppository mass is manufactured at a temperature of 120°C.
2. Care must be taken to see that molten suppository mass does not accidentally spill on the person.
3. The inside of the vessel should not be touched with the bare hand, as it is at a temperature of 120°C.
4. Sodium stearate powder is light and fluffy; avoid inhaling the dust.
5. Load item 1 into the mixer, and heat to 120°C ± 2°C while stirring at low speed.
6. Load item 2 into the mixer containing item 1.
7. Mix until complete solubilization is achieved.
8. Cool to 105°C ± 2°C.

9. Add item 3 slowly to the mixer containing the mass while stirring.
10. Mix for 20 minutes.
11. Immediately transfer the hot mass to the heated storage vessel or heated vessel of a Sarong SAAS suppository-filling machine.
12. Check the temperature; it should be 105°C ± 2°C.
13. Fill weight: 2077 mg per suppository.

GLYCERIN SUPPOSITORIES FOR CHILDREN

Bill of Materials			
Scale (mg/ suppository)	Item	Material Name	Qty/1000 Suppositories (g)
900.00	1	Glycerin (glycerol) (0.06% excess)	900.50
089.00	2	Sodium stearate	89.00
049.50	3	Purified water	49.50

MANUFACTURING DIRECTIONS

1. Fill weight: 1039 mg per suppository.
2. See manufacturing directions for glycerin suppositories.

GLYCOL FOAM (NONAQUEOUS)

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
40.00	1	Polawax A31	40.00
710.00	2	Propylene glycol	710.00
150.00	3	Ethanol DEB100	150.00

MANUFACTURING DIRECTIONS

1. Dissolve Polawax in propylene glycol/ethanol.
2. Pack into containers, and pressurize.
3. Ethanol may be omitted if desired.
4. In aerosol pack, 90% concentrate and 10% propellant 12/114 may be used.
5. Propylene glycol is a suitable vehicle for glycol-soluble medicaments.
6. This formulation provides a mousse for such a system.

GUAIFENESIN, PSEUDOEPHEDRINE, CARBINOXAMINE, AND CHLOPHEDIANOL DROPS

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Quantity/L (g)
20.00	1	Guaifenesin	20.00
400.00	2	Sucrose	400.00
240.00	3	Glucose liquid	240.00
120.00	4	Sorbitol solution	120.00
3.00	5	Saccharin sodium	3.00
2.50	6	Sodium benzoate (powder)	2.50
30.00	7	Pseudoephedrine hydrochloride	30.00
1.00	8	Carbinoxamine maleate	1.00
6.60	9	Chlophedianol hydrochloride	6.60
105.00	10	Red E123 (Amaranth)	0.105
3.75	11	FD&C Blue No. 1	3.75 mg
QS	12	Acid, hydrochloric	QS
50.00	13	Menthol crystals	50.00 mg
2.75	14	Flavors	2.75
65.00	15	Orange oil terpeneless	65.00 mg
5.66	16	Alcohol (190 proof)	5.66
QS	17	HyFlo filter aid	0.526
QS	18	Purified water	~420.00

MANUFACTURING DIRECTIONS

1. Charge 260 mL purified water into a suitable tank.
2. Begin heating water to 70°C to 80°C while adding guaifenesin and sucrose with stirring.
3. Continue stirring to dissolve ingredients.
4. Remove heat. Add glucose liquid and sorbitol to solution from preceding step with stirring.
5. Add saccharin sodium, sodium benzoate, pseudoephedrine hydrochloride, carbinoxamine maleate, and chlophedianol hydrochloride to solution from preceding step.
6. Stir well to dissolve all ingredients.
7. Dissolve Red E123 and FD&C Blue No. 1 in 10 mL warm purified water.
8. Add dye solution to solution from preceding step with stirring.
9. Cool solution to 30°C to 35°C.
10. QS to 975 mL using purified water. Mix well.
11. Adjust to pH 4.25 (range: 4.0–4.5) with hydrochloric acid (approximately 0.65 g/L of drops).
12. Stir well after each addition of acid.

13. Dissolve menthol, flavors, and orange oil in alcohol. Add mixture to solution from previous step with good stirring.
14. Stir the solution slowly for 2 hours.
15. Allow to stand overnight to cool and remove entrapped air.
16. QS to 1 L with purified water. Stir well.
17. Add HyFlo filter aid to solution, and mix well.
18. Recirculate through filter press or equivalent until sparkling clean.

GUAIFENESIN TABLETS

MANUFACTURING DIRECTIONS

1. Inner tablet: guaifenesin, 175.0 mg; microcrystalline cellulose, 35.1 mg; crospovidone, 35.0 mg; PVP, 7.3 mg; talc, 2.3 mg; zinc stearate, 2.3 mg; total, 257 mg.
2. Outer tablet: guaifenesin, 425.0 mg; hydroxypropylmethylcellulose K4M, 139.9 mg; stearic acid, 30.0 mg; zinc stearate, 5.4 mg; total, 600.3 mg.
3. Make the inner tablet by oscillating guaifenesin and half of the PVP through a 30 mesh screen.
4. Transfer the blend to a pharmaceutical-grade blender and mix until it is of uniform consistency.
5. Granulate it with PVP that had been previously dissolved in a sufficient amount of purified water to make a solution of approximately 8% to 12% of PVP.
6. Discharge this mixture and dry in a forced air oven at 40°C until the water content is less than 1%.
7. Oscillate the dried granulation through a 12 mesh screen and return to the blender.
8. Add the remaining PVP, microcrystalline cellulose, and talc to this dried granulation and mix until it is of uniform consistency.
9. Finally, add zinc stearate, and mix the mixture until it is of uniform consistency.
10. Compress this mixture into inner tablets using a standard tableting press.
11. Make the outer tablet by first passing guaifenesin through an oscillator equipped with a 30 mesh screen.
12. After this step, transfer guaifenesin to a blender, and hydroxypropylmethylcellulose K4M and stearic acid are added to it. It is mixed until uniform.
13. Add zinc stearate and blend the mixture until uniform.
14. Compress the mixture of ingredients that comprise the outer tablet around the already formed inner tablet on a standard compression coating tablet press.

GUAIFENESIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g) Percent (w/w)
69.77	1	Guaifenesin USP	69.77
16.00	2	Starch 1500	16.00
9.48	3	Microcrystalline cellulose NF	9.48
4.00	4	Starch 1500	4.00
0.50	5	Stearic acid NF	0.50
0.25	6	Magnesium stearate	0.25
100.00	7	Total	100.00

MANUFACTURING DIRECTIONS

1. Granulation: Preblend items 1 and 2 for 2 minutes prior to granulating with water to appropriate moisture.
2. Wet mass for 3 minutes.
3. Size the granulation.
4. Pass lubricant through a 60 mesh screen prior to blending.
5. Pass colloidal silicon dioxide through a 30 mesh screen along with the MCC.
6. Blend all the ingredients, except the lubricant, for 10 minutes.

HEMORRHOID CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
20.00	1	Lanolin alcohol (Ivarlan 3310)	20.00
448.00	2	Petrolatum	448.00
450.00	3	Petrolatum amber	450.00
30.00	4	Shark liver oil	30.00
10.00	5	Live yeast cell derivative (Biodyne's TRF)	10.00
10.00	6	Deionized water	10.00
20.90	7	Lanolin	20.90
1.00	8	Thyme oil	1.00
0.10	9	Phenyl mercuric nitrate	0.10

MANUFACTURING DIRECTIONS

1. Mix and heat items 1 to 4 to 70°C. Cool to 50°C, and hold.
2. Separately combine items 5 to 7, heat to 40°C, and mix until homogeneous dispersion is achieved. With rapid mixing, add this mixture to previous mixture. Mix again, and cool to 40°C. Add items 8 and 9.
3. Continue mixing while cooling to 35°C.

HERBAL HEMORRHOID TABLETS

MANUFACTURING DIRECTIONS

1. Initially, wash genera *Glycyrrhizae radix*, *Rhei rhizoma*, *Ephedrae herba*, *Moutan radicis cortex*, *Menthae herba*, *Pinelliae rhizoma*, *Pasoniae radix*, *Aconiti tuber*, *Corni fructus*, gypsum, *Ginseng radix*, and *Pelladendri radix*, respectively, with water to remove sand, clay, dust, and the like.
2. Clean and dry these natural substances to a moisture content of approximately 5%.
3. Cut 168 g of *G. radix*, 104 g of *R. rhizoma*, 104 g of *E. herba*, 168 g of *M. radicis cortex*, 104 g of *M. herba*, 168 g of *P. rhizoma*, 56 g of *P. radix*, 56 g of *A. tuber*, 56 g of *C. fructus*, 168 g of *G. radix*, and 104 g of *P. radix* into a particle size of approximately 1 cm and mix together.
4. To this mixture add 104 g of *Testudinis carapax*, 56 g of *Natrii sulfas*, 168 g of gypsum, 56 g of cinna-baris, and 256 g of talcum.
5. Thereafter, place this mixture in an extractor with an aromatic vapor collector.
6. Add 12 L of water to approximately 2 kg of the mixture in the extractor.
7. Heat the mixture in the extractor to approximately 80°C for 1 hour and then extract.
8. Filter the aqueous mixture first in a centrifugal separator and then again in a microfilter.
9. Condense the aromatic vapor distilled from the aqueous mixture and add as an aromatic liquid to the filtrate.
10. Evaporate the filtrate through an automatic vacuum evaporator to a moisture content of approximately 30% to produce an extract, which is useful as an antihemorrhoidal composition in extract form.
11. At this time, dry the concentrated liquid through a dry sprayer to produce a granulated formulation, a tablet formulation, a pill formulation, an ointment formulation, or the like, for use as an antihemorrhoid medicine.

HORSETAIL EXTRACT TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
450.00	1	Horsetail extract (powder), with excess	456.00
14.00	2	Kollidon® VA 64	14.00
5.00	3	Lutrol F 68	5.00
QS	4	Isopropanol	~120.00
14.00g	5	Kollidon® CL	14.00
QS	6	Magnesium stearate	QS

MANUFACTURING DIRECTIONS

1. Granulate the extract (item 1) with solution of items 2 to 4, dry, pass through a 0.8 mm sieve, mix with items 5 and 6, and press with high compression force.
2. Compress 489 mg using 12 mm biplanar punches.

HYDROCORTISONE AQUEOUS GEL

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
10.00	1	Hydrocortisone acetate	10.00
100.00	2	Lutrol E 400	100.00
50.00	3	Cremophor RH 40	50.00
5.00	4	Carbopol 940 (Goodrich)	5.00
495.00	5	Water	495.00
QS	6	Preservative	QS
260.00	7	Water	260.00
8.00	8	Triethanolamine	8.00
—	9	Water	7.20

MANUFACTURING DIRECTIONS

1. Heat item 6 in item 7 to 80°C, prepare a solution of items 3 and 4 in item 5, and add to the solution of preservative.
2. Add and suspend item, and mix.
3. Prepare a solution of item 8 in item 9, add to the previous solution at 70°C, and cool to form gel.

HYDROCORTISONE AQUEOUS GEL

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
10.00	1	Hydrocortisone acetate	10.00
150.00	2	Cremophor A 25	150.00
20.00	3	Cremophor RH 40	20.00
QS	4	Preservative	QS
640.00	5	Water	640.0000

MANUFACTURING DIRECTIONS

1. Suspend item 1 in a mixture of items 2 and 3 at 70°C.
2. Prepare solution of item 4 by heating item 5 to 70°C, and add it slowly to the hot item 4.
3. Continue to stir until the gel is cool to form clear, colorless gels.

HYDROCORTISONE CREAM

Bill of Materials			
Scale (g/100 g)	Item	Material Name	Qty/kg (g)
1.00	1	Hydrocortisone, micronized (3% excess)	10.30
6.00	2	Propylene glycol	60.00
0.10	3	Chlorocresol	1.00
5.00	4	Mineral oil (liquid paraffin)	50.00
2.00	5	Poloxyl 20 cetostearyl ether (Cetomacrogol 1000)	20.00
8.00	6	Cetostearyl alcohol	80.00
18.00	7	Petrolatum (white soft paraffin)	180.00
0.29	8	Monobasic sodium phosphate	2.90
0.035	9	Propylparaben	0.35
0.10	10	Methylparaben	1.00
59.60	11	Purified water	596.00

MANUFACTURING DIRECTIONS

1. Load 10 g of item 5 and items 4, 6, and 7 in fat-melting vessel.
2. Heat to 70°C to 75°C while stirring.
3. Cool down the temperature to 65°C.
4. Maintain temperature at 65°C to 70°C.
5. Heat item 11 to 90 °C in mixer.
6. Dissolve items 9 and 10 to a clear solution by stirring.
7. Cool down the temperature to 65°C.
8. Maintain temperature to 65°C to 70°C.
9. Add 10 g of item 5 and items 3 and 8 to the parabens solution to dissolve.
10. Mix for 15 minutes.
11. Maintain temperature at 65°C to 70°C.
12. Transfer oil phase to the aqueous phase in mixer vessel through mesh under vacuum while stirring at manual mode (10 rpm) at a temperature of 60°C.
13. Homogenize at high speed.
14. Maintain temperature of 60°C.
15. Vacuum at 0.4 bar for 10 minutes.
16. Cool temperature to 45°C.
17. Mix item 1 in 48 g of item 2 in a separate container at 45°C using homogenizer to make slurry.
18. Add to the dispersed phase while mixing at 10 rpm, and keep temperature at 45°C.
19. Rinse the container with 12 g of item 2, and add to the dispersed phase.
20. Mix and homogenize under vacuum at 0.4 bar for 10 minutes, low speed (10 rpm), at a temperature of 45°C.
21. Cool the temperature to 30°C while mixing at 10 rpm in automode under a vacuum of 0.4 bar.

HYDROCORTISONE CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
70.00	1	Cetylstearyl alcohol	70.00
15.00	2	Cremophor A 6	15.00
15.00	3	Cremophor A 25	15.00
120.00	4	Liquid paraffin	120.00
2.00	5	Paraben	2.00
688.00	6	Water	688.00
80.00	7	Propylene glycol	80.00
10.00	8	Hydrocortisone	10.00

MANUFACTURING DIRECTIONS

1. Heat the mixture of items 1 to 5 and the water separately to approximately 80°C.
2. Add the water to the obtained solution of items 1 to 5 with vigorous stirring.
3. Heat items 7 to 8 until the active ingredient is dissolved, mix with step 2, and continue to stir while cooling to room temperature to produce a white cream.

HYDROCORTISONE ETHANOLIC GEL

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
5.00	1	Hydrocortisone acetate	5.00
60.00	2	Cremophor RH 40	60.00
9.00	3	Triethanolamine	9.00
76.00	4	Water	76.00
600.00	5	Ethanol, 96%	600.00
5.00	6	Carbopol 940 (Goodrich)	5.00
245.00	7	Water	245.00

MANUFACTURING DIRECTIONS

1. Prepare solution of items 6 and 7, and mix slowly with solution of items 1 to 5 to produce a clear, colorless gel.

HYDROCORTISONE OINTMENT

Bill of Materials			
Scale g / 100 g	Item	Material Name	Qty/kg (g)
1.00	1	Hydrocortisone, micronized (6% excess)	10.60
91.50	2	Petrolatum (white soft paraffin)	915.00
7.00	3	Mineral oil (liquid paraffin)	70.00
0.50	4	Sorbitan sesquioleate (Arlacel 83)	5.00

MANUFACTURING DIRECTIONS

1. Melt items 2 and 4 at 75°C in fat-melting vessel.
2. Start heating mixer vessel to 75°C.
3. Transfer molten items from first step to mixer through stainless steel mesh under vacuum at 0.4 to 0.6 bar.
4. Start mixer at 10 rpm in manual mode.
5. Cool down to 50°C.
6. Disperse item 1 in 60 g of item 3 using a spatula in a water bath at 60°C.
7. Homogenize for 6 minutes using homogenizer.
8. Add this to mixer while mixing.
9. Rinse the homogenizer and container with 10 g of item 3, and transfer the rinsings to the mixer.
10. Homogenize the dispersion under vacuum at 0.4 to 0.6 bar while stirring at 10 rpm in homogenizer at high speed for 10 minutes.
11. Cool the temperature to 30°C using a mixer speed 10 rpm and vacuum of 0.4 to 0.6 bar in automode.
12. Transfer the ointment to stainless steel container.

HYDROGEN PEROXIDE BLEACHING DENTIFRICE PASTE

MANUFACTURING DIRECTIONS

1. Add to 50 g purified water, 1.5 g of emulsifier Carbopol 934/PVP in 75:25 ratio, and dissolve with gradual stirring.
2. To the mixture, 20 mL of hydrogen peroxide (50%) add and mix for an additional 5 to 10 minutes.
3. Adjust the acid composition to between pH 5.5 and 6.5 with 10% NaOH.
4. The composition thickens to a gel; set aside.
5. In a separate vessel, add 210 g of methyl methacrylate crosspolymer GMX-0610 obtained from Perspex Corp.
6. In another separate vessel, prepare the continuous phase of the invention, comprising the following ingredients: weight%, sodium fluoride, 1.05; propylene glycol, 24.10; sodium lauryl sulfate, 5.04; water, 43.40; vinyl pyrrolidone/acrylic acid,^a 1.02; hydroxyethyl cellulose, 2.01; glycerin, 18.85; sodium saccharin, 0.47; flavor, 2.76; sodium benzoate, 0.55; benzoic acid, 0.06; sodium EDTA, 0.14; sodium hydroxide (10% solution), 0.55. ^aDry blend copolymer containing 25% vinyl pyrrolidone and 75% Carbopol.
7. The vinyl pyrrolidone in the mixture delays the solubility of the emulsion further than Carbopol alone.
8. After the bleaching composition (step 1) has been prepared to the desired consistency, add 50 g of this composition to 50 g of the water-insoluble abrasive suspension (step 2). Disperse the two immiscible phases in each other in an intimate mixture and then, with the aid of the colloidal mill, agitate until an extremely fine homogeneous dispersion is obtained.

9. Add 100 g of the dispersion so obtained to 50 g of the continuous phase (step 3), mix the two phases in a colloidal mill. The resultant composition comprises the discontinuous phases (step 1) dispersed homogeneously throughout the continuous phase (step 2) and (step 3) of the present invention.
10. The final formulation is expressed as weight in percentage as follows: water, purified, 15.75; methyl methacrylate crosspolymer GMX-0610, 53.71; hydrogen peroxide, 10.00; Carbopol 934, 0.37; hydroxyethyl cellulose, 0.73; sodium fluoride, 0.38 (0.17% F ions); sodium lauryl sulfate, 1.83; propylene glycol, 8.75; glycerin, 6.84; sodium saccharin, 0.17; sodium benzoate, 0.20; benzoic acid, 0.02; sodium EDTA, 0.05; flavor, 1.00; sodium hydroxide (10%), QS (pH 6.5), 0.20.
11. Carbopol in this composition sufficiently retards the dissolution of the emulsified hydrogen peroxide to allow the abrasive agent methyl methacrylate crosspolymer GMX-0610 to remove the dental plaque and pellicles from the enamel surface and thus allow the bleaching active hydrogen peroxide to diffuse through the plaque-free enamel with ease.

IBUPROFEN FAST-DISSOLVE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Ibuprofen coated (equivalent of ibuprofen)	121.90
11.00	2	Citric acid	11.00
3.90	3	Magnasweet 135	3.90
6.50	4	Aspartame	6.50
7.80	5	Cherry flavor	7.80
39.00	6	Croscarmellose sodium	39.00
1.95	7	Silicon dioxide	1.95
3.25	8	Magnesium stearate	3.25
457.90	9	Fast-dissolving granulation (see manufacturing directions)	457.90

MANUFACTURING DIRECTIONS

1. Make a fast-dissolving granulation by combining 400 g of melted PEG-900 with fructose powder (100 g) in a planetary mixer (low shear mixer) and mixing until the granules form.
2. Allow the granulations to cool and then screen.
3. Screen ingredients are screened and then mix in a V-blender.

4. Compress tablets (653.7 mg) at 600 lb (approximately 2.7 kN).
5. The tablets should have hardness of 0.2 to 0.5 kp and disintegrate in less than 15 seconds.

IBUPROFEN-COATED FAST-CRUMBLING GRANULE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Quantity/1000 Tablets (g)
200.00	1	Ibuprofen	200.00
16.00	2	Sodium croscarmellose (AGG)	16.00
27.50	3	Aspartame	27.50
12.20	4	Precipitated silica	12.20
35.00	5	Ethylcellulose	35.00
8.00	6	Hypromellose	8.00
1.33	7	Sodium (AGM) croscarmellose	1.33
	8	Pharmacoat® 606	

MANUFACTURING DIRECTIONS

1. Obtain a suspension by mixing ethylcellulose, 80% precipitated silica, and 30% aspartame in ethyl alcohol until a homogeneous suspension is obtained.
2. Fluidize the powder mixture consisting of ibuprofen, item 7, 70% aspartame, and 20% precipitated silica.
3. Start the granulation by spraying the mixture for approximately 15 to 20 minutes at a spraying rate of 25 g/min and a suspension atomization pressure of 0.8 bar.
4. Perform the actual coating by spraying the remainder of the mixture over approximately 1 hour 30 minutes at a spraying rate of 15 to 20 g/min and a suspension atomization pressure of 1.5 bar.
5. Spray 15% of the mixture during the granulation step, and spray the remainder to 100% during the coating step.
6. Formulate the granules obtained as fast-crumbling multiparticulate tablets, the composition of which is as follows: coated granules, 300 mg; mannitol, 344 mg; sodium croscarmellose, 21 mg; precipitated silica, 7 mg; aspartame, 20 mg; mint flavoring, 4 mg; magnesium stearate, 4 mg.

IBUPROFEN PEDIATRIC SUSPENSION

Bill of Materials			
Scale (mg/ 5 mL)	Item	Material Name	Qty/L (g)
100.00	1	Ibuprofen, low-density ^a	20.00
3000.00	2	Sucrose	600.00
10.00	3	Sodium benzoate	2.00
5.00	4	Saccharin sodium	1.00
5.00	5	Edetate disodium (sodium EDTA)	1.00
500.00	6	Glycerin (glycerol)	100.00
500.00	7	Sorbitol (70% solution)	100.00
10.00	8	Xanthan gum (Keltrol®-F)	2.00
20.00	9	Microcrystalline cellulose (Avicel™ RC-591)	4.00
5.00	10	Polysorbate 80 (Tween 80)	1.00
8.50	11	Citric acid	1.70
1.35	12	FD&C Red No. 40	0.27
7.50	13	Mixed fruits flavor	1.50
5.00	14	Strawberry flavor	1.00
QS	15	Purified water	QS to 1 L

^a Meets USP criteria with the following additional requirements: 100% particle size less than 50 µm and tapped density of 0.3 to 0.4 g/mL.

MANUFACTURING DIRECTIONS

- Heat 302 g of item 15 to 90°C, and dissolve item 2 while mixing in mixer.
- Cool to approximately 50°C.
- Add items 3, 4, 5, 7, and 11 to mixer while mixing, and dissolve.
- Filter the syrup through Seitz Supra 2600 filters in clean stainless steel tank.
- In a clean stainless steel vessel, dissolve item 10 in 35 g of item 15 (40°C).
- Add item 1 slowly while mixing with stirrer.
- Mix for 30 minutes to make uniform dispersion.
Caution: Avoid excessive foaming.
- Disperse items 8 and 9 in item 6 in a clean and dry stainless steel container using stirrer.
- Add 75 g of hot item 15 (70–90°C) at once while mixing.
- Mix for 20 minutes to make a homogeneous smooth mucilage.
- Add approximately 500 g syrup, ibuprofen dispersion, and mucilage to the mixer.
- Rinse the containers of ibuprofen dispersion and mucilage with 50 g of item 15 (40°C).
- Add the rinsings to the mixer.
- Set the mixer: temperature, 25°C; speed, 18 rpm; and manual mode vacuum, 0.5 bar.
- Mix for 3 minutes at low homogenizer speed.
- Mix for 2 minutes at high homogenizer speed. Check the suspension for uniformity of dispersion.

- Homogenize for additional 3 minutes at high speed, if required.
- Add the balance of the syrup (approximately 507.6 g) from previous step to the mixer.
- In a separate container, dissolve item 12 in 6 g of cooled item 15 (40°C), and transfer to the mixer.
- Add items 13 and 14 to the mixer.
- Set the mixer: temperature, 25°C; speed, 18 rpm; manual mode vacuum, 0.5 bar.
- Mix for 15 minutes.
- Mix for 5 minutes at low homogenizer speed.
- Mix for 5 minutes at high homogenizer speed.
- Check the suspension for uniformity.
- Adjust the final volume to 1 L by using purified water.

IBUPROFEN CHEWABLE TABLETS**MANUFACTURING DIRECTIONS**

- Dissolve PVAP and PVP-K90, equivalent to a 2:1 weight ratio, in minimum volumes of an aqueous ammonium hydroxide solution (28% v/v) and water, respectively, and then mix.
- In the resulting mixture, dissolve ibuprofen, equal to the amount of PVAP used, and then add 0.1 N HCl solution dropwise until the pH of the solution is 1.
- Filter the white solid precipitate, wash with water, and then vacuum dry.
- Use the entrapped granules containing 39.06% ibuprofen in the preparation of tablets.
- Accurately weigh appropriate amounts of the granules and the cherry vehicle, corresponding to 200 mg of ibuprofen per 668 mg of tablet, and then mix and compress tablets.

IBUPROFEN SUSTAINED-RELEASE BILAYER TABLETS**MANUFACTURING DIRECTIONS**

- Immediate-Release Layer Composition
 - Part I: Ibuprofen USP, 160.0 mg; microcrystalline cellulose NF, 32.0 mg (Avicel™ PH 101); starch NF, 32.0 mg; pregelatinized starch NF (Starch 1500), 16.0 mg; sodium starch glycolate NF, 6.4 mg.
 - Part II: Hydroxypropylmethylcellulose 2910 USP (Methocel™ E-5), 1.6 mg; purified water USP, QS.
 - Part III: Sodium starch glycolate NF, 1.6 mg; (Explotab) colloidal silicon dioxide NF, 0.8 mg; total, 250.4 mg.
 - Weigh the components of part I, and preblend them in a high-shear mixer (Fielder: impeller speed of approximately 118 rpm for 3 minutes).

5. Prepare the granulating agent (part II) by dissolving the hydroxypropylmethylcellulose 2910 USP into the purified water USP (a ratio of 3.2 g of hydroxypropylmethylcellulose to 200 g water).
 6. Deliver the granulating agent to the powders of part I in the high shear mixer.
 7. Granulate the mixture for 20 minutes (Fielder: impeller speed of approximately 118 rpm).
 8. Remove the completed wet granulation from the high-shear mixer, and load into the product bowl of a fluid-bed apparatus (e.g., Aeromatic or Glatt).
 9. With an inlet air temperature of approximately 60°C, dry the granulation to a moisture level of 0.5% to 1.1% as determined by LOD (e.g., Computrac). The wet granulation can also be dried on trays in drying ovens.
 10. Sieve the dried granulation (e.g., Glatt Quick Sieve: Stator No. 3, Screen No. 1, 5 mm, 1000 rpm). Other machines, such as a Fitzpatrick Communion Mill, can be used.
 11. Blend the sieved and dried granulation with the powders of part III using a suitable mixer, such as a twin-shell, ribbon, or planetary mixer.
2. Sustained-Release Layer
1. Povidone USP (Plasdone K 29/32), 14.7 mg; alcohol USP and purified water USP (QS); 1:1 mixture.
 2. Pregelatinized starch NF (Starch 1500 LM), 0.8 mg; microcrystalline cellulose NF (Avicel™ PH101), 7.3 mg; magnesium stearate NF, 5.0 mg; colloidal silicon dioxide NF (Cab-O-Sil), 5.0 mg, total, 523.3 mg; total tablet weight, 773.7 mg.
 3. Weigh the components of part I, and preblend them in a high-shear mixer (Fielder: impeller speed of approximately 250 rpm for 1 minute).
 4. Prepare the granulating agent (part II) by dissolving Povidone USP in a 1:1 mixture of alcohol USP and purified water USP (a ratio of 12.25 g of povidone to 100 g of alcohol/water).
 5. Spray the granulating agent at a rate of 600 mL/min onto part I in the high-shear mixer.
 6. Granulate the mixture for 1 minute after the addition of part II (Fielder: impeller speed of approximately 250 rpm).
 7. Remove the completed wet granulation from the high-shear mixer, and load it into the product bowl of a fluid-bed apparatus (e.g., Aeromatic or Glatt).
 8. With an inlet air temperature of approximately 60°C, dry the granulation to a moisture level of 0.3% to 0.8% as determined by LOD (e.g., Computrac).
 9. The wet granulation can also be dried on trays in drying ovens.

10. Sieve the dried granulation (Fitzpatrick Communion Mill, Model D6: medium speed, knives forward, 0.093 screen). Other machines, such as Glatt Quick Sieve, can also be used.
 11. Blend the sieved and dried granulation with the powders of part III using a suitable mixer such as a twin-shell, ribbon, or planetary mixer.
3. Compression of Tablets or Caplets
1. Load the granulation of the immediate-release layer into one hopper and the granulation of the sustained-release layer into the second hopper of a bilayer tableting machine (e.g., Stokes Versapress).
 2. Compress tablets using 0.749 × 0.281 × 0.060 extra deep concave capsule-shaped tooling. (Tablet tooling of other shapes, such as oval or round, can also be used.)
 3. The sustained-release layer has a target weight of 523.3 mg, and the immediate-release layer has a target weight of 250.4 mg. Ideal tablet hardness immediately after compression is 11 to 12 kp.

IBUPROFEN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
200.00	1	Ibuprofen	200.00
88.00	2	Maize starch	88.00
30.00	3	Maize starch	30.00
12.80	4	Maize starch (dried) ^a	12.80
1.60	5	Stearic acid (fine powder)	1.60
—	6	Purified water	144.00

^a LOD: NMT 4.5% when dried at 120°C for 4 hours.

MANUFACTURING DIRECTIONS

1. Pass item 3 through a 250 µm sieve using a sifter.
2. Prepare a slurry of item 3 with 10.67 g of cold item 6 (25–30°C) in a stainless steel container.
3. Pour the slurry into a vessel containing 37.33 g of hot item 6 (70–90°C).
4. Heat to 80°C to 90°C, and mix until mixture swells and becomes translucent.
5. Cool to 50°C.
6. Check weight (theoretical weight, 58.00 g). If required, adjust with hot purified water. Record the quantity of extra water added.
7. Pass items 1 and 2 through sifter using 250 µm sieve.
8. Load it into a mixer (if required, grind item 1 through a 1 mm sieve).
9. Mix the powder for 15 minutes at high speed.

10. Add binding solution to the dry powder in the mixer, and mix for 15 minutes at high speed. Check for satisfactory wet mass.
11. Pass the wet mass through a Fitz mill using sieve 24207, knives forward, medium speed.
12. Collect and spread the granules onto the trays, one-third the thickness of the tray.
13. Load the trolleys into the oven, and dry the granules at 55°C for 36 hours.
14. After 12 hours of drying, stir the granules in the trays, and change the position of the trays for uniform drying.
15. Check the moisture of the dried granules. The limit NMT is 2.5%. Dry further if required to obtain moisture content of 2.5%.
16. Check the weight of dried granules (theoretical weight = 318.00 g).
17. Pass the dried granules through a 1.5 mm sieve using a granulator. Collect in a stainless steel drum, and add to the blender.
18. Pass items 4 and 5 through a 250 µm sieve using a sifter.
19. Add the sieved material to the granules in a blender, and mix for 5 minutes.
20. Compress 330 mg in 10 mm convex punches at 4 to 9 kp.
21. Coat the tablets using one of the PVP coating solutions provided in the Appendix, or use the sugar-coating formulation given here.

Bill of Materials: Sugar Coating

Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
7.06	1	Sandrac varnish (WMR)	7.06
3.33	2	Povidone (PVP K-25)	3.33
1.86	3	Povidone (PVP K-25)	1.86
175.85	4	Sucrose	175.85
0.16	5	Titanium dioxide	0.16
1.20	6	Polishing emulsion	1.20
1.33	7	Talc (fine powder)	1.33
—	8	Purified water	87.10

22. Load the tablets into the pan.
23. Start the tablets rolling with the exhaust on and air supply off.
24. Pour the item 1 solution onto the rolling tablets, and allow the tablets to roll, using hand agitation if required, permitting the solution to spread well over the tablet bed.
25. Permit the tablets to roll until tack develops, at which point item 7 should be quickly sprinkled over the tablets.
26. Allow to roll freely for 2 minutes at 45°C.
27. Do not roll too long, as the seal may be worn from the tablet edges.

28. After 2 minutes of rolling, jog the tablets every 1 minute over a period of 15 minutes with exhaust and drying air on at 45°C.
29. Continue jogging for a further 15 minutes. Jog every 3 minutes with exhaust and drying air temperature on at 45°C.
30. Dissolve 2.40 g of item 2 in 28.80 g of item 8.
31. Apply a half quantity of it to the tablets over 5 minutes. Allow to dry, and apply the remainder over a 15 minute period.
32. Heat 11.52 g of item 8 to boiling, dissolve 26.88 g of item 4, and cool down to 25°C.
33. Check weight (theoretical weight, 38.40 g). If lower, adjust weight to 38.40 g with purified water.
34. Apply sugar coat over a 30 minute period.
35. Dry the tablets in the coating pan at 30°C, jogging every 1 hour for 6 hours.
36. Heat 72 g of item 8 in mixer to boiling.
37. Dissolve 168 g of item 4, and then cool to 25°C.
38. Filter the syrup through a 180 µm stainless steel sieve.
39. Dissolve item 3 in 3.68 g of item 8.
40. Dissolve 4.53 g of item 4 in item 6.
41. Disperse item 5 in approximately 10.67 g of sugar syrup from the previous step, and homogenize.
42. Mix these steps with sugar syrup. Check for evenness of the dispersion.
43. Apply sugar coating.

Bill of Materials: Polishing Coat

Scale (mg/g)	Item	Material Name	Qty/kg (g)
28.75	1	Beeswax, bleached (white beeswax)	28.75
70.00	2	Polyethylene glycol (PEG-6000)	70.00
57.50	3	Carnauba wax	57.50
125.00	4	Talc (fine powder)	125.00
718.75	5	Ethanol, 95%	718.75

44. Melt items 1, 2, and 3 in a steam-heated vessel by gentle heating to 70°C or in a stainless steel container on a hotplate heater.
45. Add item 4 to the vessel or stainless steel container, and stir manually.
46. Add item 5 to the vessel or stainless steel container, and stir manually.
47. Pass the mixture through a homogenizer.
48. Store the polishing emulsion in a closed container at room temperature.
49. Apply gloss solution.
50. Add item 6 without air to the tablet bed carefully to get a uniform distribution while rolling.
51. After 5 minutes of distribution, turn on the cold air, and roll further until a shine appears.
52. Once the desired polish appears, stop rolling the pan.
53. Dry the tablets in the pan at 30°C for 30 minutes. Final tablet weight should be 480 mg.

INOSIN TABLETS

Bill of Materials			
Scale (g/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
200.00	1	Inosin (Ribaxin, Russia)	200.00
51.00	2	Lactose monohydrate	51.00
6.00	3	Kollidon® 90 F	6.00
QS	4	Isopropanol	60.00 mL
10.00	5	Kollidon® CL	10.00
3.00	6	Magnesium stearate	3.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 3 with the solvent mixture of item 4.
2. Dry and pass through a 0.8 mm sieve, add items 5 and 6, and press with low compression force.
3. Compress 270 mg in 9 mm biconvex punches.

INSECT BITE CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
180.00	1	Trilaneth-4 phosphate, glyceryl stearate, and PEG-2 stearate	180.00
20.00	2	Hydrogenated palm/kernel oil PEG-6 esters	20.00
80.00	3	Mineral oil	80.00
0.30	4	Sodium methylparaben	0.30
0.70	5	Sorbic acid	0.70
646.70	6	Deionized water	646.70
10.00	7	Benzocaine	10.00
10.00	8	Butamben	10.00
2.00	9	Menthol	2.00
0.30	10	Resorcinol	0.30
50.00	11	Ethoxydiglycol	50.00

MANUFACTURING DIRECTIONS

1. Dissolve items 7 to 10 in item 11.
2. Mix and heat items 1 to 6 to 75°C.
3. Allow to cool slowly with constant stirring.
4. At 35°C, add this to previous mixture.
5. Homogenize if necessary.

IRON INFANT DROPS

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
0.18	1	Propylparaben	0.18
0.022	2	Methylparaben	0.02
1000.00	3	Sorbitol solution	1.00 kg
4.00	4	Citric acid (hydrous powder)	4.00
125.00	5	Iron sulfate	125.00
0.106	6	Sodium metabisulfite	0.10
0.50	7	Guarana flavor (artificial)	0.50
20.00	8	Alcohol (ethanol)	20.00
0.14	9	Dye	0.14
QS	10	Sodium hydroxide	QS
QS	11	Citric acid (powder)	QS
QS	12	Purified water	QS to 1 L
QS	13	HyFlo filter aid	1.00
QS	14	Liquid nitrogen	QS
QS	15	Carbon dioxide gas	QS

MANUFACTURING DIRECTIONS

The product is susceptible to oxidation. No effort should be spared to protect it from atmospheric air. Maintain carbon dioxide (CO₂) or nitrogen atmosphere where indicated. The product must be manufactured and held in a glass-lined or stainless steel tank. Product waiting to be filled should be either in a closed tank with a CO₂ atmosphere or in an open tank covered with polyethylene sheeting taped tightly with a constant slow stream of CO₂ gas flowing into the tank head-space. Avoid vortex formation throughout processing.

1. Place 144 mL of purified water into a mixing tank.
2. Heat to 95°C to 100°C, and add parabens with strong agitation.
3. Add sorbitol solution and citric acid (item 4) while mixing.
4. Bring solution to 90°C while mixing.
5. Cool the solution while mixing to 60 °C to 65 °C, and hold at this temperature with CO₂ or nitrogen gas bubbling into it.
6. CO₂ gas protection is continued for the remainder of the manufacturing process.
7. Add ferrous sulfate and dissolve while mixing, holding at 60°C to 65°C.
8. Cool to 25°C with mixing.
9. Add sodium metabisulfite, and dissolve while mixing.
10. Avoid vortex formation.
11. Dissolve dye in 2 mL of freshly boiled purified water, and add to the tank. Mix.

12. Dissolve the guarana flavor in alcohol, add to the tank, and mix.
13. Check pH (range: 1.8–2.2). Adjust if necessary with a solution of 10% sodium hydroxide or a solution of 10% citric acid.
14. Make up to volume with freshly boiled purified water, and mix.
15. Readjust to volume if necessary with freshly boiled purified water, and mix.
16. Add HyFlo filter aid, and mix. Filter through press until clear.
17. Bubble CO₂ or nitrogen gas into the clear filtrate for 5 minutes; then, seal tank, and hold product under CO₂ or nitrogen protection.

IRON (POLYMER-COATED PARTICLE) TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Elemental iron; use ferrous sulfate polymer-coated particles (233 mg iron per gram ferrous sulfate)	450.60
200.00	2	Cellulose microcrystalline	200.00
254.40	3	Lactose monohydrate	254.40
36.00	4	Sodium starch glycolate	36.00
9.00	5	Magnesium stearate	9.00

Note: Factor in potency of ferrous sulfate polymer-coated particles. Adjust with item 3. Item 1 is prepared by first granulating ferrous sulfate using alcohol and water, drying, and sieving particles over 1200 μ m in size. Regranulate smaller particles. Apply enteric (HPMC) coating to the granules in a fluid-bed dryer.

MANUFACTURING DIRECTIONS

1. Load a suitable mixer/blender with microcrystalline cellulose, and disperse the ferrous sulfate polymer-coated powder.
2. To this mix, add about half the lactose (item 3), and blend for 5 minutes.
3. Pass the sodium starch glycolate through a 500 μ m sieve followed by about half of the remaining lactose.
4. Add to the mix.
5. Blend for further 5 minutes.
6. Pass the magnesium stearate (item 5) through a 500 μ m sieve followed by the remaining lactose.
7. Add to the previous mix.
8. Blend for further 5 minutes.
9. Compress 950 mg per tablet at 8 to 14 kpi using 8 mm $\times$ 16 mm punches. Do not rework tablets.
10. Coat the tablets using a HPMC coating solution (see Appendix).

IRON POLYSTYRENE AND VITAMIN C SYRUP

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
125.00	1	Glycerin	125.00
1.40	2	Methylparaben	1.40
0.16	3	Propylparaben	0.16
79.61	4	Sorbitol; use sorbitol solution	364.33
3.30	5	Xanthan gum	3.30
10.00	6	Sucrose (granulated)	10.00
0.20	7	Saccharin (insoluble)	0.200
105.00	8	Elemental iron; use iron polystyrene sulfonate	530.31
50.00	9	Ascorbic acid, USP (35% excess)	61.95
0.10	10	Flavor	1.00 mL
0.10	11	Flavor (artificial guarana)	1.00 mL
QS	12	Sodium hydroxide	12.00
QS	13	Dye	2.00
9.50	14	Distilled purified water	~95.00 mL
10.00	15	Sorbitol solution	~10.00

MANUFACTURING DIRECTIONS

1. Add glycerin (item 1) to the tank.
2. Commence heating with agitation.
3. Add and disperse parabens.
4. Continue heating to 70°C to 80°C, and mix until solution is complete.
5. Force cool to 30°C; then, add and disperse xanthan gum (item 5).
6. Add sorbitol solution (item 4) and 80 mL of purified water (item 14), and heat with mixing to 60°C to 70°C until the xanthan gum is fully dissolved.
7. Add and disperse saccharin and sugar (items 6 and 7).
8. Mix at 60°C to 70°C until dispersion is complete.
9. Force cool to 25°C to 30°C with continuous mixing.
10. Commence N₂ gas protection, and maintain for the remainder of the manufacturing process.
11. Add and disperse ascorbic acid.
12. Continue mixing for 30 minutes at 25°C to 30°C.
13. *Note:* Use suitable stainless steel high-powered stirrer.
14. Mix the iron polystyrene sulfonate milled slurry in the original epoxy-lined drums under N₂ gas protection until uniform.
15. Add the slurry to the main batch, and mix for 30 minutes at 25°C to 30°C.
16. *Note:* Avoid scraping the epoxy lining of the steel drum while mixing, and use a plastic or rubber scraper to assist in complete transfer of the mixed slurry.) Add and disperse the flavors. Mix well.
17. Check and record pH. Adjust pH using a 20% sodium hydroxide solution (1 g in 5 mL water) to a value of 3 (range: 2.8–3.2).

18. Dissolve the dye in 5 to 7 mL of water at 40°C to 45°C by stirring for 10 minutes.
19. Add this solution to the main batch through a 420 μm screen with mixing.
20. Rinse container with 2 to 3 mL water at 40°C to 45°C, and add to bulk through a 420 μm screen.
21. Continue to mix under vacuum until mixture is uniform.
22. Pass the suspension through the colloid mill at a gap setting of 100 to 150 μm .
23. Adjust the flow rate such that the temperature rise of the suspension does not exceed 10°C.
24. Collect the milled suspension in a stainless steel jacketed tank with vacuum.
25. Mix at 25°C to 30°C under vacuum until a uniform suspension is achieved.
26. Flush the bulk suspension with nitrogen, and seal.
27. Hold at 25°C to 30°C.

KAOLIN-PECTIN SUSPENSION

Bill of Materials			
Scale (mg/ 5 mL)	Item	Material Name	Qty/L (g)
5.40	1	Sodium methylparaben	4.92
0.6	2	Sodium propylparaben	1.08
36.00	3	Magnesium aluminum silicate type IA	0.11
5832.00	4	Kaolin (powder)	194.40
130.00	5	Pectin	4.33
120.00	6	Sodium CMC (premium, low-viscosity)	4.00
210.00	7	Cyclamate calcium	7.00
21.00	8	Saccharin calcium (powder)	0.70
15.375	9	Flavor	0.51
1.234	10	Flavor	41.13
QS	11	Distilled purified water (approx.)	QS
QS	12	Citric acid (anhydrous powder)	QS

MANUFACTURING DIRECTIONS

1. Charge 600 mL of water into a suitable jacketed mixing tank.
2. Add the methylparaben and propylparaben to the tank, and heat to 90°C to 95°C.
3. Cool to 70°C, add the magnesium aluminum silicate, and mix for 30 minutes or until evenly dispersed.
4. Hold temperature at 70°C.
5. Add kaolin with constant mixing at 70°C until evenly dispersed.
6. Add pectin and mix for 2 hours, maintaining a temperature of 70°C.
7. Add the premium, low-viscosity sodium CMC, and mix for at least 30 minutes, maintaining a temperature of 70°C.

8. Cool to 60°C, and hold at this temperature.
9. Add, in order, the cyclamate calcium and saccharin calcium, and mix thoroughly for 20 minutes.
10. While mixing, cool to room temperature, and allow to stand overnight to hydrate.
11. After overnight standing (minimum 12 hours), mix for 30 minutes.
12. Add flavors while mixing.
13. Check and record pH (range: 4.5–7.5). If pH is more than 7.5, adjust with a 60% solution of citric acid to the desired pH.
14. Add water to 1 L, and mix thoroughly for 3 hours.
15. Strain product through muslin cloth into holding tanks, and cover.

KAOLIN-PECTIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
QS	1	Distilled purified water	300 mL
50.00	2	Cornstarch	50.00
50.00	3	Povidone (K-29-32)	50.00
QS	4	Distilled purified water	0.50 L
630.00	5	Hydrated aluminum–magnesium silicate	630.00
100.00	6	Kaolin (powder)	100.00
50.00	7	Pectin	50.00
80.00	8	Cornstarch	80.00
80.00	9	Sodium lauryl sulfate	80.00
10.00	10	Magnesium stearate	10.00

MANUFACTURING DIRECTIONS

1. Heat purified water (item 1) to 75°C to 80°C, and add cornstarch (item 2) with continuous stirring until a translucent paste is formed. Use this paste within 1 hour.
2. Dissolve povidone in purified water (item 4) in a separate container. Ensure that dissolution is complete.
3. Charge the following into a suitable planetary mixer: hydrated aluminum–magnesium silicate, kaolin, and pectin.
4. Mix for 5 minutes.
5. Add freshly prepared starch paste from the first step and the povidone solution to the powder blend from the third step. Mix until a mass of suitable consistency is obtained.
6. Add extra-purified water, if needed.
7. Spread the wet mass on paper-lined trays, and dry in the oven at 50°C for 2 hours.
8. Pass the semidried mass through a 4.8 mm (4 mesh) screen by hand or by using a suitable granulator, and load the granule mass onto paper-lined trays.

9. Dry in the oven at 50°C until the moisture content is between 10% and 15%.
10. Pass the dried granules through a 1 mm (18 mesh) screen on a comminuting mill at medium speed, knives forward, into clean, tared, polyethylene-lined drums. Seal and weigh.
11. Transfer the dried granules to a suitable blender.
12. Screen the following items through a 595 µm (30 mesh) screen, and add to the blender: cornstarch (item 8), sodium lauryl sulfate, and magnesium stearate.
13. Blend for 5 to 10 minutes.
14. Compress on a suitable compression machine using 1/2 in. round standard concave punches, upper punch with logo, and lower punch with a bisect line.
15. Compress 977 mg at 10 to 18 kpi.
16. Coat using an aqueous Methocel™ coating, and polish as desired.

KERATOLYTIC CREAM

Bill of Materials			
Scale (mg/10 g)	Item	Material Name	Qty/kg (g)
150.00	1	Polawax (self-emulsifying wax)	15.00
150.00	2	PPG-2 myristyl ether propionate (Crodamol PMP)	15.00
50.00	3	Sorbitol isostearate	5.00
35.00	4	Safflower oil, super-refined	3.50
20.00	5	Avocado oil, super-refined	2.00
20.00	6	Cetyl palmitate	2.00
50.00	7	Salicylic acid	5.00
1.50	8	Propylparaben	0.15
1.00	9	Butylated hydroxyl anisole	0.10
487.50	10	Deionized water	48.75
10.00	11	Sodium borate	1.00
3.00	12	Methylparaben	0.30
2.00	13	Imidazolidinyl urea	0.20
20.00	14	Hydrolyzed collagen + hyaluronic acid (Cromoist HTA)	2.00

MANUFACTURING DIRECTIONS

1. Dissolve item 7 in item 2 with mixing and heating to 70°C.
2. Add balance of items 1 to 9, and mix with heat to 80°C. Add items 10 to 13 together in a separate container, and heat to 80°C.
3. Add this mixture to the first mixture with mixing, and cool to 40°C.
4. Add item 14 with mixing, and cool to the desired fill temperature.
5. Adjust pH if necessary to 3 to 4 with 10% triethanolamine solution.

KHELLIN TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
25.00	1	Khellin	25.00
124.00	2	Ludipress®	124.00
1.00	3	Magnesium stearate	1.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix intensively, and press.
2. Compress 150 mg in 8 mm biplanar punches.

LIDOCAINE GEL

Bill of Materials			
Scale (mg/10 g)	Item	Material Name	Qty/kg (g)
20.00	1	Lidocaine hydrochloride	2.00
560.00	2	Water	56.00
200.00	3	Propylene glycol (pharma)	20.00
220.00	4	Lutrol F 127	22.00

MANUFACTURING DIRECTIONS

1. Prepare solution of items 1 to 3 at room temperature, heat to 70°C or cool to 6°C, and slowly add item 4 to the well. Stir solution until it is dissolved.
2. Maintain the temperature until the air bubbles escape to obtain a clear, colorless gel.

LIDOCAINE GEL CREAM

Bill of Materials			
Scale (mg/10 g)	Item	Material Name	Qty/kg (g)
50.00	1	Lidocaine hydrochloride	5.00
500.00	2	Water	50.00
150.00	3	Propylene glycol (pharma)	15.00
100.00	4	Liquid paraffin	10.00
200.00	5	Lutrol F 127	20.00

MANUFACTURING DIRECTIONS

1. Prepare solution of items 1 to 3 at room temperature, and mix with item 4.
2. Heat to 70°C or cool to 6°C, and slowly add item 5 to the well. Stir solution until it is dissolved.
3. Maintain the temperature until the air bubbles escape.

LIDOCAINE OINTMENT

Bill of Materials			
Scale (g/ 100 g)	Item	Material Name	Qty/kg (g)
5.00	1	Lidocaine base	50.00
28.00	2	PEG-3350	280.00
40.00	3	PEG-400	400.00
25.00	4	Propylene glycol	250.00
2.00	5	Purified water	20.00

MANUFACTURING DIRECTIONS

1. Load items 2 and 3 into a fat-melting vessel.
2. Heat to 70°C.
3. Cool to 40°C while stirring at slow speed (10–12 rpm).
4. Maintain the temperature between 40°C and 45°C under continuous stirring.
5. Heat 200 g of item 4 to 40°C to 45°C in a stainless steel container.
6. Dissolve item 1 by stirring with stirrer.
7. Add item 5 under continuous stirring.
8. Maintain the temperature between 40°C and 45°C under continuous stirring.
9. Filter through cloth filter.
10. Transfer the drug solution into a mixer previously set with a temperature of 40°C to 45°C.
11. Rinse the stainless steel container with 50 g of item 4.
12. Add the rinsings into the mixer.
13. Transfer the molten mass from the fat-melting vessel at 40 °C through a stainless steel filter to the mixer containing the drug solution while mixing at 10 to 12 rpm.
14. When the transfer is over, start the homogenizer at low speed with a vacuum of 0.6 bar and stirrer speed of 10 rpm (manual mode).
15. Mix and homogenize for 10 minutes with recirculation.
16. Maintain temperature at 40°C to 45°C.
17. Stop the homogenizer, and set the mixer at temperature 25°C and stirrer speed at 10 rpm (manual mode).
18. Cool the cream to 25°C.
19. When the ointment is cooled to 25°C, unload the ointment into a stainless steel container.

LIDOCAINE, EUGENOL, AND MENTHOL DENTAL OINTMENT

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
55.20	1	Beeswax (white, slabs)	55.20
150.00	2	Anhydrous lanolin (regular)	150.00
723.70	3	Petrolatum (white, regular)	723.70
40.00	4	Lidocaine base	40.00
1.20	5	Saccharin sodium (powder)	1.20
QS	6	Deionized, purified water	3.00 mL
1.00	7	Eugenol	1.00
5.00	8	Menthol (crystals)	5.00
0.80	9	Peppermint oil	0.80
20.16	10	Metaphen ointment base	20.16

MANUFACTURING DIRECTIONS

1. Melt beeswax, lanolin, and petrolatum together at 70°C to 80°C, and strain into a suitable container.
2. Do not heat above 70°C to 80°C.
3. Mix together.
4. Melt lidocaine base, and strain into the container while mixing.
5. Dissolve the sodium saccharin in purified water heated to 70°C.
6. Add to the container while mixing.
7. Cool down to 45°C to 50°C while mixing.
8. Mix the eugenol, menthol, and peppermint oil together, and liquefy.
9. Warm gently to 35°C to 40°C if necessary.
10. Strain into the container while mixing.
11. Gently melt metaphen ointment base, and strain into the container while mixing.
12. Mix thoroughly until congealed.

LOPERAMIDE HYDROCHLORIDE FAST-MELT TABLET**MANUFACTURING DIRECTIONS**

1. Prepare granules by using loperamide hydrochloride, 5%; sodium bicarbonate, 27%; citric acid anhydrous, 27%; tartaric acid, 3%; microcrystalline cellulose, 15%; anhydrous lactose, 8%; xylitol, 12%; and Crodesta F160, 3%.
2. Dry the ingredients at elevated temperature in the presence of a desiccant to significantly reduce the moisture content of each material.

- Blend the ingredients for 10 minutes and extrude in a hot melt extruder at 70°C to 100°C to soften and melt the thermal binders (sucrose stearate and xylitol) to form granules containing the effervescent ingredients.
- Pass the granules through a screen and then blend with the following ingredients: LH-EFG (30–80 mesh), 50%; microcrystalline cellulose, 31%; mannitol, 8%; Ac-Di-Sol, 5%; L-HPC LH-11, 2%; aspartame, 3%; redberry flavor, 0.4%; magnesium stearate, 0.5%; Cab-o-Sil M5P, 0.1%. These are mixed for 5 minutes prior to compression.
- Compress loperamide FICI tablets to a hardness of approximately 1 to 3 kg and tablets disintegrate in purified water in approximately 15 to 35 seconds.

LORATADINE AND PSEUDOEPHEDRINE SULFATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
25.00	1	Loratadine	25.00
180.00	2	Pseudoephedrine sulfate	180.00
5.00	3	PVP	5.00
75.00	4	Low-substituted hydroxypropyl cellulose	75.00
75.00	5	Crospovidone	75.00
1.50	6	Colloidal silicon dioxide	1.50
25.00	7	Microcrystalline cellulose	25.00
250.00	8	Crystalline sugar seeds	250.00
120.00	9	Purified water	120.00

MANUFACTURING DIRECTIONS

- Prepare a binder solution by dissolving 5 g of PVP in 120 g of water.
- Mix and screen 25 g of loratadine, 180 g of pseudoephedrine sulfate, 25 g of microcrystalline cellulose, 75 g of low-substituted hydroxypropyl cellulose, 75 g of crospovidone, and 1.5 g of colloidal silicon dioxide through a 20 mesh sieve to give a mixed powder.
- Spray the binder solution of step 1 onto 250 g of crystalline sugar seeds in a centrifugal granulator, and dust the mixed powder onto the crystalline sugar seeds in the centrifugal granulator to afford pellets using the rotation panel rate of 140 to 200 rpm, the spraying rate of the binder solution of 2 to 20 mL/min, air spraying pressure of 1 to 2 kg/cm², air spraying volume of 5 to 300 L/min, and powder (step 2) spraying rate of 5 to 30 g/min.

LORATADINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
10.00	1	Loratadine	10.00
69.93	2	Pregelatinized starch	69.93
69.63	3	Microcrystalline cellulose	69.63
0.37	4	Colloidal silicon dioxide	0.37
0.25	5	Magnesium stearate	0.25

MANUFACTURING DIRECTIONS

- Use a multistep blending process to ensure proper distribution of the active. Initially, combine half of the pregelatinized starch with the drug and colloidal silicon dioxide.
- Blend this mixture in a twin-shell V-blender for 5 minutes.
- Discharge the mixture and pass through a 40 mesh screen by hand.
- This step not only breaks up the silicon dioxide but also helps to distribute the active.
- Return the screened mixture to the blender, and add the remainder of the Starch 1500 and blend for an additional 5 minutes.
- Add the MCC and blend for 10 minutes.
- Add the magnesium stearate last and blend for 5 minutes.
- Pass the magnesium stearate through a 60 mesh screen prior to weighing.
- Compress tablets at 100 mg or proportionally for different strengths.

LORATADINE FASTAB

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
10.00	1	Loratadine (micronized)	10.00
180.60	2	Pharmaburst	180.60
2.70	3	Acesulfame K	2.70
2.00	4	Magnesium stearate	2.00
2.00	5	Talc (fine powder)	2.00
2.70	6	Dry anise flavor	2.70

MANUFACTURING DIRECTIONS

- Sift and mix items 1, 2, 3, and 6.
- Lubricate with magnesium stearate and fine talc powder.
- Compress 200 mg in 6 mm punches.

LORATADINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
10.00	1	Loratadine	10.00
67.30	2	Lactose monohydrate	67.30
22.00	3	Maize starch	22.00
10.00	4	Maize starch	10.00
5.00	5	Maize starch, dried	5.00
0.70	6	Magnesium stearate	0.70
QS	7	Purified water	QS

MANUFACTURING DIRECTIONS

1. Sift items 1 to 3 through a 630 μm stainless steel sieve, load in mixer, and mix for 5 minutes.
2. In a separate container, prepare binder solution by mixing item 4 using purified water at 30°C to 40°C, heat translucent slurry to 90°C to 95°C, and cool to 45°C to 50°C.
3. Mix the binder solution with the first step and granulate, dry on trays at 55 °C for 8 hours, and dry to LOD of 2% to 3% (2 hours after beginning drying, crush mixture for uniform drying).
4. Heat additional 1 hour at 55°C if LOD is not within limits.
5. Add magnesium stearate, tumble mix, and compress using 7 mm round punches to 10-tablet weight of 1.15 (within 3%) to achieve thickness of 2.3 ± 0.3 mm and hardness of 4 to 7 kp.

LYCOPENE TABLET CORES (6 MG)**FORMULATION**

Lycovit 10% dry powder, 60 g; Ludipress®, 330 g; Kollidon® CL, 6 g; magnesium stearate, 4 g.

MANUFACTURING DIRECTIONS

1. Mix the Lycovit dry powder with the other components.
2. Sieve through a 0.8 mm screen, and press with medium to high compression force at 400 mg.

MAGALDRATE CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Magaldrate, USP	500.00
400.00	2	Lactose monohydrate	400.00
50.00	3	Orange flavor (FDO)	50.00
20.00	4	Kollidon® 90 F	20.00
6.00	5	Banana flavor (FDO)	6.00
6.00	6	Cocoa flavor (FDO)	6.00
1.00	7	Saccharin sodium	1.00
180.00	8	Water	180.00
5.00	9	Aerosil® 200	5.00
3.00	10	Magnesium stearate	3.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 3 with solution of items 4 to 8, pass through a 0.8 mm sieve, dry, mix with items 9 and 10, and press with low compression force.
2. Compress 1 g in 16 mm biplanar punches.

MAGALDRATE CHEWABLE TABLETS (500 MG)**FORMULATION**

1. Magaldrate USP, 500 g; lactose monohydrate, 400 g; orange flavor (FDO), 50 g.
2. Kollidon® 90 F, 20 g; banana flavor (FDO), 6 g; cocoa flavor (FDO), 6 g; saccharin sodium, 1 g; water, 180 g.
3. Aerosil® 200, 5 g; magnesium stearate, 3 g.

MANUFACTURING DIRECTIONS

1. Wet granulation: Granulate mixture 1 with solution 2, pass through a 0.8 mm sieve, dry, mix with 3, and press with low compression force at 1000 mg.

MAGALDRATE CHEWABLE TABLETS (1000 MG)**FORMULATION**

Magaldrate (Reheis), 1000 g; Ludipress® LCE, 930 g; Lutrol E4000F, 60 g; aspartame, potassium (Searle), 10 g; peppermint flavor, QS.

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with medium compression force at 2 g.

MAGALDRATE DISPERSIBLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
700.00	1	Magaldrate	700.00
435.00	2	Lactose monohydrate	435.00
10.00	3	Kollidon® 90 F	10.00
50.00	4	Kollidon® CL	50.00
5.00	5	Magnesium stearate	5.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8-mm sieve, mix, and press with low compression force (4–6 kN).
2. Compress 1.2 g in 16 mm biplanar punches.

**MAGALDRATE INSTANT
POWDER OR DRY SYRUP**

Bill of Materials			
Scale (mg/ Sachet)	Item	Material Name	Qty/1000 Sachets (g)
800.00	1	Magaldrate, USP	800.00
640.00	2	Kollidon® CL-M	640.00
200.00	3	Sorbitol (crystalline)	200.00
40.00	4	Orange flavor	40.00
40.00	5	Kollidon® 90 F	40.00
4.00	6	Coconut flavor	4.00
4.00	7	Banana flavor	4.00
0.80	8	Saccharin sodium	0.80
QS	9	Water	~280.00 mL

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 4 with solution of items 5 to 9, and pass through a 0.8 mm sieve to obtain free-flowing granules.
2. Fill 2 g in sachets or 20 g in a 100 mL flask.
3. Instant granules in sachets: suspend 2 g (= one sachet) in a glass of water (= 800 mg magaldrate).

MAGALDRATE SUSPENSION

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
100.00	1	Magaldrate USP	100.00
80.00	2	Kollidon® CL-M	80.00
20.00	3	Kollidon® 90 F	20.00
10.00	4	Orange flavor	10.00
0.50	5	Coconut flavor	0.50
0.80	6	Banana flavor	0.80
0.20	7	Saccharin sodium	0.20
QS	8	Preservatives	QS
QS	9	Water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Dissolve or suspend all the solids in water under aseptic conditions; pH should be approximately 9.

MAGALDRATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
400.00	1	Magaldrate (powder, 100 mesh)	400.00
325.00	2	Sucrose	325.00
60.00	3	Cellulose (microcrystalline) (Avicel™ PH101)	60.00
30.00	4	Cornstarch	30.00
8.84	5	Guar gum	8.84
0.50	6	Saccharin sodium	0.50
–	7	Purified water	100.00 mL
–	8	Alcohol SD 3A (200 proof)	100.00 mL
QS	9	Flavor	0.60 mL
QS	10	Flavor	1.00 mL
0.06	11	Ethyl vanillin	0.06
8.00	12	Talc	8.00
16.00	13	Magnesium stearate	16.00

MANUFACTURING DIRECTIONS

1. Pass granulated sugar (take approximately 10% excess) through 500 µm stainless steel screen on comminuting mill (impact forward, high speed).
2. Screen the milled sugar through 250 µm aperture on sieve shaker.
3. Weigh the required quantity, and charge into a suitable mixer.
4. Discard remaining sugar.
5. Screen magaldrate powder (take approximately 5% excess) through 150 µm stainless steel screen on sieve shaker.

6. Weigh the required quantity, and add to the previous blend.
7. Mix well.
8. Screen, if necessary, microcrystalline cellulose, cornstarch, and guar gum through 500 μm aperture on sieve shaker.
9. Add to the first step, and mix well.
10. Dissolve saccharin sodium in water.
11. To this, add alcohol, and mix well.
12. Add this hydroalcoholic solution to magaldrate blend, and knead well.
13. Add more water, if necessary, and QS to mass.
14. Pass wet mass through 2.8 mm aperture on sieve shaker or oscillating granulator, and spread uniformly on stainless steel trays.
15. Tray dry granules at 70°C to 75°C.
16. After 3 to 4 hours of drying, screen semidried granules through 1.4 mm aperture on sieve shaker, and reload for further drying.
17. (This step helps in drying granules faster and more uniformly.) Dry to LOD of 1% to 1.5%.
18. Screen dry granules through 1 mm aperture on sieve shaker and store in drums doubly lined with polyethylene bags.
19. Charge half of the granulation into a suitable blender.
20. From the balance of the granules, take out the fines (approximately 40 g of fines for a batch of 1000 tablets) through 250 μm aperture on sieve shaker.
21. Retain coarse particles for later use.
22. Mix together the flavors in a suitable vessel.
23. Add and dissolve the ethyl vanillin.
24. Check that the solution is clear before proceeding.
25. Charge a suitable mixer with the fines from step 20.
26. While mixing, disperse the flavor solution.
27. Add magnesium stearate and talc, and mix thoroughly.
28. Pass the blend through a 250 μm aperture on sieve shaker.
29. Add the dispersed flavor blend to the granules.
30. Add remaining granules, and blend for 8 to 10 minutes.
31. Discharge blended granules into suitable airtight containers doubly lined with polyethylene bags.
32. Compress on a suitable machine fitted with 14.4 mm diameter round punches with beveled edges.
33. Weight: 8.5 g/10 tablets, thickness: approximately 3.6 to 3.8 mm, hardness: 8 to 10 kPa.

MAGALDRATE WITH SIMETHICONE SUSPENSION

Bill of Materials			
Scale (mg/5 mL)	Item	Material Name	Qty/L (g)
QS	1	Distilled purified water	285.00 mL
9.00	2	Methylparaben	1.80
1.00	3	Propylparaben	0.20
5.00	4	Benzoic acid	1.00
3.75	5	Saccharin sodium (dehydrate powder)	0.75
400.00	6	Magaldrate (wet cake; 18–20%)	400.00
1.00 g	7	Sorbitol solution (70%)	260.00
12.50	8	Silicon dioxide (colloidal) (international)	2.50
QS	9	Citric acid (hydrous powder)	QS
200.00	10	Dimethyl polysiloxane emulsion (30%)	40.00
0.005 mL	11	Flavor	1.00 mL
1.26 g	12	Glycerin	252.00
25.00 g	13	Potassium citrate monohydrate	5.00
13.30	14	Xanthan gum	2.66

MANUFACTURING DIRECTIONS

This product is highly prone to microbial contamination. All equipment coming into contact with the product should be treated with a freshly prepared sodium hypochlorite solution (100 ppm) made with freshly boiled and cooled-down water on the day of use. Bottles and caps should also be so treated. Freshly boiled and cooled deionized water should be used for rinsing.

1. Place 285 mL purified water into a suitable jacketed tank, and heat to 90°C to 95°C.
2. Add and dissolve parabens, benzoic acid, saccharin sodium, and potassium citrate.
3. While maintaining temperature at 85°C to 90°C, add, in small quantities, half the quantity of magaldrate cake or powder, if used, and disperse well.
4. (Adjust speed of the agitator and homogenizer to ensure effective mixing and to maintain free mobility of the suspension.) Add sorbitol solution, and mix well.
5. Raise the temperature, if necessary, maintaining temperature at 85°C to 90°C.
6. Add, in small quantities, the remaining half of the magaldrate cake or powder, and disperse well.
7. Mix for 1 hour, and then remove heat. (Adjust speed of the agitator and homogenizer to maintain the mobility of suspension.) Separately blend colloidal silicon dioxide with xanthan gum, and disperse the blend in glycerin with constant mixing.

8. While maintaining temperature at 85°C to 95°C, add and disperse the suspension from the previous step to the main tank, and mix well.
9. Avoid lump formation at any stage.
10. Cool to room temperature.
11. Add dimethyl polysiloxane emulsion, and mix well.
12. Add flavor, and mix well.
13. Dissolve citric acid in twice the quantity of purified water, and adjust pH if necessary.
14. Check and record pH (range: 7.5–8.0). Add purified water to volume, and mix well for a minimum of 30 minutes.
15. Filter through a 180 µm aperture nylon cloth, and store in a suitable tank.

MAGALDRATE WITH SIMETHICONE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
525.00	1	Sucrose, NF	525.00
15.00	2	Lactose monohydrate, NF	15.00
60.00	3	Simethicone, USP	60.00
60.00	4	Cellulose microcrystalline (Avicel™ PH101), NF	60.00
12.00	5	Silicon dioxide colloidal (International)	12.00
400.00	6	Magaldrate, USP	400.00
40.00	7	Acacia (special grade), NF	40.00
0.05	8	Dye	0.05
–	9	Distilled purified water, USP	100.00 mL
–	10	Alcohol SD 3A (200 proof)	100.00 mL
1.50	11	Flavor	1.50
0.15	12	Ethyl vanillin, NF	0.15
5.00	13	Silicon dioxide (colloidal)	5.00
30.00	14	Starch monohydrate	30.00
10.00	15	Lactose monohydrate	10.00
80.00	16	Talc powder, USP	80.00
5.30	17	Magnesium stearate	5.30

MANUFACTURING DIRECTIONS

1. Pass the granulated sucrose (with approximately 10% excess) through a 500 µm aperture stainless steel screen on comminuting mill (impact forward, high speed).
2. Screen the milled sugar through a 250 µm screen on sieve shaker.
3. Weigh the required quantity, and charge into a suitable mixer (planetary mixer or dough mixer). Discard the remainder.
4. Screen lactose (item 2) through a 250 µm aperture screen on sieve shaker, and add to powdered sugar from preceding step. Mix well.
5. While mixing vigorously, add and disperse simethicone (add slowly in a fine stream of flow to avoid lump formation). Mix well.

6. Rough blend colloidal silicon dioxide (item 5) and microcrystalline cellulose, and add to the simethicone dispersed mass from previous step.
7. Mix initially at low speed for 4 to 5 minutes, and thereafter, mix vigorously for 5 to 10 minutes.
8. Either screen simethicone dispersed mass through a 1.0 mm aperture on sieve shaker or pass through a comminuting mill using a 1.4 mm aperture screen (impact forward, medium speed).
9. Load into a mass mixer, and continue mixing.
10. Screen magaldrate powder (with approximately 7% excess) through a 150 µm aperture screen on sieve shaker, and weigh the required quantity.
11. To this quantity, add acacia, and rough blend.
12. Add this blend in the dough mixer, dispersing in small quantities, and mix well for 30 to 40 minutes until simethicone is well absorbed in the dry blend. Discard remaining magaldrate powder.
13. Dissolve dye in water; then, add alcohol, and mix well.
14. Wet down mass with colored hydroalcoholic solution, and knead well.
15. Add more hydroalcoholic solution, if necessary (water : alcohol, 1:1), to mass.
16. Screen wet mass through a 2.8 mm aperture screen on sieve shaker or oscillating granulator, and spread uniformly on trays.
17. Tray dry granules at 71°C to 74°C until LOD is within 1% to 1.5% (test at 105°C for 1 hour).
18. After approximately 3 to 4 hours of drying, screen semidried granules through a 1.4 mm aperture on sieve shaker, and reload for further drying.
19. (*Note:* This step helps in drying granules faster and more uniformly and avoids color mottling on final product.) Screen dried granules through a 1.0 mm aperture screen on sieve shaker, and store in drums lined with double polyethylene bags. Alternatively, drying can be done in a fluid-bed dryer.
20. Pass dried granules through a 1 mm aperture screen on sieve shaker.
21. Pass coarse granules through a comminuting mill using a 1.4 mm aperture screen (knives forward, slow speed) and then through 1.0 mm aperture on sieve shaker.
22. Store granules in drums lined with double polyethylene bags.
23. Charge half of the base granulation into a suitable blender.
24. From the balance of the granules, take out fines (approximately 50 g of fines for a batch of 1000 tablets) through a 250 µm aperture on sieve shaker, and hold in a suitable vessel.
25. Add and dissolve ethyl vanillin in liquid flavor.
26. Check for clarity, and only then disperse over dried starch.
27. Rough blend colloidal silicon dioxide (item 13) with lactose monohydrate (item 15), talc, and magnesium stearate, and add to the flavored starch.

28. To this mixture, add fines from step 24 and mix well by hand or in a suitable mixer.,
29. Screen through a 250 µm aperture on sieve shaker.
30. Add this flavored, dispersed blend to the base granulation (first step) in a blender.
31. Add the remaining bulk granules from the second step to the base granulation, and blend well for 8 to 10 minutes. (*Caution:* Do not mix for too long, as the granules may crumble to a finer size, which may adversely affect hardness during compression.) Discharge blended granules into suitable airtight containers lined with double polyethylene bags until ready for compressing.
32. Compress on a suitable machine fitted with 14.4 mm diameter round punches with beveled edges. Compress 1244 mg per tablet.

MAGNESIUM CARBONATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
260.00	1	Magnesium carbonate, USP	262.00
238.00	2	Ludipress®	238.00
4.00	3	Magnesium stearate	4.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with medium compression force.
2. Compress 500 mg in 12 mm biplanar punches.

MEDICATED FOOT CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
5.00	1	Lanolin	5.00
90.00	2	Stearic acid	90.00
5.00	3	Cetyl alcohol	5.00
40.00	4	Isopropyl palmitate	40.00
10.00	5	Oleyl alcohol	10.00
20.00	6	Mineral oil and lanolin alcohol (liquid base CB3929)	20.00
7.50	7	Oil of wintergreen	7.50
3.00	8	Oil of thyme	3.00
5.00	9	Oil of pine	5.00
5.00	10	Menthol	5.00
5.00	11	Camphor	5.00
QS	12	Deionized water	QS to 1 kg
80.00	13	Glycerin	80.00
18.00	14	Triethanolamine 99%	18.00
QS	15	Preservative, color	QS

MANUFACTURING DIRECTIONS

1. Heat oil and water phases separately at 65°C to 70°C.
2. Add water phase to oil phase while stirring.
3. Add the triethanolamine dropwise.
4. Stir to cool.
5. This product can be used as a disinfecting and soothing cream for the feet.

MENTHOL MOUTHWASH

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
10.00	1	Menthol	10.00
10.00	2	Eucalyptus oil	10.00
40.00	3	Cremophor RH 40	40.00
4.50	4	Saccharin sodium	4.50
2.00	5	Sodium citrate	2.00
5.00	6	Citric acid	5.00
50.00	7	Lutrol F 127	50.00
67.00	8	Ethanol 96%	67.00
QS	9	Sicovit colorant	QS
QS	10	Water	801.00

MANUFACTURING DIRECTIONS

1. Mix items 1 to 3, and heat to approximately 60°C.
2. Prepare solution of items 4 to 10, heat it to approximately 60°C, and add it slowly to the well-stirred mixture of items 1 to 3.
3. Clear, colored liquid has a fresh mint taste.

METHYL SALICYLATE ANALGESIC CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
30.00	1	Tromethamine magnesium aluminum silicate (Veegum® PRO)	30.00
30.00	2	Hydroxypropylcellulose	30.00
350.00	3	Deionized water	350.00
350.00	4	Ethanol	350.00
40.00	5	Cocoyl sarcosine (Vanseal CS)	40.00
25.00	6	Oleath-10	25.00
25.00	7	PEG-25 hydrogenated castor oil	25.00
50.00	8	Isopropyl myristate	50.00
20.00	9	Triethanolamine	20.00
5.00	10	Camphor	5.00
5.00	11	Menthol	5.00
2.00	12	Eucalyptus oil	2.00
65.00	13	Methyl salicylate	65.00
QS	14	Preservatives	QS

MANUFACTURING DIRECTIONS

1. Dry blend item 1 and item 2, and slowly add them to items 3 and 4, agitating to ensure homogenous dispersion.
2. Combine items 5 to 9 separately and items 10 to 14 separately; then, mix them together.
3. Finally, add this mixture to the first mixture, and mix until uniform.

METHYL SALICYLATE ANALGESIC CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
15.00	1	Magnesium aluminum silicate (Veegum®)	15.00
547.00	2	Deionized water	547.0
2.00	3	Simethicone emulsion	2.00
30.00	4	Propylene glycol	30.00
150.00	5	Methyl salicylate	150.00
50.00	6	Menthol	50.00
6.00	7	Polysorbate	6.00
50.00	8	C18-C36 acid	50.00
150.00	9	Glyceryl stearate and PEG-100 stearate	150.00
QS	10	Preservatives	QS

MANUFACTURING DIRECTIONS

1. Add item 1 to water slowly, and mix vigorously to smooth dispersion.
2. Add items 3 and 4, mixing one at a time. Heat to 75°C to 80°C.
3. Separately mix and heat items 5 to 9 to 75°C to 80°C, and combine the two parts while mixing.
4. Cool while mixing, and add item 10 at 40°C.

METHYL SALICYLATE AND MENTHOL GEL

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
110.00	1	Methyl salicylate	110.00
50.00	2	Menthol	50.00
200.00	3	Lutrol E 400	200.00
60.00	4	Cremophor RH 40	60.00
70.00	5	Propylene glycol (pharma)	70.00
320.00	6	Lutrol F 127	320.00
QS	7	Water	190.00

MANUFACTURING DIRECTIONS

1. Dissolve item 6 in solution of items 1 to 5, and mix with item 7.
2. The clear gel can be diluted with water.
3. Because of the high concentration of the active ingredients and of Lutrol F 127, the consistency of the colorless clear gel is extremely hard.
4. By reducing the concentration of the active ingredients, the amount of Lutrol F 127 can also be reduced, and the consistency of the gel will be normal.

METHYL SALICYLATE HEAT RUB LOTION

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
25.00	1	PPG-5-cetech-10-phosphate (Crodafos SG)	25.00
40.00	2	Emulsifying wax, NF (Polawax)	40.00
45.00	3	PPG-1 cetyl ether (Procetyl 10)	45.00
10.00	4	Menthol	10.00
10.00	5	Camphor	10.00
75.00	6	Methyl salicylate	75.00
30.00	7	Glycerin	30.00
10.00	8	Gelatin, NF (Crodyne BY-19)	10.00
3.00	9	Diethanolamine	3.00
742.00	10	Deionized water	742.00
10.00	11	Propylene glycol, diazolidinyl urea, methylparaben, and propylparaben	10.00

MANUFACTURING DIRECTIONS

1. Premix items 4, 5, and 6 with item 3.
2. When completely dissolved, add items 1 and 2, and heat to 75°C to 80°C.
3. Dissolve item 8 in water, and add items 7 and 9.
4. Heat to 80°C; slowly add this part to previous part using good mechanical mixing.
5. Allow to cool while mixing to 40°C, and then add item 11.
6. Cool to 30°C, and fill.

METOCLOPRAMIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
10.00	1	Anhydrous metoclopramide hydrochloride; use metoclopramide hydrochloride	10.54
7.00	2	Maize starch (dried)	7.00
1.00	3	Silicon dioxide (colloidal)	1.00
0.76	4	Magnesium stearate	0.76
5.00	5	Starch (pregelatinized)	5.00
101.24	6	Lactose	101.24
QS	7	Purified water	~ 15.00 mL

MANUFACTURING DIRECTIONS

1. Dried maize starch must be used for lubrication.
2. Dry the starch at 80 °C for 36 hours prior to its use in manufacturing.
3. Check LOD of starch; the LOD must be less than 2%.
4. Pass the lactose, pregelatinized starch, and metoclopramide hydrochloride through a 1.25 mm aperture screen, and transfer to a suitable mass mixer. Mix for 5 minutes.
5. Add the water slowly to the mixer, and mix for 30 minutes or until a suitable consistency is obtained. Add extra water if required.
6. Pass the mass through a 4.8 mm aperture screen or an oscillating granulator (or by hand), and dry in a tray dryer or fluid-bed dryer at 50 °C until the moisture content is less than 5.5%.
7. Pass the granules through an 875 µm aperture screen on an oscillating granulator (or comminuting mill at medium speed, knives forward) into tared, polyethylene-lined drums. Seal and weigh.
8. Carry out remaining steps at an RH less than 50% and temperature less than 26°C.
9. Transfer the dried granulation to a suitable blender.
10. Screen the starch (item 2), magnesium stearate, and silicon dioxide through a 250 µm aperture screen on a sieve shaker, and add to the blender.

11. Blend for 10 minutes.
12. Discharge the granules into polyethylene-lined drums. Seal, and weigh for yield.
13. Compress 1.255 g per 10 tablets in 6.35 or 7.14 mm standard concave punches.

MICONAZOLE NITRATE CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
21.00	1	Miconazole nitrate (5% excess)	21.00
200.0	2	Tefose® 63	200.0
30.00	3	Labrafil® M ^a	30.00
30.00	4	Mineral oil (liquid paraffin)	30.00
0.05	5	Butylated hydroxyanisole	0.05
2.00	6	Benzoic acid	2.00
720.00	7	Purified water	720.00

^a Synonyms: Labrafil® M 1944 CS, oleoyl macrogolglycerides, apricot kernel oil PEG-6 complex.

MANUFACTURING DIRECTIONS

1. Melt items 2, 3, and 4 (fatty phase) in fat-melting vessel.
2. Heat to 65°C to 70°C.
3. Disperse items 1 and 5 in the fatty phase while mixing at high speed for 20 minutes.
4. Add item 7 to the mixer, and heat to 80°C to 90°C.
5. Dissolve item 6, and cool down to 65°C to 70°C.
6. Transfer the fatty phase to the mixer with vacuum at 0.2 to 0.3 bar.
7. Start cooling down while mixing at 10 rpm, and homogenize at high speed for 20 minutes; then, cool down to 25°C to 28°C while mixing at a vacuum of 0.2 to 0.3 bar (65–45°C) or 0.5 to 0.7 bar (45–25°C).

MINERAL AND MULTIVITAMIN SYRUP

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
6.65	1	Hypophosphorous acid	6.65
16.47	2	Calcium hypophosphite	16.47
31.68	3	Calcium lactate (powder)	31.68
1.00	4	Methylparaben	1.00
0.20	5	Propylparaben	0.20
1.00	6	Benzoic acid	1.00
150.00	7	Sucrose (granular)	150.00
5.20	8	Ferrous gluconate	5.20
2.00	9	Niacinamide (5% excess)	2.10
0.33	10	Riboflavin-5-phosphate sodium	0.33
1.00	11	D-pantothenyl alcohol (dexpantenol; 20% excess)	1.20
0.60 µg	12	Vitamin B ₁₂ (cyanocobalamin) (35% excess)	0.81 mg
0.20	13	Pyridoxine hydrochloride	0.20
0.30	14	Thiamine hydrochloride (regular powder) (55% excess)	0.46
4.782	15	Flavor, raspberry blend	4.78
1.945	16	Flavor, chocolate	1.945
0.64	17	Orange oil (terpeneless, No. 54125)	0.64
0.21	18	Lime oil, distilled	0.21
4.28	19	Alcohol	4.28
2.50	20	Saccharin sodium	2.50
10.00	21	Ascorbic acid (white powder/EP) (45% excess)	14.50
3.00	22	Caramel (acid proof)	3.00
2.00	23	Anhydrous citric acid	2.00
10.0 µg	24	Butylated hydroxyanisole (BHA)	10.0 mg
3.39	25	Corn oil	3.39
0.40	26	Vitamin A palmitate (1.5 million U/g) (40% excess)	0.56
0.08	27	Viosterol in corn oil (syn. oleovitamin D; 1000 mg/g) (40% excess)	0.112
1.5 g	28	Acacia (special grade)	1.50
0.127	29	Sodium lauryl sulfate (acetone-washed)	0.127
171.00	30	Deionized, purified water	~171.00
QS	31	Glucose liquid (corn syrup)	QS to 1 L

MANUFACTURING DIRECTIONS

Do not expose this preparation during manufacturing to direct sunlight. Riboflavin is sensitive to light.

- Add 83.7 mL purified water to a stainless steel jacketed tank.
- Add calcium hypophosphite, calcium lactate, the parabens, and benzoic acid.
- Heat mixture to 60°C with agitation.
- Shut off mixer, and wash tank until free of all powders with 25.9 mL purified water.
- Heat to and maintain a maximum temperature of 100°C until solution is complete. Do not agitate. Avoid loss of water through evaporation. Cover opening of tank.
- After solution occurs, take sample from bottom of tank and examine for clarity. Solution must be clear.
- Add hypophosphorous acid (if used) with mixing.
- Turn off heat, add 222 g glucose, and start agitator. (*Caution:* Use CO₂ cover throughout. Wherever water is used, it should be CO₂-saturated water.) Dissolve ferrous gluconate in 7.4 mL water CO₂-saturated by heating.
- Add 278 g glucose with mixing. Add and dissolve sugar.
- Allow solution to cool to 35°C, and mix well.
- To 29.6 mL water, add and dissolve nicotinamide, riboflavin, D-pantothenyl alcohol, vitamin B₁₂, pyridoxine, and thiamine. Mix until solution is complete, and add to tank. Dissolve by heat if necessary.
- Charge raspberry blend flavor and chocolate flavor into tank. Charge saccharin into tank, and mix until dissolved.
- Charge ascorbic acid into tank. Mix well.
- Charge caramel into tank, and mix well.
- Dissolve citric acid in 3 mL water, and add.
- Heat corn oil to 50°C to 60°C, and add and dissolve BHA. Be sure the BHA is completely dissolved before continuing.
- Cool to room temperature. While cooling oil mixture, saturate with CO₂, and maintain heavy CO₂ coverage for balance of operation.
- Set aside a small amount of this mixture as a rinse for the vitamin A and viosterol containers in preceding step.
- Add vitamin A palmitate and viosterol to the cool corn oil mixture, rinsing the containers with the reserved oil.
- Add the rinse to the bulk. Mix well.
- Add the acacia to the oil mixture with good mixing.
- Dissolve sodium lauryl sulfate in 3 mL CO₂-saturated purified water. To avoid excessive foaming, do not bubble CO₂ gas through the water/sodium lauryl sulfate solution.
- Add the sodium lauryl sulfate solution to the oil mixture, and stir to a thick creamy emulsion.
- Add 7.56 g glucose to the emulsion with mixing.
- Blend 13.33 mL CO₂-saturated purified water with 77.04 g glucose, and add emulsion with stirring.
- Recycle primary emulsion back into holding tank while setting mill.
- Homogenize until all oil globules are less than 8 µm in diameter using colloid mill with a fine setting. Do not change mill setting after removing sample unless samples are unacceptable.

28. Add primary emulsion to syrup solution with mixing. Add glucose QS to 965 mL, and mix well. Allow to stand overnight to vent entrapped air.
29. Adjust the volume to 1 L using glucose or glucose and CO₂-saturated water.
30. Strain through 149 µm aperture or similar screen into clean reserve tank, and recheck volume.

MINT-MENTHOL MOUTHWASH

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
20.00	1	Mint oil	20.00
0.40	2	Menthol	0.40
0.90	3	Eucalyptus oil	0.90
10.00	4	Alpha-bisabolol (BASF)	10.00
0.60	5	Thymian oil	0.60
40.00	6	Cremophor RH 40	40.00
4.50	7	Saccharin sodium	4.50
2.00	8	Sodium citrate	2.00
5.00	9	Citric acid	5.00
0.20	10	Sodium fluoride	0.20
50.00	11	Glycerol	50.00
50.00	12	Lutrol F 127	50.00
0.60	13	Salicylic acid	0.60
1.00	14	Benzoic acid	1.00
175.00	15	Sorbitol, crystalline	175.00
216.00	16	Ethanol 96%	216.00
QS	17	Sicovit colorant	QS
QS	18	Water	48.40

MANUFACTURING DIRECTIONS

1. Mix items 1 to 6, and heat to approximately 60°C.
2. Prepare solution of items 7 to 18, heat it to approximately 60 °C, and add it slowly to the well-stirred mixture of items 1 to 6.
3. Clear, colored liquids have a fresh mint taste.

MINT OIL SOLUTION

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
35.00	1	Peppermint oil	35.00
138.00	2	Cremophor RH 40	138.00
520.00	3	Ethanol 96%	520.00
QS	4	Water	307.00

MANUFACTURING DIRECTIONS

1. Mix the peppermint oil with Cremophor RH 40, stir well, and slowly add ethanol and water.
2. Clear, colorless liquid is of low viscosity.

MULTIVITAMIN AND BETA-CAROTENE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
7.00	1	Beta-carotene; use beta-carotene dry powder (10%, Pharma)	70.00
2.20	2	Thiamine mononitrate	2.20
2.20	3	Riboflavin	2.20
6.50	4	Nicotinamide	6.50
11.50	5	Calcium D-pantothenate	11.50
2.20	6	Pyridoxine hydrochloride	2.20
0.06	7	Cyanocobalamin; use cyanocobalamin dry powder (0.1%)	6.00
85.00	8	Ascorbic acid (powder)	85.00
32.00	9	Vitamin E acetate (dry powder; SD 50)	32.00
210.00	10	Ludipress®	210.00
7.00	11	Kollidon® VA 64	7.00
3.00	12	Magnesium stearate	3.00
7.00	13	Orange flavor	7.00
2.50	14	Saccharin sodium	2.50

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, mix, and press with medium compression force.
2. Compress 448 mg using 12 mm planar punches.

MULTIVITAMIN AND CALCIUM SYRUP

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/100 g (mg)
0.10	1	Vitamin A palmitate	10.00
0.50 µg	2	Vitamin D 40 mio IU/g	0.05
1.00	3	Vitamin E acetate, BASF	100.00
0.02	4	BHT	2.00
45.00	5	Cremophor RH 40	4.50 g
100.00	6	Water	10.00 g
450.00	7	Saccharose	45.00 g
2.00	8	Methyl paraben	200.00
0.80	9	Citric acid	80.00
96.00	10	Glycerol	9.60 g
0.70	11	Calcium gluconate	70.00
250.00	12	Water	25.00 g
0.15	13	Thiamine hydrochloride, BASF	15.00
0.15	14	Riboflavin 5'-phosphate sodium	15.00
0.55	15	Nicotinamide	55.00
0.15	16	Pyridoxine hydrochloride	15.00
3.00	17	Ascorbic acid, crystalline	300.00
1.00	18	Sorbic acid	100.00
50.00	19	Propylene glycol (pharma)	5.00 g

MANUFACTURING DIRECTIONS

1. Heat items 1 to 5 and item 6 separately to approximately 60 °C, and mix slowly, stirring well to obtain a clear solution.
2. Dissolve items 7 to 9 in the hot solution of items 10 to 12 to obtain a clear solution.
3. Mix all the solutions upon cooling, and add solutions of items 13 to 19. Adjust the pH value to 4.0 to 4.1.
4. Pass nitrogen through the solution for 10 minutes, and fill in bottles under nitrogen cover.

MULTIVITAMIN AND CARBONYL IRON TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
5000 IU	1	Vitamin A acetate (dry powder; 500,000 IU/g)	10.00
2.20	2	Thiamine mononitrate, BASF	2.20
2.20	3	Riboflavin	2.20
16.50	4	Nicotinamide	16.50
11.50	5	Calcium D-pantothenate	11.50
2.20	6	Pyridoxine hydrochloride	2.20
6.00	7	Cyanocobalamin (dry powder; 0.1%)	6.00
85.00	8	Ascorbic acid (powder)	85.00
31.00	9	Vitamin E acetate (dry powder; SD 50)	31.00
311.00	10	Ludipress®	311.00
10.00	11	Carbonyl iron (powder OF)	10.00
3.00	12	Magnesium stearate	3.00
7.20	13	Orange flavor	7.20
2.50	14	Saccharin sodium	2.50

MANUFACTURING DIRECTIONS

1. Mix all ingredients, pass through a 0.8 mm sieve, mix, and press with high compression force (20 kN).
2. Compress 500 mg in 12 mm biplanar punches.

MULTIVITAMIN AND FLUORIDE CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
1.20	1	Riboflavin; use coated riboflavin (25% excess)	5.28
0.30	2	Folic acid (powder)	0.31
1.00	3	Fluoride; use sodium fluoride (powder)	2.21
19.50	4	Starch (bright yellow 2 LA)	19.50
1.05	5	Pyridoxine; use pyridoxine hydrochloride (6% excess)	4.02
1.05	6	Thiamine HCl; use coated thiamine mononitrate (5% excess)	3.21
13.50	7	Niacin; use nicotinamide	40.20
4.50 µg	8	Vitamin B ₁₂ ; use cyanocobalamin oral powder in starch (10% excess)	5.17
20.00	9	Ascorbic acid; use surface-coated ascorbic acid	21.00
40.00	10	Sodium ascorbate; use surface- coated sodium ascorbate (5% excess)	47.25
7.49	11	Anhydrous citric acid	7.49
15 IU	12	Vitamin E; use vitamin E (D,L- α -tocopherol) (5% excess)	31.50
400 IU (10 µg)	13	Vitamin D; use vitamin D ₃ beadlets (25% excess)	0.65
9.36	14	Flavor	9.36
2500 IU or 0.75 mg	15	Vitamin A; use vitamin A palmitate beadlets (500 mU/g), USP (60% excess)	8.25
500.60	16	Sugar (compressible)	500.60

MANUFACTURING DIRECTIONS

Manufacture this product at less than 40% RH and a temperature less than 26.7°C.

1. If lumpy, hand screen riboflavin through an 8 mesh screen, and mix with folic acid, sodium fluoride powder, and approximately 3.5 g of bright yellow starch in a suitable blender until the yellow color of premix is uniform.

2. Cross-feed the premixed items, pyridoxine hydrochloride, thiamine mononitrate, nicotinamide, cyanocobalamin oral powder in starch, ascorbic acid, citric acid, and vitamin E through an 846 μm screen on a comminuting mill (knives forward, medium speed).
3. Transfer the powders to a suitable blender.
4. Clear mill with a part of the compressible sugar, and transfer to the blender.
5. Charge vitamin D₃ beadlets, sodium ascorbate, flavor, and vitamin A palmitate into the blender.
6. Blend for 10 minutes.
7. Discharge the contents of the blender into polyethylene-lined drums.
8. Pass the remaining compressible sugar through an 846 μm screen on a comminuting mill (knives forward, medium speed).
9. Transfer to the blender.
10. Screen the material from previous step, the magnesium stearate, and the remaining bright yellow starch through an 846 μm screen, and transfer to the blender. (*Note:* Mill material not passing through the screen through an 846 μm screen on a comminuting mill at medium speed with knives forward.) Blend for 20 minutes.
11. Discharge blender into polyethylene-lined drums, and weigh for yield.
12. Use precompression, if available, to obtain a tablet with adequate friability.
13. Coat as needed (see Appendix).

MULTIVITAMIN AND MINERAL SYRUP

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/L (g)
6.65	1	Hypophosphorous acid (50% pure)	6.655
16.47	2	Calcium hypophosphite	16.47
31.68	3	Calcium lactate (powder)	31.68
1.00	4	Methylparaben	1.00
0.20	5	Propylparaben	200.00 mg
1.00	6	Acid benzoic	1.00
150.00	7	Sucrose	150.00
5.20	8	Ferrous gluconate	5.20
2.00	9	Niacinamide (white powder) (5% excess)	2.10
0.32	10	Riboflavin-5-phosphate sodium	328.77 mg
1.00	11	D-Pantothenyl alcohol (dexpanthenol; 20% excess)	1.20
0.00060	12	Vitamin B ₁₂ (cyanocobalamin; 35% excess)	810.00 μg
0.20	13	Pyridoxine hydrochloride	200.00 mg
0.30	14	Thiamine hydrochloride (powder, regular) (55% excess)	465.00 mg
4.78	15	Flavor, raspberry blend	4.782
1.94	16	Flavor, chocolate	1.945
0.64	17	Orange oil, terpeneless No. 54125	642.00 mg
0.21	18	Lime oil (distilled)	214.975 mg
4.28	19	Alcohol (ethanol, 190 proof)	4.28
2.50	20	Saccharin sodium	2.50
10.00	21	Acid ascorbic (45% excess)	14.50
3.00	22	Caramel (acid proof)	3.00
2.00	23	Anhydrous citric acid	2.00
0.0010	24	Butylated hydroxyanisole (BHA)	10.0 mg
3.39	25	Corn oil	3.39
0.56	26	Vitamin A palmitate (1.5 million UA/g, 40% excess)	560.00 mg
0.08	27	Vioosterol in corn oil (syn. oleovitamin D; 1000 mD/g; D3 in arachis oil) (40% excess)	112.00 mg
1.50	28	Acacia	1.50
0.12	29	Sodium lauryl sulfate (acetone washed)	127.41 mg
171.00	30	Purified water	~171.00
QS	31	Glucose liquid	QS to 1 L

MANUFACTURING DIRECTIONS

Do not expose this preparation during manufacturing to direct sunlight. Riboflavin is sensitive to light.

1. Add 83.7 mL of purified water to a stainless steel jacketed tank.
2. Add calcium hypophosphite, calcium lactate, parabens, and benzoic acid.
3. Heat mixture to 60°C with agitation.

4. Shut off mixer, and wash tank free of all powders with 25.9 mL purified water.
5. Heat to and maintain a maximum temperature of 100°C until solution is complete. Do not agitate. Avoid loss of water through evaporation. Cover opening of tank. After solution occurs, take sample from bottom of tank and examine for clarity. Solution must be clear.
6. Add acid hypophosphorous (if used) with mixing.
7. Turn off heat, add 222 g glucose, and start agitator. (*Caution:* Use CO₂ cover throughout. Wherever water is used, it should be CO₂-saturated water.) Dissolve ferrous gluconate in 7.4 mL water CO₂ saturated by heating.
8. Add 278 g glucose with mixing. Add and dissolve sugar.
9. Allow solution to cool to 35°C, and mix well.
10. To 29.6 mL water, add and dissolve nicotinamide, riboflavin, D-pantothenyl alcohol, vitamin B₁₂, pyridoxine, and thiamine.
11. Mix until solution is complete, and add to tank. Dissolve by heat if necessary.
12. Charge raspberry blend flavor and chocolate flavor into tank.
13. Charge saccharin into tank, and mix until dissolved.
14. Charge ascorbic acid into tank, and mix well.
15. Charge caramel into tank, and mix well.
16. Dissolve citric acid in 3 mL water, and add this solution to the mixture.
17. Heat corn oil to 50°C to 60°C, and add and dissolve BHA. Be sure the BHA is completely dissolved before continuing.
18. Cool to room temperature. While cooling oil mixture, saturate with CO₂, and maintain heavy CO₂ coverage for balance of operation.
19. Set aside a small amount of this mixture as a rinse for the vitamin A and viosterol containers in previous step.
20. Add vitamin A palmitate and viosterol to the cool corn oil mixture, rinsing the containers with the oil reserved earlier.
21. Add the rinse to the bulk, and mix well.
22. Add the acacia to the oil mixture with good mixing.
23. Dissolve sodium lauryl sulfate in 3 mL CO₂-saturated purified water. To avoid excessive foaming, do not bubble CO₂ gas through the water/sodium lauryl sulfate solution.
24. Add the sodium lauryl sulfate solution to the oil mixture, and stir to a thick creamy emulsion.
25. Add 7.56 g glucose to the emulsion with mixing.
26. Blend 13.33 mL CO₂-saturated purified water with 77.04 g glucose, and add emulsion with stirring.
27. Recycle primary emulsion back into the holding tank while setting mill.

28. Homogenize until all oil globules are less than 8 µm in diameter using colloid mill with a fine setting. After setting mill, sample. Do not change mill setting after removing sample unless samples are unacceptable.
29. Add primary emulsion to syrup solution with mixing. Add glucose QS to 965 mL, and mix well.
30. Allow to stand overnight to vent entrapped air. Adjust the volume to 1 L using glucose or glucose and CO₂-saturated water.
31. Strain through 149 µm aperture or similar screen into clean reserve tank, and recheck volume.

MULTIVITAMIN AND MINERAL TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
4000 IU/400 IU	1	Vitamin A/vitamin D crystallites (500,000 A/50,000 D/g) (25% excess)	10.00
40.00	2	Vitamin A acetate (powder; 500 MA) (20% excess)	50.00
10.00	3	Thiamine hydrochloride (10% excess)	11.00
5.00	4	Riboflavin	5.00
100.00	5	Nicotinamide niacinamide (white powder)	100.00
200.00	6	Ascorbic acid (white powder) (10% excess)	220.00
20.00	7	Calcium pantothenate (dextro) (30% excess)	26.00
5.00	8	Pyridoxine hydrochloride	5.00
7.33	9	Povidone (K-29-32) ^a	7.33
29.16	10	Anhydrous refined alcohol isopropyl	29.16
24.20	11	Talc powder	24.20
6.07	12	Magnesium stearate (impalpable powder)	6.07
4.75	13	Stearic acid (fine powder)	4.75
10.0	14	Iron; use iron sulfate (dried)	31.26
1.00	15	Copper ^a	1.00
0.15	16	Iodine ^a	0.15
1.00	17	Manganese ^a	1.00
5.00	18	Magnesium ^a	5.00
1.50	19	Zinc ^a	1.50
0.10	20	Cobalt; use cobalt sulfate	0.47
5.00	21	Potassium; use potassium sulfate	11.14
0.20	22	Molybdenum; use sodium molybdate (dihydrate)	0.50
6.00 µg	23	Vitamin B ₁₂ ; use cyanocobalamin (1000 µg/g oral powder in gelatin; 5% excess)	6.30

^a Provided as mineral mix (includes 3% excess).

Bill of Materials for Mineral Mix

Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
13.85	1	Copper sulfate	14.28
0.01175	2	Calcium iodate monohydrate	0.01212
0.1228	3	Manganese sulfate monohydrate	0.1267
0.1480	4	Zinc sulfate (pure dry powder)	0.1526

MANUFACTURING DIRECTIONS

Mineral mix processing:

1. Grind copper sulfate, calcium iodate, manganese sulfate, and zinc sulfate through Fitz mill screen 0 band (high speed, impact forward).
2. *Note:* Vitamin A is susceptible to destruction by oxidation and excessive exposure to actinic light and moisture. Compression of this tablet should be done where RH is less than 40%. Protect granulation with CO₂ if material is not to be compressed soon after granulation.
3. Hand screen vitamins A and D crystallets and vitamin A acetate through 1.2 mm aperture screen.
4. Load into mass mixer (screen using 1.2 mm aperture screen if necessary) thiamine HCl, riboflavin, nicotinamide, ascorbic acid, calcium pantothenate, pyridoxine HCl, and the vitamins A and D mix.
5. Blend for 10 minutes.
6. Dissolve povidone in alcohol (approximately 26 mL).
7. Add povidone solution to blended materials, and mix for 5 minutes.
8. Scrape mixer; then, add alcohol to mass (approximately 11 mL).
9. Pass wet mass through a 15.88 mm aperture (or similar) band-fitted to rotary granulator. (*Note:* Wet mass can set hard; therefore, granules should be spread quickly onto trays.) Dry the granulation at 49°C until LOD is less than 1.0%.
10. Pass the dried granulation through a 1.2 mm aperture screen fitted to an oscillating granulator.
11. Mill the talc (item 11), magnesium stearate, stearic acid, iron sulfate, mineral mix, cobalt sulfate, potassium sulfate, and sodium molybdate through a 595 µm aperture screen at high speed, impact forward.
12. Load half the granulation into a suitable blender. Add mineral mix and cyanocobalamin oral powder.
13. Add balance of granulation, and blend for 30 minutes.
14. Compress and coat using a sealing subcoating of PVP (see Appendix) followed by HPMC coating solution and clear MethocelTM gloss.

MULTIVITAMIN AND MINERAL TABLETS WITH BETA-CAROTENE

Bill of Materials

Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
150.00	1	Beta-carotene (dry powder; 10%)	150.00
2.50	2	Thiamine mononitrate	2.50
2.90	3	Riboflavin	2.90
2.00	4	Pyridoxine hydrochloride	2.00
22.00	5	Nicotinamide	22.00
12.00	6	Calcium D-pantothenate	12.00
110.00	7	Ascorbic acid for direct compression	110.00
550.00	8	Calcium phosphate (dibasic)	550.00
82.00	9	Ferrous fumarate	82.00
166.00	10	Magnesium oxide	166.00
2.50	11	Cupric sulfate	2.50
13.80	12	Manganese sulfate	13.80
57.20	13	Potassium chloride	57.20
37.00	14	Zinc sulfate	37.00
57.00	15	Avicel TM PH102	57.00
50.00	16	Kollidon [®] CL	50.00
5.70	17	Stearic acid	5.70
5.00	18	Magnesium stearate	5.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with high compression force.
2. Compress 1300 mg per tablet using 16 mm biplanar punches.

MULTIVITAMIN, CALCIUM, AND IRON TABLETS

Bill of Materials

Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
5.00	1	Vitamin A acetate (dry powder)	5.00
2.00	2	Vitamin D (dry powder; 500,000 IU/g)	2.00
1.20	3	Thiamine mononitrate (100,000 IU/g)	1.20
1.80	4	Riboflavin, BASF	1.80
12.00	5	Nicotinamide	12.00
4.00	6	Vitamin E acetate (dry powder, SD 50)	4.00
50.00	7	Ascorbic acid (powder), BASF	50.00
60.00	8	Ferrous fumarate	60.00
200.00	9	Dibasic calcium phosphate granulated with 5% Kollidon [®] 30	200.00
125.00	10	Calcium carbonate	125.00
45.00	11	Avicel TM PH101	45.00
1.50	12	Aerosil [®] 200	1.50

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a sieve, and press to tablets.
2. Compress 500 mg in 11 mm biplanar punches.

**MULTIVITAMIN + CALCIUM + IRON
TABLETS (1 RDA OF VITAMINS)**
FORMULATION

Vitamin A acetate dry powder, 500,000 IU/g (BASF), 5.0 g; vitamin D dry powder, 100,000 IU/g, 2.0 g; thiamine mononitrate, 1.2 g; riboflavin, 1.8 g; nicotinamide, 12.0 g; vitamin E acetate dry powder SD 50, 4.0 g; ascorbic acid, powder, 50.0 g; ferrous fumarate, 60.0 g; dibasic calcium phosphate, 200.0 g; granulated with 5% Kollidon® 30; calcium carbonate, 125.0 g; Avicel™ PH 101, 45.0 g; Aerosil® 200, 1.5 g.

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a sieve, and press to tablets at 500 mg.

**MULTIVITAMIN + CARBONYL IRON
TABLETS (1–2 RDA OF VITAMINS)**
FORMULATION

Vitamin A acetate dry powder, 500,000 IU/g, 10.0 g; thiamine mononitrate, 2.2 g; riboflavin, 2.2 g; nicotinamide, 16.5 g; calcium D-pantothenate, 11.5 g; pyridoxine hydrochloride, 2.2 g; cyanocobalamin, dry powder 0.1%, 6.0 g; ascorbic acid, powder, 85.0 g; vitamin E acetate dry powder SD 50, 31.0 g; Ludipress®, 311.0 g; carbonyl iron powder OF, 10.0 g; magnesium stearate, 3.0 g; orange flavor, 7.2 g; saccharin sodium, 2.5 g.

MANUFACTURING DIRECTIONS

1. Mix all ingredients, pass through a 0.8 mm sieve, mix, and press with high compression force (20 kN) at 500 mg.

**MULTIVITAMIN CHEWABLE
TABLETS FOR CHILDREN**
FORMULATION

Vitamin A acetate dry powder, 500,000 IU/g, 7.0 g; thiamine mononitrate, 1.2 g; riboflavin, 1.2 g; nicotinamide, 20.0 g; pyridoxine hydrochloride, 1.8 g; cyanocobalamin, 0.1% dry

powder, 6.5 g; ascorbic acid, powder, 60.0 g; vitamin D₃ acetate dry powder, 100,000 IU/g, 5.0 g; vitamin E acetate, 31.0 g, dry powder SD 50; sorbitol, crystalline [10], 200.0 g; sucrose, crystalline, 200.0 g; Kollidon® VA 64, 20.0 g; Aerosil® 200, 1.0 g; orange flavor, dry powder, 30.0 g; raspberry flavor, dry powder, 6.0 g; passion fruit flavor, dry powder, 3.0 g; cyclamate sodium, 2.0 g.

MANUFACTURING DIRECTIONS

1. Mix all ingredients, pass through a 0.8 mm sieve, and press with medium to high compression force (20 kN) at 575 mg.

**MULTIVITAMIN CHEWABLE
TABLETS FOR CHILDREN**

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
3500 IU	1	Vitamin A acetate (dry powder; 500,000 IU/g)	7.00
1.20	2	Thiamine mononitrate	1.20
1.20	3	Riboflavin	1.20
20.00	4	Nicotinamide	20.00
1.80	5	Pyridoxine hydrochloride	1.80
6.50	6	Cyanocobalamin (dry powder; 0.1%), BASF	6.50
60.00	7	Ascorbic acid (powder)	60.00
5.00	8	Vitamin D ₃ acetate (dry powder; 100,000 IU/g)	5.00
31.00	9	Vitamin E acetate (dry powder, SD 50)	31.00
200.00	10	Sorbitol (crystalline)	200.00
200.00	11	Sucrose (crystalline)	200.00
20.00	12	Kollidon® VA 64	20.00
1.00	13	Aerosil® 200	1.00
30.00	14	Orange flavor (dry powder)	30.00
6.00	15	Raspberry flavor (dry powder)	6.00
3.00	16	Passion fruit flavor (dry powder)	3.00
2.00	17	Cyclamate sodium	2.00

MANUFACTURING DIRECTIONS

1. Mix all ingredients, pass through a 0.8 mm sieve, and press with medium to high compression force (20 kN).
2. Compress 575 mg using 12 mm biplanar punches.

MULTIVITAMIN DROPS

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
13,600 IU	1	Vitamin A palmitate (1.7 MM IU/g)	8.00
5200 IU	2	Vitamin D ₃ (40 MM IU/g)	0.13
5.00	3	Vitamin E acetate	5.00
150.0	4	Cremophor EL (or Cremophor RH 40)	150.00
2.00	5	Parabens (methyl and propyl)	2.00
525.00	6	Water purified	525.00
4.00	7	Thiamine hydrochloride	4.00
2.00	8	Riboflavin 5-phosphate sodium	2.00
2.00	9	Pyridoxine hydrochloride	2.00
2.00	10	Nicotinamide	2.00
0.20	11	Sodium bisulfite	0.20
200.00	12	Propylene glycol	200.00
QS	13	Water purified	10.00
QS	14	Hydrochloric acid	QS

MANUFACTURING DIRECTIONS

1. Heat mixture of items 1 to 4 to approximately 60°C, stir strongly, and slowly add solution of items 5 and 6 (60°C).
2. To the obtained clear solution, add solution of items 7 to 13.
3. Adjust the pH with item 14 to approximately 4, and QS to volume.

MULTIVITAMIN EFFERVESCENT GRANULES

Bill of Materials			
Scale (mg/sachet)	Item	Material Name	Qty/1000 Sachets (g)
2.60	1	Thiamine hydrochloride	0.26
3.00	2	Riboflavin	0.30
11.00	3	Nicotinamide	1.10
2.50	4	Pyridoxine hydrochloride	0.25
15.00	5	Calcium D-pantothenate	1.50
200.00	6	Ascorbic acid (powder)	20.00
500.00	7	Citric acid	50.00
1300.00	8	Sucrose	130.00
800.00	9	Fructose	80.00
200.00	10	Kollidon® CL-M	20.00
250.00	11	Flavors	25.00
20.00	12	Cyclamate sodium	2.00
1.00	13	Saccharin sodium	0.10
150.00	14	Kollidon® VA 64	15.00
350.00	15	Isopropanol	35.00
5000 IU	16	Vitamin A acetate (dry powder; 325,000 IU/g cold water dispersible [CWD])	1.50
800 IU	17	Vitamin D ₃ (dry powder; 100,000 IU/g CWD)	0.80
21.00	18	Vitamin E acetate (dry powder; 50%)	2.10
0.0660	19	Cyanocobalamin (gelatin-coated; 0.1%)	0.66
400.00	20	Sodium bicarbonate	40.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 13 with solution of items 14 and 15.
2. Pass through a 0.8 mm sieve, dry well, and mix with items 16 to 20.
3. Fill 4 g in sachets.

MULTIVITAMIN EFFERVESCENT TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
13.00	1	Thiamine mononitrate	13.00
4.00	2	Riboflavin	4.00
11.00	3	Pyridoxine hydrochloride	11.00
66.00	4	Nicotinamide	66.00
17.00	5	Calcium D-pantothenate	17.00
360.00	6	Tartaric acid (powder)	360.00
550.00	7	Sodium bicarbonate	550.00
300.00	8	Sucrose (crystalline)	300.00
300.00	9	Sucrose (powder)	300.00
35.00	10	Kollidon® 30	35.00
5.00	11	Kollidon® 30	5.00
QS	12	Isopropanol	~80.00
6.00	13	Riboflavin	6.00
550.00	14	Ascorbic acid (powder)	550.00
20.00	15	Cyanocobalamin (dry powder, 0.1%)	20.00
12.00	16	Vitamin A palmitate (250,000 IU/g dry powder CWD)	12.00
60.00	17	Vitamin E acetate (dry powder; 50%)	60.00
80.00	18	PEG-6000 (powder)	80.00
100.00	19	Kollidon® CL	100.00

MANUFACTURING DIRECTIONS

1. Granulate the mixture of items 1 to 10 with solution of items 11 and 12. Dry at 60°C with vacuum.
2. Mix with items 13 to 19, and press with high compression force at maximum 30% of relative atmospheric humidity.
3. Compress 2.5 g per tablet using 20 mm biplanar punches.

MULTIVITAMIN EFFERVESCENT TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
5.50	1	Thiamine mononitrate	5.50
5.50	2	Riboflavin	5.50
6.50	3	Pyridoxine hydrochloride	6.50
60.00	4	Nicotinamide	60.00
30.00	5	Calcium D-pantothenate	30.00
200.00	6	Ascorbic acid (powder)	200.00
0.20	7	Cyanocobalamin (dry powder, 0.1%)	20.00
30.00	8	Vitamin A acetate (dry powder; 325,000 IU/g CWD)	30.00
55.00	9	Vitamin E acetate (dry powder; 50%)	110.00
500.00	10	Citric acid (powder)	500.00
400.00	11	Tartaric acid (powder)	400.00
500.00	12	Sodium bicarbonate	500.00
600.00	13	Ludipress®	600.00
70.00	14	PEG-6000 (powder)	70.00
0.50	15	Saccharin sodium	0.50
40.00	16	Cyclamate sodium	40.00
200.00	17	Sucrose, crystalline	200.00
200.00	18	Fructose	200.00
100.00	19	Flavors (Firmenich)	100.00

MANUFACTURING DIRECTIONS

1. Mix all components, and sieve through a 0.8 mm screen.
2. Press with high compression force at maximum 30% relative atmospheric humidity.
3. Compress 3 g in 20 mm biplanar punches.

MULTIVITAMIN EFFERVESCENT
TABLETS I, DC (1–2 RDA OF VITAMINS)

FORMULATION

Lucarotene dry powder 10%, 23.0 g; CWD G/Y, dry vitamin E acetate 50% DC, 40.0 g; thiamine mononitrate, 2.0 g; riboflavin C, 2.0 g; nicotinamide, 22.0 g; calcium D-pantothenate, 11.0 g; pyridoxine hydrochloride, 2.0 g; cyanocobalamin 0.1% dry powder, 6.0 g; ascorbic acid, powder, 85.0 g; Ludipress® LCE, 477.0 g; sodium bicarbonate, 600.0 g; tartaric acid, 400.0 g; polyethylene glycol 6000, powder, 90.0 g; orange flavor (Dragoco), 60.0 g; aspartame (Searle), 30.0 g.

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, mix, and press with high compression force at a maximum of 30% of relative atmospheric humidity at 1850 mg.

MULTIVITAMIN EFFERVESCENT TABLETS II, DC (3–4 RDA OF VITAMINS)**FORMULATION**

Thiamine mononitrate, 5.5 g; riboflavin, 5.5 g; pyridoxine hydrochloride, 6.5 g; nicotinamide, 60.0 g; calcium D-pantothenate, 30.0 g; ascorbic acid, powder, 200.0 g; cyanocobalamin 0.1% dry powder, 20.0 g; vitamin A palmitate dry powder, 325,000 IU/g CWD, 30.0 g; vitamin E acetate dry powder 50%, 110.0 g; tartaric acid, powder, 400.0 g; sodium bicarbonate, 500.0 g; Ludipress®, 600.0 g; polyethylene glycol 6000, powder, 70.0 g; saccharin sodium, 0.5 g; cyclamate sodium, 40.0 g; sucrose, crystalline, 200.0 g; fructose, 200.0 g; flavors (Firmenich), 100.0 g.

MANUFACTURING DIRECTIONS

1. Mix all components, sieve through a 0.8 mm screen, and press with high compression force at maximum 30% relative atmospheric humidity.

MULTIVITAMIN EFFERVESCENT TABLETS WITH BETA-CAROTENE

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
2.00	1	Thiamine mononitrate	2.00
2.00	2	Riboflavin	2.00
2.00	3	Pyridoxine hydrochloride	2.00
22.00	4	Nicotinamide	22.00
11.00	5	Calcium D-pantothenate	11.00
400.00	6	Tartaric acid (powder)	400.00
300.00	7	Lactose monohydrate	300.00
100.00	8	Cornstarch	100.00
3.00	9	Cornstarch	3.00
50.00	10	Water	50.00
23.00	11	Beta-carotene (dry powder; 10% CWD; food grade)	23.00
6.00	12	Cyanocobalamin (powder; 0.1%)	6.00
85.00	13	Ascorbic acid (powder)	85.00
40.00	14	Vitamin E acetate (dry powder; 50%)	40.00
600.00	15	Sodium bicarbonate	600.00
80.00	16	Flavors	80.00
QS	17	Saccharin sodium	QS

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 6 with solution of items 9 and 10 prepared at 70°C.
2. Dry and sieve, add items 11 to 17, pass through a 0.4 mm sieve, and press with high compression force at maximum 30% of relative atmospheric humidity.
3. Compress 1.63 g using 16 mm biplanar punches.

MULTIVITAMIN INFANT DROPS

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
1125 IU	1	Vitamin A palmitate (1.7 MM IU/g, 50% excess)	1.324
416 IU	2	Vitamin D (40 MM IU/g, cholecalciferol, 25% excess)	0.013
5.00	3	Vitamin E (oily; alpha-tocopheryl acetate)	5.00
52.50	4	Ascorbic acid (50% excess)	78.75
0.375	5	Thiamine hydrochloride (50% excess)	0.75
0.40	6	Pyridoxine hydrochloride	0.40
8.00	7	Nicotinamide	8.00
0.00125	8	Cyanocobalamin (50% excess)	0.001875
0.82	9	Riboflavin sodium phosphate (5% excess as riboflavin)	0.865
2.50	10	Polyoxyl 20 cetostearyl ether (Cetomacrogol 1000)	2.50
12.50	11	Polysorbate 80 (Tween 80)	12.50
0.50	12	Edetate disodium (sodium EDTA)	0.50
3.75	13	Sodium hydroxide	3.75
0.25	14	Saccharin sodium	0.25
300.00	15	Glycerin (glycerol)	300.00
500.00	16	Sorbitol (70% solution)	500.00
50.00	17	Propylene glycol	50.00
1.50	18	Flavor	1.50
3.00	19	Flavor	3.00
1.50	20	Flavor	1.50
–	21	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

The product is a microemulsion and thermolabile. The temperature of solution must not exceed 25°C at the time of processing. Store bulk at temperature 15°C to 20°C under nitrogen protection to avoid discoloration and precipitation. Period of storage should not exceed 48 hours prior to filling in the bottle.

1. Check and record pH of item 21 (limit: 5.0–6.5), and collect 250 g of it in manufacturing vessel. Heat to 90°C to 95°C for 10 minutes; then, cool to 20°C to 25°C.
2. Bubble nitrogen gas into cooled item 21 for 20 minutes.
3. Load 200 g of item 21 from first step to the manufacturing vessel.

4. Bubble nitrogen gas during all stages of the process.
5. Add items 4 to 9 and 12 to 14 one by one to the manufacturing vessel while mixing.
6. Check that all materials are dissolved completely. Solution should be clear.
7. Add item 11 in a separate stainless steel container, and heat to 45°C.
8. Mix items 1, 2, 3, and 10 one by one.
9. Mix for 1 hour at slow speed.
10. Add oil phase preparation to the aqueous phase at a rate of 2 mL/min while mixing. Keep on bubbling nitrogen gas throughout the process.
11. Add items 15 and 16 to the manufacturing vessel one by one while mixing.
12. Keep on bubbling nitrogen gas throughout the process.
13. Add items 18, 19, and 20 in item 17, and add to the manufacturing vessel while mixing.
14. Adjust the volume to 1 L using nitrogen-bubbled item 21.
15. Mix for 10 minutes at slow speed without aeration.
16. Check pH (limit: 3.7–4.5).
17. Filter the product at 1.5 bar.
18. Recirculate approximately 100 to 150 mL of product.
19. Transfer the filtered product to the storage vessel under a nitrogen blanket.

MULTIVITAMIN INFANT DROPS

Bill of Materials			
Scale (mg/ 0. mL)	Item	Material Name	Qty/L (g)
675.00	1	Glycerin, USP (96%)	675.00
10.00	2	Nicotinamide niacinamide (white powder) (5% excess)	17.50
2.74	3	Riboflavin-5'-phosphate sodium (0% excess)	2.74
0.50	4	Methyl paraben (powder)	500.00 mg
1.00	5	Benzoic acid	1.00
2.10	6	Saccharin sodium (powder)	2.10
1.50	7	Thiamine HCl (45% excess)	3.625
0.60	8	Pyridoxine HCl	833.34 mg
50.00	9	Ascorbic acid (white powder) (20% excess)	100.00
0.257	10	Orange oil terpeneless No. 54125	257.789 mg
0.095	11	Alcohol (ethanol)	95.50 mg
80.00	12	Polysorbate 80	80.00
0.186	13	Butylated hydroxyanisole	186.92 mg
400 IU	14	Vitamin D viosterol in corn oil (oleovitamin D) (25% excess)	833.34 mg
5000 IU	15	Vitamin A; use vitamin A palmitate (1,500,000 AU/g) (50% excess ^a)	16.66
QS	16	Purified water	329
QS	17	Carbon dioxide gas	QS

^a Excess includes 20% manufacturing loss and 30% stability excess.

MANUFACTURING DIRECTIONS

Use carbon dioxide cover at all times, and use stainless steel 316 or higher resistant equipment.

1. Add 300 mL of purified water and the glycerin into a suitable jacketed tank. Start mixing.
2. Add, in this order, nicotinamide, riboflavin-5'-phosphate sodium, Aspetoform M (paraben), benzoic acid, and saccharin sodium.
3. Continue mixing for balance of process.
4. Heat to 90°C to 100°C to dissolve ingredients.
5. In a separate tank, boil at least 15 mL of purified water for at least 15 minutes.
6. Cool while bubbling CO₂ gas into it, and hold at 30°C or lower for use later for making up the volume.
7. Start cooling the main tank. When the temperature reaches 50°C to 60°C, start bubbling CO₂ gas through the solution from the bottom of the tank.
8. Continue cooling to 25°C. Continue the CO₂ gas protection for the balance of the process.
9. Add and dissolve thiamine HCl, pyridoxine HCl, and ascorbic acid.
10. Dissolve orange oil in alcohol, and add.
11. Load approximately 5.25 g of Polysorbate 80 into a separate stainless steel container.
12. Heat to 50°C to 60°C. Add the butylated hydroxyanisole and dissolve with mixing. Remove heat.
13. Add remaining Polysorbate 80 into the container, setting aside a sufficient quantity for rinsing the vitamin containers.
14. Bubble in CO₂ gas while mixing slowly. Stop mixing.
15. Add viosterol and vitamin A palmitate.
16. Rinse bottles with remaining Polysorbate 80, and drain.
17. Mix slowly for at least 30 minutes or longer, if necessary, to provide a clear solution. Continue to bubble CO₂ gas for the entire mixing period.
18. Change CO₂ gas protection on main mixing tank to the top to prevent excessive foaming upon addition of Polysorbate 80 solution.
19. Add Polysorbate 80 solution to the main tank from the bottom of the tank to the top to prevent excessive foaming. Stop mixing.
20. If the volume is less than 1000 mL, adjust the volume with CO₂-saturated purified water made previously to 1000 mL. Mix for at least 1 hour.
21. In a separate tank, boil at least 115 mL of purified water for at least 15 minutes.
22. Cool while bubbling CO₂ gas into it, and hold at 30°C or lower for use later. Stop mixing.
23. Allow to stand for at least 4 hours to eliminate entrapped CO₂ gas.
24. Readjust volume to 1000 mL with CO₂-saturated purified water. Mix for at least 1 hour. Stop mixing.
25. Filter through lint-free paper; do not use filter aids.
26. Recirculate product back to mixing tank until clear.
27. Flush storage tank with CO₂ gas, and continue CO₂ gas protection until product has been filled.
28. Average intake dose is 0.60 mL.

MULTIVITAMIN INSTANT GRANULES

Bill of Materials			
Scale (mg/ sachet)	Item	Material Name	Qty/30 kg (g)
40.00	1	Vitamin A and vitamin D (dry powder + 50,000 IU/g CWD)	200.00
5.00	2	Thiamine mononitrate, with excess	26.00
6.00	3	Riboflavin, with excess	33.00
22.00	4	Nicotinamide	110.00
4.50	5	Pyridoxine hydrochloride	22.00
30.00	6	Calcium D-pantothenate	150.00
0.013	7	Cyanocobalamin; use cyanocobalamin (gelatin-coated, 0.1%)	66.00
230	8	Ascorbic acid powder	1150.00
–	9	Vitamin E acetate dry powder	210.00
4000	10	Sucrose (finely ground)	20,000.00
1000	11	Kollidon® CL-M	5000.00
200	12	Orange flavor	1000.00
400	13	Kollidon® VA 64	2000.00
–	14	Ethanol or isopropanol	~7.00 L

MANUFACTURING DIRECTIONS

1. Pass mixture through a 0.8 mm sieve, and granulate with solution of items 13 and 14 in the fluidized bed.
2. Fill 6 to 12 g of the granules in sachets.
3. If the technology of a fluidized bed is not available, the dry powders of vitamins A, B₁₂, and E should be added after granulation of the other components.
4. Suspend 6 to 12 g (= 1 sachet) in a glass of water (corresponds to 2 to 4 RDA of vitamins).

MULTIVITAMIN MINERAL SYRUP

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
6.65	1	Acid hypophosphorous (50% pure)	6.65
16.47	2	Calcium hypophosphite	16.47
31.68	3	Calcium lactate (powder)	31.68
1.00	4	Methylparaben	1.00
0.20	5	Propylparaben	200.00 mg
1.00	6	Benzoic acid	1.00
150.00	7	Sucrose (granular)	150.00
5.20	8	Ferrous gluconate	5.20
2.00	9	Niacinamide (5% excess)	2.10
0.32	10	Riboflavin-5-phosphate sodium	328.77 mg
1.00	11	D-Pantothenyl alcohol (dexpanthenol) (20% excess)	1.20
0.60	12	Vitamin B ₁₂ (cyanocobalamin) (35% excess)	810.00 µg
0.20	13	Pyridoxine hydrochloride	200.00 mg
0.30	14	Thiamine hydrochloride (regular powder) (55% excess)	465.00 mg
4.78	15	Flavor	4.78
1.94	16	Flavor	1.94
0.64	17	Orange oil, terpeneless	642.00 mg
0.21	18	Lime oil, distilled	214.97 mg
4.28	19	Alcohol (190 proof)	4.28
2.50	20	Saccharin sodium	2.50
14.50	21	Acid ascorbic (white powder/EP) (45% excess)	14.50
3.00	22	Caramel (acid proof)	3.00
2.00	23	Anhydrous citric acid (powder/EP)	2.00
0.01	24	Butylated hydroxyanisole (BHA)	10.00 mg
3.39	25	Corn oil	3.39
0.40	26	Vitamin A palmitate (TN, 1.5 MM UA/g) (40% excess)	560.00 mg
0.08	27	Viosterol in corn oil (syn. oleovitamin D; 1000 mD/g; D ₃ in arachis oil) (40% excess)	112.00 mg
1.50	28	Acacia	1.50
0.12	29	Sodium lauryl sulfate (acetone washed)	127.41 mg
171.00	30	Deionized, purified water	171.00
QS	31	Glucose liquid	QS to 1 L

MANUFACTURING DIRECTIONS

Do not expose this preparation during manufacturing to direct sunlight. Riboflavin is sensitive to light.

1. Add 83.7 mL of purified water to a stainless steel jacketed tank.
2. Add calcium hypophosphite, calcium lactate, parabens, and benzoic acid.
3. Heat mixture to 60 °C with agitation.

4. Shut off mixer, and wash tank free of all powders with 25.9 mL purified water.
5. Heat mixture to and maintain a maximum temperature of 100°C until solution is complete. Do not agitate. Avoid loss of water through evaporation. Cover opening of tank.
6. After solution occurs, take sample from bottom of tank and examine for clarity. Solution must be clear.
7. Add acid hypophosphorous (if used) with mixing.
8. Turn off heat, add 222 g glucose, and start agitator. (*Caution:* Use CO₂ cover throughout. Wherever water is used, it should be CO₂-saturated water.) Dissolve ferrous gluconate in 7.4 mL water CO₂ saturated by heating.
9. Add 278 g glucose with mixing. Add and dissolve sugar.
10. Allow solution to cool to 35°C, and mix well.
11. To 29.6 mL water, add and dissolve nicotinamide, riboflavin, D-pantothenyl alcohol, vitamin B₁₂, pyridoxine, and thiamine. Mix until solution is complete, and add to tank. Dissolve by heat if necessary.
12. Charge flavors into tank.
13. Charge saccharin into tank, and mix until dissolved.
14. Charge ascorbic acid into tank, and mix well.
15. Charge caramel into tank, and mix well. Dissolve citric acid in 3 mL water, and add to mixture.
16. Heat corn oil to 50°C to 60°C, and add and dissolve BHA. Be sure the BHA is completely dissolved before continuing.
17. Cool to room temperature. While cooling oil mixture, saturate with CO₂, and maintain heavy CO₂ coverage for balance of operation.
18. Set aside a small amount of this mixture as a rinse for the vitamin A and viosterol containers.
19. Add vitamin A palmitate TN and viosterol to the cool corn oil mixture, rinsing the containers with the reserved oil.
20. Add the rinse to the bulk. Mix well.
21. Add the acacia to the oil mixture with good mixing.
22. Dissolve sodium lauryl sulfate in 3 mL CO₂-saturated purified water.
23. To avoid excessive foaming, do not bubble CO₂ gas through the water/sodium lauryl sulfate solution.
24. Add the sodium lauryl sulfate solution to the oil mixture, and stir to a thick creamy emulsion.
25. Add 7.56 g glucose to the emulsion with mixing.
26. Blend 13.33 mL CO₂-saturated purified water with 77.04 g glucose, and add emulsion with stirring.
27. Recycle primary emulsion back into holding tank while setting mill.
28. Homogenize until all oil globules are less than 8 µm in diameter using colloid mill with a fine setting.
29. Add primary emulsion to syrup solution with mixing. Add glucose QS to 965 mL, and mix well.
30. Allow to stand overnight to vent entrapped air.

31. Adjust the volume to 1 L using glucose or glucose and CO₂-saturated water.
32. Strain through 149 µm aperture or similar screen into clean reserve tank, and recheck volume.
33. Seal tank under heavy CO₂ until filled.

MULTIVITAMIN + MINERALS TABLETS WITH BETA-CAROTENE (1 RDA OF VITAMINS)

FORMULATION

Beta-carotene dry powder, Betavit 20%, 16.5 g; thiamine mononitrate, 1.7 g; riboflavin, 1.9 g; nicotinamide (Degussa), 22.0 g; calcium D-pantothenate, 12.0 g; pyridoxine hydrochloride, 2.2 g; ascorbic acid, crystalline, 72.0 g; vitamin E acetate dry powder 50%, 66.0 g; ferrous fumarate, 54.7 g; magnesium oxide, high-density type, 165.8 g; copper II oxide, powder, 2.5 g; manganese sulfate, 6.9 g; zinc oxide, 18.7 g; potassium chloride (Baker), 76.3 g; dicalcium phosphate, DI-TAB, 550.0 g; Avicel™ PH 102, 60.0 g; croscarmellose, 32.0 g; Syloid® 244 FP (Grace), 6.0 g; stearic acid, 6.0 g; magnesium stearate, 6.0 g.

MANUFACTURING DIRECTIONS

1. Pass all ingredients through a 0.8 mm sieve, blend in a mixer, and then compress with medium to high compression force at 1193 mg.

MULTIVITAMIN ORAL GEL

FORMULATION

- I. Vitamin A palmitate, 1.7 million IU/g, 110 mg; vitamin E acetate, 1060 mg; butylated hydroxytoluene (BHT), 500 mg; Cremophor RH 40, 20 g.
- II. Water, 725 g.
- III. Thiamine hydrochloride, 355 mg; riboflavin, 35 mg; pyridoxine hydrochloride, 177 mg; cyanocobalamin gelatin coated 1%, 35 mg; nicotinamide, 353 mg; folic acid, 35 mg; dexpantenol, 353 mg; EDTA sodium, 300 mg; ferrous sulfate (7H₂O), 438 mg; manganese chloride (4H₂O), 638 mg; potassium iodide, 115 mg.
- IV. Kollidon® 90 F, 50 g; Lutrol F 127, 100 g; Lutrol F 127 [1], 100 g; Total amount: approximately 1000 g.

MANUFACTURING DIRECTIONS

1. Heat mixture I to approximately 60°C to obtain a clear solution.
2. Slowly add the water II to the well-stirred solution I.
3. Dissolve III and IV in this mixed solution (step 2) at room temperature, cool to approximately 6°C, add IV, and stir until all Lutrol F 127 is dissolved.
4. Maintain the cool temperature until the air bubbles escape.

MULTIVITAMIN ORAL GEL VETERINARY

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (mg)
18,700 IU	1	Vitamin A palmitate (1.7 MM IU/g)	110.00
1.06	2	Vitamin E acetate	1060.00
0.50	3	BHT	500.00
20.00	4	Cremophor RH 40	20.00 g
725.00 g	5	Water	725.00 g
0.355	6	Thiamine hydrochloride	355.00
0.035	7	Riboflavin	35.00
0.177	8	Pyridoxine hydrochloride	177.00
0.035	9	Cyanocobalamin (gelatin coated, 1%)	35.00
0.353	10	Nicotinamide	353.00
0.035	11	Folic acid	35.00
0.353	12	Dexpanthenol	353.00
0.30	13	EDTA sodium	300.00
0.438	14	Ferrous sulfate (7H ₂ O)	438.00
0.638	15	Manganese chloride (4H ₂ O)	638.00
0.115	16	Potassium iodide	115.00
50.00	17	Kollidon® 90 F	50.00 g
100.00	18	Lutrol F 127	100.00 g
100.00	19	Lutrol F 127	100.00 g

MANUFACTURING DIRECTIONS

1. Heat mixture of items 1 to 4 to approximately 60°C to obtain a solution.
2. Slowly add the water (item 5) to the well-mixed solution.
3. Dissolve items 6 to 16 and item 17 separately in this mixed solution at room temperature, cool to approximately 6°C, add item 19, and stir until all Lutrol F127 clear is dissolved.
4. Maintain the cool temperature until the air bubbles escape.

MULTIVITAMIN ORAL GEL WITH LINOLEIC AND LINOLENIC ACID

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/100 mL (mg)
0.05	1	Evening primrose oil (Epopure®, Prima Rosa/SA)	5.00 mL
0.30	2	Vitamin A palmitate (1.7 million IU/g)	30.00
0.19	3	Vitamin E acetate	19.00
0.00150	4	Vitamin D ₃ (40 million IU/g)	150.00 µg
200.00	5	Cremophor RH 40	20.00 g
550.00	6	Water	55.00 g
0.03	7	Thiamine hydrochloride	3.00
0.03	8	Riboflavin	3.00
0.15	9	Pyridoxine hydrochloride	15.00
0.001	10	Cyanocobalamin (crystalline)	10.00 µg
0.001	11	Calcium D-pantothenate	10.00
0.005	12	Nicotinamide	50.00
10.00	13	Ascorbic acid (crystalline)	1.00 g
140.00	14	Lutrol F 127	14.00 g
50.00	15	Lutrol F 127	5.00 g

MANUFACTURING DIRECTIONS

1. Prepare mixture of items 1 to 5, and heat to approximately 65°C.
2. Slowly add the warm water (item 6) (65°C) to the well-stirred mixture as before.
3. Dissolve items 7 to 14 at 20°C to 25°C in this clear solution.
4. Cool the obtained solution to approximately 5°C, and dissolve the rest of the Lutrol F 127 (item 15).
5. Maintain the cool temperature until the air bubbles escape.
6. A clear yellow gel is obtained. 5 mL of evening primrose oil Epopure® contains 3.5 g linoleic acid and 0.45 g gamma-linolenic acid.

MULTIVITAMIN SYRUP

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/100 mL (mg)
170 IU	1	Vitamin A palmitate (1.7 million IU/g)	10.00
2.00 IU	2	Vitamin D (40 million IU/g)	0.05
1.00	3	Vitamin E acetate	100.00
0.02	4	BHT	2.00
45.00	5	Cremophor RH 40	4.50 g
100.00	6	Water	10.00 g
450.00	7	Saccharose	45.00 g
2.00	8	Methylparaben	200.00
0.08	9	Citric acid	80.00
9.60	10	Glycerol	9.60 g
250.00	11	Water	25.00 g
0.15	12	Thiamine hydrochloride	15.00
0.15	13	Riboflavin 5'-phosphate sodium	15.00
0.55	14	Nicotinamide	55.00
0.15	15	Pyridoxine hydrochloride	15.00
3.00	16	Ascorbic acid (crystalline)	300.00
1.00	17	Sorbic acid	100.00
5.00	18	Propylene glycol (Pharma)	5.00 g

MANUFACTURING DIRECTIONS

1. Mix items 1 through 5 and heat to 60°C.
2. Separately heat item 2 to approximately 60°C.
3. Mix these two solutions slowly, stirring well to obtain a clear solution.
4. Dissolve items 7 to 9 in the hot solution of items 10 and 11 to obtain a clear solution.
5. Add to previous solution.
6. Add items 12 to 18, and adjust the pH to 4.0 to 4.2.
7. Pass nitrogen through the solution for 10 minutes, and fill under nitrogen cover.
8. Provides 1 to 2 RDA/20 mL.

MULTIVITAMIN SYRUP

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/100 mL (mg)
0.17	1	Vitamin A palmitate (1.7 MM IU/g)	17.00
0.001	2	Vitamin D ₃ (40 MM IU/g)	0.10
0.01	3	BHT	1.00
30.00	4	Cremophor RH 40	3.00 g
1.00	5	Parabens	100.00
170.00	6	Water	17.00 g
0.50	7	Thiamine hydrochloride	50.00
0.20	8	Riboflavin phosphate sodium	20.00
0.20	9	Pyridoxine hydrochloride	20.00
2.50	10	Ascorbic acid (crystalline)	250.00
50.00	11	Water	5.00 g
–	12	Sugar syrup	Add 100 mL

MANUFACTURING DIRECTIONS

1. Heat mixture of items 1 to 4 to approximately 65°C.
2. Stir well, and very slowly add item 6 to warm solution (65°C).
3. Mix with solution of items 7 to 11, and add item 12 to make up the volume.
4. *Note:* Parabens are generally a 1:10 ratio of methyl and propyl parabens.

MULTIVITAMIN TABLET CORES WITH BETA-CAROTENE (1–2 RDA OF VITAMINS)

FORMULATION

Vitamin A acetate dry powder, 500,000 IU/g, 1.27%; beta-carotene dry powder Betavit 10%, 11.50%; thiamine mononitrate, 1.24%; riboflavin, 0.96%; nicotinamide, 11.50%; calcium D-pantothenate, 1.91%; pyridoxine hydrochloride, 1.15%; cyanocobalamin gelatin coated 1%, 2.86%; D-biotin, 1% trituration, 1.91%; folic acid, 0.09%; ascorbic acid, 38.20%; vitamin D₃ dry powder, 100,000 IU/g, 0.76%; vitamin E acetate dry powder 50 DC, 28.40%; phytomenadione dry powder 5% GFP, 0.19%, 270.2 g; Ludipress®, 69.1 g; magnesium stearate, 3.3 g.

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with high compression force at 459 mg.

MULTIVITAMIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Thiamine mononitrate (powder), USP (5% excess; 5–10%)	10.50
5.00	2	Riboflavin, USP	5.00
100.00	3	Nicotinamide niacinamide (white powder), USP	100.00
200.00	4	Ascorbic acid; use sodium ascorbate (microcrystalline) (2% excess)	229.47
40.00	5	Calcium pantothenate; use calcium pantothenate racemic (20% excess)	48.00
5.00	6	Pyridoxine hydrochloride, USP	5.00
6.10	7	Povidone (PVP K-25), USP	6.10
–	8	Alcohol dehydrated (200 proof), USP	25.00 mL
21.90	9	PEG-8000, NF	21.90
25,000 IU	10	Vitamin A (275,000 IU ^a) (20% excess)	7.50 mg
400 IU	11	Vitamin D as D ₂ powder (850 mD ^a)	1.77
6.00	12	Vitamin B ₁₂ oral powder in gelatin (5% excess)	6.30
16.00	13	PEG-8000 (milled), NF	16.00
5.30	14	Magnesium stearate	5.30
23.20	15	Talc	23.20

^a Adjust quantities according to regulatory allowance for OTC label.

MANUFACTURING DIRECTIONS

Vitamin A is susceptible to destruction by oxidation and also excessive exposure to actinic light and moisture. Oxidation and destruction are catalyzed by traces of copper and other heavy metals. Dry granulation and compression of this tablet should be done where RH is less than 40%. Protect with CO₂ at blending and storage stages.

1. Load the following into a suitable mixer (screen if necessary): thiamine mononitrate, riboflavin, nicotinamide, sodium ascorbate, calcium pantothenate, and pyridoxine HCl.
2. Dissolve the PVP (item 7) in approximately 16 mL alcohol.
3. Add PVP solution to the powders from first step, and QS with alcohol to mass.
4. Granulate the mass through a 4 mesh (4.76 mm aperture or similar) screen.
5. Dry at 50°C until the LOD is less than 1%.
6. Grind to 16 mesh (1.2 mm or similar).

7. Melt the PEG-8000 (item 10), and incorporate vitamins A and D with thorough agitation.
8. Mix until mass cools and becomes granular.
9. Screen through a 16 mesh (1.2 mm aperture or similar) screen, and grind coarse material through a Fitz mill or similar No. 2 band (1.59 mm aperture or similar) at slow speed or a 16 mesh (1.2 mm aperture or similar).
10. Reserve for lubrication.
11. Mix milled PEG-8000 (item 13) with talc and magnesium stearate, and pass through a Fitz mill using a 60 mesh (250 µm aperture or similar) screen (impact forward, high speed).
12. If a Fitz mill is unavailable, pass the mixture through a 30 mesh (595 µm aperture or similar) screen.
13. Load base granulation into a mixer along with vitamin B₁₂, the preceding mixture, and the PEG-coated vitamins A and D mixture from the first step. Blend thoroughly.
14. Store dry mixed granulation with CO₂ protection.
15. Compress.
16. Apply a PVP subcoat, a CAP-carbowax, or other aqueous coating, and finish with a polish coat (see Appendix).

MULTIVITAMIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
10.00	1	Riboflavin	10.00
100.00	2	Niacinamide (white powder)	100.00
5.00	3	Pyridoxine hydrochloride (15% excess)	5.75
15.00	4	Thiamine mononitrate (powder) (5% excess)	15.75
500.00	5	Ascorbic acid, EP	500.00
100.00	6	Lactose	100.00
40.00	7	Povidone (K-29-32)	40.00
100.00	8	Cellulose microcrystalline (Avicel™ PH101)	100.00
–	9	Alcohol SD 3A (200 proof)	QS
20.00	10	Calcium pantothenate; use racemic calcium pantothenate, USP (80 mesh; 15% excess)	46.00
11.50	11	Magnesium oxide (light powder calcined)	11.50
500.00	12	Ascorbic acid	500.00
3.83	13	Povidone (K-29-32)	3.83
–	14	Alcohol SD 3A (200 proof)	QS
4.00 µg	15	Vitamin B ₁₂ ; use vitamin B ₁₂ oral powder in gelatin (15% excess)	4.60
28.00	16	Acid stearic	28.00
9.60	17	Magnesium stearate	9.60

MANUFACTURING DIRECTIONS

1. Dry blend the riboflavin, niacinamide, pyridoxine hydrochloride, thiamine mononitrate, ascorbic acid (item 5), and lactose for 10 minutes.
2. Dissolve the povidone (item 7) in 75 mL of alcohol (item 9).
3. While mixing in mass mixer, add the povidone solution to mass, and continue mixing for 10 minutes or until a satisfactory granule mass is obtained.
4. Additional alcohol may be added if required.
5. Granulate the mass through a 15.9 mm screen using a comminuting mill (knives forward, slow speed) or a 4 mm screen on an oscillating granulator.
6. Dry the granules between 41°C and 49°C in a hot air oven (for approximately 8 hours) or fluid-bed dryer until moisture content is less than 1.5%.
7. Dry screen the granule through a 1 mm screen on an oscillating granulator.
8. Dry blend the calcium pantothenate and magnesium oxide in a suitable mixer for 10 minutes.
9. Dissolve the povidone (item 13) in 20 mL alcohol (item 14).
10. While mixing, add the povidone solution, and mix to produce a suitable mass.
11. Additional alcohol may be added if required.
12. Granulate the mass through a 15.9 mm aperture screen using a comminuting mill (knives forward, slow speed) or a 4 mm screen on an oscillating granulator.
13. Dry the granule at 45 ° C in a hot air oven until moisture content is less than 1.5%.
14. Dry screen granule through a 1.0 mm screen on an oscillating granulator.
15. Mix the two granules made separately in a suitable mixer.
16. Add vitamin B₁₂ powder, and blend for 10 minutes. If necessary, screen the stearic acid and magnesium stearate through a 250 µm screen.
17. Add the remainder of the granule together with the magnesium stearate and stearic acid to the mixer, and blend for 10 minutes.
18. Compress and coat (see Appendix).

MULTIVITAMIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
10.00	1	Riboflavin	10.00
100.00	2	Niacinamide (white powder)	100.00
5.00	3	Pyridoxine hydrochloride (15% excess)	5.75
15.00	4	Thiamine mononitrate (powder) (5% excess)	15.75
40.00	5	Povidone (K-29-32)	40.00
25.00	6	Povidone (K-29-32)	25.00
–	7	Alcohol SD 3A (200 proof)	QS
13.50	8	Stearic acid (fine powder)	13.50
2.70	9	Magnesium stearate	2.70

MANUFACTURING DIRECTIONS

1. Mill the niacinamide, riboflavin, pyridoxine hydrochloride, and thiamine mononitrate through a 500 µm screen on a comminuting mill (impact forward, slow speed).
2. Load screened material from previous step into a mass mixer, add the povidone (item 5) and the cellulose microcrystalline, and dry blend for 5 to 15 minutes.
3. While mixing in the mass mixer, add alcohol (item 7) to mass, and continue mixing for 10 minutes or until a satisfactory granule mass is obtained.
4. If necessary, granulate the mass through a 15.9 mm screen using a comminuting mill (knives forward, slow speed) or a 4 mm screen on an oscillating granulator.
5. Dry the granule between 41°C and 49°C in a hot air oven (for approximately 8 hours) or fluid-bed dryer until moisture content is less than 1.5%.
6. Dry screen the granules through a 1 mm screen on an oscillating granulator.
7. Load ascorbic acid and povidone (item 6) into the mixer, and dry-blend for 10 minutes.
8. While mixing, add 15 mL of alcohol (item 7), and mix until a satisfactory mass is formed, adding more alcohol if necessary. If necessary, screen through a 4.00 mm screen, and load onto trays.
9. Dry at 49°C for 8 hours.
10. Dry screen the granules through a 1 mm aperture screen on an oscillating granulator.
11. Screen the magnesium stearate and stearic acid through a 500 µm aperture screen.
12. Mix the two granules, add the screened lubricants, and blend for 20 minutes.
13. Coat with a protective subcoat, a color coat, and a polish coat (see Appendix).

MULTIVITAMIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
10.00	1	Vitamin A acetate (dry powder; 500,000 IU/g)	10.00
2.20	2	Thiamine mononitrate	2.20
2.20	3	Riboflavin	2.20
16.50	4	Nicotinamide	16.50
11.50	5	Calcium D-pantothenate	11.50
2.20	6	Pyridoxine hydrochloride	2.20
6.00	7	Cyanocobalamin (dry powder, 0.1%)	6.00
85.00	8	Ascorbic acid (powder)	85.00
31.00	9	Vitamin E acetate (dry powder; SD 50)	31.00
321.00	10	Ludipress ^{®a}	321.00
21.00	11	Kollidon [®] VA 64	21.00
3.00	12	Magnesium stearate	3.00
7.20	13	Orange flavor	7.20
2.50	14	Saccharin sodium	2.50

^a Can be replaced with 300 g of microcrystalline cellulose (Vitalcel[®]).

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, mix, and press with medium compression force (15 kN).
2. Compress 500 mg in 12 mm biplanar punches.

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
2.00	1	Thiamine hydrochloride	2.20
2.20	2	Riboflavin	2.20
11.00	3	Calcium D-pantothenate	11.00
2.20	4	Pyridoxine hydrochloride	2.20
300.00	5	Mannitol	300.00
20.00	6	Kollidon [®] 30 or Kollidon [®] VA 64	20.00
—	7	Isopropanol	~80
5000 IU vitamin A, 500 IU vitamin D	8	Vitamins A and D; use crystallites of vitamin A acetate + vitamin D ₃ dry powder (500,000 + 50,000 IU/g) (10% excess)	11.00
31.00	9	Vitamin E acetate (dry powder; SD 50)	31.00
0.06	10	Cyanocobalamin; use gelatin- coated cyanocobalamin (0.1%)	6.00
80.00	11	Ascorbic acid (crystalline)	80.00
20.00	12	Nicotinamide	20.00
65.00	13	Avicel [™] PH101	65.00
7.00	14	Orange flavor	7.00
2.00	15	Saccharin sodium	2.00
3.00	16	Magnesium stearate	3.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 5 with solution of items 6 and 9.
2. Pass through a 0.8 mm sieve, mix with items 8 to 16, and press with medium compression force.
3. Compress 560 mg in 12 mm biplanar punches.

MULTIVITAMIN TABLETS, DC
(1–2 RDA OF VITAMINS)

FORMULATION

Vitamin A acetate dry powder, 500,000 IU/g, 10.0 g; thiamine mononitrate, 2.2 g; riboflavin, 2.2 g; nicotinamide, 16.5 g; calcium D-pantothenate, 11.5 g; pyridoxine hydrochloride, 2.2 g; cyanocobalamin, 0.1% dry powder, 6.0 g; ascorbic acid, powder, 85.0 g; vitamin E acetate dry powder SD 50, 31.0 g; Ludipress[®], 321.0 g; magnesium stearate, 3.0 g; orange flavor, 7.2 g; saccharin sodium, 2.5 g.

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, mix, and press with medium compression force (15 kN).

MULTIVITAMIN TABLETS FOR DOGS

FORMULATION

Vitamins A and D₃ dry powder, 500,000 and 50,000 IU/g, 4.0 g; thiamine mononitrate, 0.5 g; riboflavin, 0.7 g; nicotinamide, 5.0 g; calcium D-pantothenate, 1.0 g; pyridoxine hydrochloride, 0.5 g; cyanocobalamin gelatin coated 1%, 0.5 g; folic acid, 0.05 g; choline bitartrate, 20.0 g; vitamin E acetate dry powder SD 50, 20.0 g; Ludipress[®], 196.0 g; magnesium stearate, 2.0 g.

MANUFACTURING DIRECTIONS

Pass all components through a 0.8 mm sieve, mix, and press with low compression force at 250 mg.

MULTIVITAMIN TABLETS FOR DOGS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
2000 IU Vitamin A, 200 IU Vitamin D	1	Vitamin A + vitamin D ₃ (dry powder; 500,000 + 50,000 IU/g)	4.00
0.50	2	Thiamine mononitrate	0.50
0.70	3	Riboflavin	0.70
5.00	4	Nicotinamide	5.00
1.00	5	Calcium D-pantothenate	1.00
0.50	6	Pyridoxine hydrochloride	0.50
0.50	7	Cyanocobalamin (gelatin coated, 1%)	0.50
0.05	8	Folic acid	0.05
20.00	9	Choline bitartrate	20.00
20.00	10	Vitamin E acetate (dry powder, SD 50)	20.00
196.00	11	Ludipress®	196.00
2.00	12	Magnesium stearate	2.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with low compression force.
2. Compress 250 mg using 8 mm biplanar punches.

MULTIVITAMIN TABLETS WITH BETA-CAROTENE

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
1.00	1	Beta-carotene; use beta-carotene dry powder (Betavit, 10%)	10.00
2.00	2	Thiamine mononitrate	2.00
2.00	3	Riboflavin	2.00
16.00	4	Nicotinamide	16.00
11.00	5	Calcium D-pantothenate	11.00
2.00	6	Pyridoxine hydrochloride	2.00
0.06	7	Cyanocobalamin; use cyanocobalamin dry powder (0.1%)	6.00
85.00	8	Ascorbic acid (powder)	85.00
31.00	9	Vitamin E acetate (dry powder; SD 50)	31.00
321.00	10	Ludipress®	321.00
7.00	11	Kollidon® VA 64	7.00
3.00	12	Magnesium stearate	3.00
7.00	13	Orange flavor	7.00
2.00	14	Saccharin sodium	2.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, mix, and press with medium compression force.
2. Compress 508 mg using 12 mm planar punches.

MULTIVITAMIN TABLETS WITH COPPER AND ZINC

FORMULATION

Vitamin mixture (thiamine mononitrate), 3.9%; riboflavin 100, 0.4%; nicotinamide 10.1%; calcium D-pantothenate, 2.9%; pyridoxine hydrochloride, 1.2%; cyanocobalamin gelatin coated 0.1%, 2.6%; folic acid, 0.1%; ascorbic acid fine powder, 63.4%; vitamin E acetate dry powder 500 SD, 9.1%; copper oxide, 0.3%; zinc sulfate, 6.0%, 1000 g; Aerosil®, 200, 5 g; Ludipress®, 150 g; Avicel™ PH102, 120 g; Kollidon® VA64, 25 g; magnesium stearate, 10 g; talc, 10 g.

MANUFACTURING DIRECTIONS

Pass all components through a 0.8 mm sieve, mix, and press with high compression force at 1350 mg.

MULTIVITAMIN WITH BETA-CAROTENE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
2.85 IU	1	Vitamin A acetate (dry powder; 500,000 IU/g)	5.47
5.00	2	Beta-carotene; use beta-carotene dry powder (Betavit, 10%)	50.00
15.34	3	Thiamine mononitrate	15.34
4.13	4	Riboflavin	4.13
50.00	5	Nicotinamide	50.00
8.23	6	Calcium D-pantothenate	8.23
5.00	7	Pyridoxine hydrochloride	5.00
0.04	8	Cyanocobalamin; use gelatin-coated cyanocobalamin (1%)	4.00
0.04	9	D-Biotin; use 1% trituration	4.00
0.38	10	Folic acid	0.38
165.00	11	Ascorbic acid	165.00
327.00	12	Vitamin D ₃ (dry powder; 100,000 IU/g)	3.27
122.00	13	Vitamin E acetate (dry powder; SD 50)	122.00
0.41	14	Phytomenadione; use phytomenadione dry powder (5% GFP)	0.82

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with high compression force.
2. Compress 432 mg in 12 mm biplanar punches.

MULTIVITAMIN WITH FLUORIDE INFANT DROPS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
8.00	1	Niacin; use niacinamide (5% excess)	0.82
0.80	2	Riboflavin, USP; use riboflavin-5-phosphate sodium (2% excess)	
0.50	3	Methylparaben	0.50
1.00	4	Benzoic acid	1.00
5000 IU	5	Vitamin E; use D-alpha-tocopheryl PEG-1000 succinate (20% excess)	13.826
400 IU	6	Vitamin D; use viosterol in corn oil (syn. oleovitamin D) (25% excess)	0.522
1500 IU (0.45)	7	Vitamin A palmitate (synthetic A palmitate, 1 MM U/g), USP	1.44
35.00	8	Ascorbic acid (white powder), USP (33% excess)	46.55
0.50	9	Thiamine hydrochloride (44% excess)	0.72
0.40	10	Pyridoxine; use pyridoxine hydrochloride	0.486
0.25	11	Fluoride; use sodium fluoride (powder)	0.5526
4.013	12	Caramel (acid proof)	4.013
0.257	13	Orange oil terpeneless	0.257
QS	14	Alcohol (ethanol; 190 proof)	10.00 mL
QS	15	Distilled purified water	QS
QS	16	Hydrochloric acid	QS
QS	17	Sodium hydroxide	QS
QS	18	Carbon dioxide gas	QS

MANUFACTURING DIRECTIONS

Use only stainless steel tanks, and minimize vortex formation to prevent aeration. Product attacks glass, so avoid contact with glass.

1. Place 350 mL of purified water into the stainless steel jacketed main tank.
2. Start mixing.
3. Add, in this order, niacinamide, riboflavin, sodium fluoride, methyl paraben, and benzoic acid.
4. Rinse the interior walls of the tank with approximately 16 mL purified water.
5. Continue mixing for the balance of the process.

6. Heat the main tank to 95°C to dissolve ingredients.
7. When the solution is complete, cool to less than 85°C (range: 80–90 °C).
8. The main tank will have to be heated to 85°C for this step.
9. Add vitamin E to another tank, if necessary, by heating vitamin E container.
10. Melt vitamin E in the tank.
11. Add viosterol and vitamin A, and heat to 60°C to 65°C with mixing.
12. Start bubbling in CO₂.
13. Mix slowly for 10 minutes or longer to produce a clear solution.
14. Start CO₂ gas protection on the main mixing tank, and continue for the balance of the process.
15. With the main batch at 85°C to 90°C, add the solution of vitamins A, D, and E at 60°C to 65°C, with mixing.
16. The addition may cause the temperature of the main batch to drop below the specified range, so readjust to 85°C to 90°C.
17. Mix and maintain at this temperature until solution is complete, after which cool to less than 30°C.
18. Add the glycerin with mixing.
19. Adjust the temperature to 25°C ± 5°C, and maintain at this temperature before proceeding.
20. Add and dissolve with mixing, in this order, ascorbic acid, thiamine, pyridoxine, and caramel.
21. Rinse the caramel container with approximately 3 mL of water, and add the rinsings.
22. Rinse the tank inner walls and mixer shaft with approximately 3 mL water.
23. Dissolve the orange oil with mixing in the alcohol, and add to the solution.
24. Continue mixing for at least 30 minutes to ensure a homogeneous product.
25. Stop mixing, and take pH (range: 3.1–3.3). If necessary, adjust with 10% sodium hydroxide or 10% hydrochloric acid, prepared by adding 1 mL hydrochloric acid (reagent-grade) with 3.3 mL purified water. Mix.
26. Stop mixing, and allow to stand for at least 4 hours to eliminate entrapped CO₂ gas.
27. In a properly cleaned separate tank, boil at least 65 mL of purified water for at least 15 minutes.
28. Cool while bubbling CO₂ into it, and hold at 30°C.
29. Adjust pH to the range of 3.1 to 3.3.
30. Filter using a lint-free paper. Do not use filter aids.
31. Recirculate product back to main mixing tank until clear.
32. Flush a storage tank with CO₂ for at least 10 minutes with the CO₂ valve completely open.
33. Filter product into this storage tank.
34. Fill under CO₂ cover.

MULTIVITAMIN WITH ZINC TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Niacin; use niacinamide (white powder)	100.00
750.00	2	Ascorbic acid; use microcrystalline sodium ascorbate ^a	843.68
20.00	3	Vitamin B ₆ ; use pyridoxine hydrochloride	34.03
QS	4	Povidone	40.00
15.00	5	Thiamine hydrochloride; use thiamine mononitrate (powder)	17.47
15.00	6	Riboflavin	16.50
20.00	7	Pantothenic acid; use calcium pantothenate	32.60
0.49	8	Folic acid (powder)	0.52
12.00 µg	9	Vitamin B ₁₂ ; use cyanocobalamin oral powder in gelatin 1:1000	15.00
60.00	10	Vitamin E (D,L- α -tocopherol acetate)	60.00
—	11	Alcohol SD 3A (200 proof)	138 mL
22.50	12	Elemental zinc (pure zinc sulfate powder)	55.61
4.00	13	Povidone	4.00
—	14	Alcohol SD 3A (200 proof)	4 mL
—	15	Alcohol SD 3A (200 proof)	9 mL
10.80	16	Magnesium stearate	10.80
40.00	17	Cellulose microcrystalline	40.00
3.20	18	Silicon dioxide colloidal	3.20
6.00	19	Colloidal silicon dioxide	6.00

^a May use ascorbic acid (750.00 g) instead. The quantity of povidone is reduced to 6.34 g, and the amount of alcohol SD used is adjusted.

MANUFACTURING DIRECTIONS

1. Mill niacinamide, sodium ascorbate, pyridoxine, povidone (item 4), and thiamine through a comminuting mill with hammers (impact forward) at high speed and fitted with a 0 band (686 µm aperture or similar) screen.
2. Place millings into mass mixer.
3. Screen riboflavin, calcium pantothenate, folic acid, and vitamins B₁₂ and E through an 840 µm screen.
4. Place into mass mixer, and dry mix for 5 to 10 minutes.
5. Add 89 mL alcohol to powder while mixing.
6. Add additional alcohol if required (approximately 49 mL) to achieve satisfactory granulation.
7. Pass wet mass through 5/8 in. band (15.88 mm aperture or similar) screen, and spread out on paper-lined trays.
8. Dry granulation at 49°C, and dry until LOD is NMT 1.5%.
9. Sift dry granule through 1.19 mm screen, and coarse grind granule through a No. 2 band (1.59 mm aperture or similar) screen fitted on a comminuting mill (knives forward, medium speed) to polyethylene-lined drums.
10. Mill zinc sulfate and povidone through a comminuting mill fitted with a 0 band (686 µm aperture or similar) screen at high speed with impact (hammers) forward.
11. Charge millings into mass mixer for 5 to 10 minutes.
12. Add 3.3 mL alcohol (item 14) to powders from first step while mixing.
13. If necessary, use additional alcohol (up to 0.83 mL) to achieve satisfactory granulation.
14. Granulate wet mass through 5/8 in. band (15.88 mm aperture or similar) screen, and spread out on paper-lined trays.
15. Dry granule at 49°C, and dry until LOD is NMT 1.5%.
16. Sift dry granule through 1.19 mm screen and coarse grind granule through a No. 2 band (1.59 mm aperture or similar) screen fitted on a comminuting mill (knives forward, medium speed), and transfer to polyethylene-lined drums.
17. Charge approximately one-tenth of vitamin granulation into blender.
18. Premix magnesium stearate, microcrystalline cellulose, and silicon dioxide in a bowl, and sift through 840 µm screen into blender.
19. Charge another one-tenth of vitamin granulation into blender, and blend for 5 minutes.
20. Discharge a portion of granulation from the blender, and check for white lumps.
21. If lumps are present, discharge entire granulation through a 1.68 mm aperture screen to break lumps; then, return it to blender.
22. Charge zinc granulation into the blender.
23. Charge remaining vitamin granulation into blender, and blend for 15 minutes.
24. Discharge blender into polyethylene-lined drums, tie liners, close and seal drums, and deliver to storage area.
25. Compress and coat (see Appendix).

NAPHAZOLINE EYE DROPS

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
17.71	1	Acid boric	17.71
1.50	2	Hydroxypropylmethylcellulose 2910 (400 cps)	1.50
0.36	3	Borax (sodium borate)	0.36
1.00	4	Disodium edetate	1.00
0.12	5	Naphazoline hydrochloride	0.12
0.17 mL	6	Benzalkonium chloride; use benzalkonium chloride solution (17%)	0.63 mL
QS	7	Water for injection	QS to 1 L

MANUFACTURING DIRECTIONS

Use thoroughly cleaned and rinsed, steam-jacketed glass-lined or stainless steel tank equipped with a speed-controlled agitator. The tank should have a cover. Foaming occurs because of benzalkonium chloride, which concentrates in foam. Processing and filling systems should be designed to minimize foaming and allow rapid dissipation of foaming.

1. Place 80% of final volume of water into mixing tank. Heat deionized water to 90°C.
2. While agitating, add and disperse hydroxypropylmethylcellulose by slowly sprinkling it on the surface of solution. Mix to avoid excessive foaming.
3. Allow 15 minutes for hydration of hydroxypropylmethylcellulose before discontinuing heating and allowing cooling to 40°C.
4. While agitating, add and dissolve disodium edetate, benzalkonium chloride, boric acid, and sodium borate.
5. Continue cooling to 30°C (25–30°C). Discontinue agitation, and QS to 950 mL with deionized water.
6. Start agitator, and mix for at least 15 minutes at 30°C. Discontinue agitation and cooling.
7. Naphazoline hydrochloride concentrate solution: dissolve naphazoline hydrochloride in 50 mL of deionized water, and sterile-filter solution through a previously sterilized Millipore filter unit containing 0.22 µm membrane.
8. Hold naphazoline solution under aseptic conditions for addition to bulk solution (after it has been autoclaved and cooled).
9. Prefiltration: Methylcellulose solutions filter at a slow rate, so use an appropriate filter.
10. Recirculate solution until clear, and transfer to holding or sterilization.
11. Sterilization and filling: Use either heat sterilization or sterile filtration.

12. Heat sterilization: Sterilize at 112°C to 115°C for 60 minutes, cool solution to 25°C to 30°C, and aseptically add the sterile naphazoline solution. Mix well.
13. Set up a previously sterilized filter and transfer line with 10 µm stainless steel FulFlo filter or equivalent.
14. Aseptically fill sterile solution into sterilized containers, and apply sterile closure components.
15. Sterile filtration: Use Pall cartridge AB 1 NR 7p (pr 8P) with Sartorius Cartridge 526-07 H 1. Prepare and steam sterilize the recommended filter units.
16. Aseptically fill the sterilized solution to which the naphazoline solution has been added into each sterilized container, and apply sterile closure.

NEOMYCIN GEL

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
0.50	1	Neomycin sulfate	0.50
50.00	2	Propylene glycol	50.00
5.00	3	Parabens	5.00
200.00	4	Lutrol F 127	200.00
745.00	5	Water	745.00

MANUFACTURING DIRECTIONS

1. Dissolve the parabens and Lutrol F 127 in water heated to approximately 80 °C.
2. Add the propylene glycol, and dissolve neomycin sulfate.
3. Cool to room temperature when the air bubbles escape.
4. Alternative: Dissolve parabens in hot water, cool to 5°C to 10°C, dissolve Lutrol F 127, add propylene glycol, and dissolve neomycin sulfate.
5. Maintain the cool temperature until the air bubbles escape.

NIACIN TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
1000.00	1	Niacin	1000.00
40.00	2	PVP	40.00
10.00	3	Silicon dioxide	10.00
15.00	4	Sodium stearyl fumarate	15.00
400.00	5	Water	400.00

MANUFACTURING DIRECTIONS

1. Niacin is placed in a fluidized-bed apparatus.
2. An aqueous PVP solution (in 85 g of water) is sprayed to get granules.
3. The granules thus obtained are subsequently dried and passed through a sieve (1 mm mesh), and sodium stearyl fumarate is weighed, added, and blended in a drum mixer.
4. The resulting mixture is pressed into tablets 1065 mg.
5. These tablet cores are then coated with the following formulation: ethylcellulose (Ethocel™), 10mL; PVP (povidone), 5.50 mg; stearic acid, 2.40 mg.
6. Ethocel™, povidone, and stearic acid are first dissolved in denatured alcohol (180 g).
7. The coating solution is then sprayed onto the tablet cores in a coating pan.

NICOTINAMIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
300.00	1	Nicotinamide (Degussa)	320.00
160.00	2	Avicel™ PH101	160.00
16.00	3	Kollidon® VA 64	16.00
3.00	4	Magnesium stearate	3.00
3.00	5	Aerosil® 200	3.00

MANUFACTURING DIRECTIONS

1. With medium compression force, compress 506 mg using 12 mm biplanar punches.

NICOTINIC ACID TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Quantity/1000 Tablets (g)
375.00	1	Nicotinic acid	375.00
188.70	2	Hydroxypropylmethylcellulose E10 M premium	188.70
12.90	3	Povidone K90	12.90
5.80	4	Stearic acid (Hystrene 5016)	5.80

MANUFACTURING DIRECTIONS

1. Combine one-half of the quantity of items 1 to 3, and dry mix the powder bed mixed in a Littleford granulator, with choppers on, for approximately 1 minute.

2. At the completion of the 1 minute premix cycle, slowly spray an appropriate quantity, approximately three times the quantity of item 3, for a period of 5 minutes.
3. Discharge the granulated unit into double polyethylene-lined containers and then manually load into a Glatt bowl while passing through a No. 4 mesh screen. Load the Glatt bowl into a Glatt fluid-bed drier with an inlet air temperature setting of approximately $70^{\circ}\text{C} \pm 5^{\circ}\text{C}$.
4. Dry the unit until a moisture level of approximately 1% is obtained as determined using a Computrac® Moisture Analyzer.
5. Discharge the dried granulation into appropriately labeled, double polyethylene-lined drums and reconciled.
6. Pass the dried and reconciled granulation through a Kemtec BetaGrind mill equipped with a 1.5 mm screen and running at approximately 1500 rpm.
7. Collect the milled granulation into appropriately labeled, double polyethylene-lined drums and reconciled.
8. Sample and test the milled granulation by quality control and release prior to further processing.
9. Add the released granulation units to a Patterson-Kelley 20 ft³ V-blender, after which blend together for approximately 10 ± 1 minutes and then discharge to appropriately labeled, double polyethylene-lined containers.
10. Add item 4, blend, and compress at 582.40 mg in caplet shaped punches. Compress 727.50 mg for 500 mg strength and 990.50 mg for 750 mg strength.

NICOTINIC ACID (NIACIN) TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
200.00	1	Nicotinic acid	200.00
200.00	2	Ludipress®	200.00
5.00	3	Kollidon® CL	5.00
1.50	4	Magnesium stearate	1.50
3.00	5	Aerosil® 200	3.00
10.00	6	PEG-6000	10.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.5 mm sieve.
2. Mix, and press with very low compression force.
3. Compress 410 mg using 12 mm biplanar punches.

NICOTINIC ACID (NIACIN) TABLETS (200 MG)**FORMULATION**

Nicotinic acid (Lonza), 200.0 g; Ludipress®, 200.0 g; Kollidon® CL, 5.0 g; magnesium stearate, 1.5 g; Aerosil® 200, 3.0 g; polyethylene glycol 6000, powder, 10.0 g.

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.5 mm sieve, mix, and press with very low compression force at 419 mg.

NONDETERGENT NEUTRAL DRY SKIN CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
60.00	1	Stearic acid	60.00
145.00	2	White petrolatum jelly	145.00
116.00	3	Mineral oil (25 cS)	116.00
10.00	4	Lanolin	10.00
20.00	5	Cetearyl alcohol	20.00
QS	6	Deionized water	QS to 1 kg
14.00	7	Triethanolamine (99%)	14.00
QS	8	Perfume, preservative, color	QS

MANUFACTURING DIRECTIONS

1. Heat oil and water phases separately to 70°C.
2. Add water phase to oil phase while stirring.
3. Stir to cool, adding triethanolamine at 60°C and perfuming at 40°C to 50°C.
4. This cream serves as a base for drugs as well.
5. Triethanolamine may be omitted, as it gives a higher pH.

NOREPHEDRINE SYRUP

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
40.00	1	DL-norephedrine hydrochloride	40.00
4.00	2	Parabens	4.00
5.00	3	Saccharin sodium	5.00
3.00	4	Kollidon® 90 F	3.00
500.00	5	Sorbitol solution	500.00
460.00	6	Water	460.00

MANUFACTURING DIRECTIONS

1. Dissolve the parabens in the hot water, add the sorbitol, cool to room temperature, and dissolve the other components.

2. To prevent discoloration of Kollidon® in the solution during storage, 0.1% to 0.5% cysteine could be added as an antioxidant.
3. Flavors should be added to adjust the taste as needed.

NYSTATIN CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
80.00	1	Cetostearyl alcohol	80.00
20.00	2	Polyoxyl 20 cetostearyl ether (Cetomacrogol 1000)	20.00
80.00	3	Mineral oil (liquid paraffin)	80.00
2.00	4	Methyl paraben	2.00
100,000 IU	5	Nystatin microfine ^a (30% excess) 5420 IU/mg	24.00
1.00	6	Propylparaben	1.00
100.00	7	Propylene glycol	100.00
4.86	8	Dibasic sodium phosphate	4.86
2.36	9	Monobasic sodium phosphate	2.36
180.00	10	Petrolatum (soft white paraffin)	180.00
506.00	11	Purified water	506.00

^a Particle size NLT 90% less than 45 µm and 100% less than 80 µm.

MANUFACTURING DIRECTIONS

1. Charge item 3 to the fat-melting vessel.
2. Heat to 70°C while stirring.
3. Charge items 1, 2, and 10 to the fat-melting vessel while stirring.
4. Mix well, and maintain the temperature at 65°C to 70°C.
5. Load 466 g of item 11 and item 7 into mixer, and heat to 90°C.
6. Add items 4 and 6 to dissolve while stirring on manual mode.
7. Mix for 15 minutes at 10 rpm.
8. Cool to 65°C to 70°C.
9. Add items 8 and 7 to the parabens solution (step 6) to dissolve.
10. Mix for 5 to 10 minutes at 10 rpm.
11. Maintain temperature at 65°C to 70°C.
12. Take a sample of approximately 0.40 mL from mixer, and cool to 25°C.
13. Check the pH (6.3–7.0).
14. Withdraw 80 g of preservative/buffer solution from mixer at 65°C to 70°C in a stainless steel container.
15. Cool the solution in stainless steel container to 30°C to 35°C.
16. Disperse item 5 carefully using a spatula.
17. Homogenize using homogenizer to make a smooth dispersion.
18. Transfer the molten fat to the mixer containing the preservative/buffer solution through a stainless steel

sieve by vacuum at 0.6 bar while mixing at 10 rpm in manual mode at a temperature of 65°C.

19. Homogenize, and mix the cream for 10 minutes at low speed (10 rpm, manual mode) and vacuum of 0.6 bar.
20. Cool to 40°C ± 5°C.
21. Transfer 104 g of drug phase (35°C ± 5°C) to the mixer while mixing.
22. Rinse the stainless steel container of the drug phase with 40 g of item 11 (25–35°C), and transfer to the mixer while mixing.
23. Rinse the homogenizer and the container with item 11, and transfer the rinsings to the mixer.
24. Mix for 5 minutes.
25. Set the mixer at a mixing speed of 10 rpm (manual mode) and the homogenizer at low speed with a vacuum of 0.6 bar.
26. Mix and homogenize for 15 minutes.
27. Cool to 30°C with mixer speed of 10 rpm and vacuum of 0.6 bar.
28. Transfer the cream to a stainless steel drum.

NYSTATIN OINTMENT

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100,000 IU	1	Nystatin microfine ^a , 5420 IU/mg, 15% excess	21.05
22.00	2	Cetostearyl alcohol	22.00
8.00	3	Paraffin (hard paraffin)	8.00
100.00	4	Mineral oil (liquid paraffin)	100.00
848.95	5	Petrolatum (soft white paraffin)	848.95

^a Particle size NLT 90% less than 45 µm and 100% less than 80 µm.

MANUFACTURING DIRECTIONS

1. Melt items 2, 3, and 5 at 70°C in fat-melting vessel.
2. Disperse item 1 in 80 g of item 4 in a separate stainless steel container by using a spatula.
3. Pass the dispersion through a homogenizer twice; then, transfer the dispersion to the mixer.
4. Rinse the homogenizer and container with 20 g of item 4, and transfer the rinsings to the mixer.
5. Homogenize the dispersion at high speed for 15 minutes.
6. Set the mixer at a temperature of 40°C to 45°C.
7. Transfer the molten mass from the fat-melting vessel to the mixer at a temperature of 45°C to 50°C.
8. Mix for 10 minutes in manual mode and 10 minutes in automode at 12 rpm and vacuum 0.4 to 0.6 bar.
9. Homogenize at high speed for 10 minutes with recirculation.
10. Mix until the temperature of ointment reaches 28°C to 30°C.

11. Transfer the ointment to a stainless steel drum.
12. Keep drum tightly closed.

NYSTATIN, NEOMYCIN SULFATE, GRAMICIDIN, AND TRIAMCINOLONE ACETONIDE CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100,000 IU	1	Nystatin microfine, ^a 5420 IU/mg, 20% excess	22.96
4.43	2	Neomycin sulfate ^b	4.43
0.28	3	Gramicidin ^c	0.28
1.00	4	Triamcinolone acetonide micronized	1.00
80.00	5	Cetostearyl alcohol	80.00
20.00	6	Poloxyl 20 cetostearyl ether (Cetomacrogol 1000)	20.00
80.00	7	Mineral oil (liquid paraffin)	80.00
2.00	8	Methylparaben	2.00
1.00	9	Propylparaben	1.00
60.00	10	Propylene glycol	60.00
4.86	11	Dibasic sodium phosphate	4.86
2.36	12	Monobasic sodium phosphate	2.36
180.00	13	Petrolatum (soft white paraffin)	180.00
531.86	14	Purified water	531.86

For items 1–3, actual quantity to be calculated per actual potency. Difference in quantity is to be adjusted by purified water.

^a Particle size NLT 90% less than 45 µm and 100% less than 80 µm.

^b Particle size NLT 99% less than 20 µm and 75% less than 10 µm.

^c Particle size NLT 98% less than 50 µm.

MANUFACTURING DIRECTIONS

1. Load items 5, 6, 7, and 13 in fat-melting vessel.
2. Heat to 70°C. Stir to melt.
3. Maintain temperature at 70°C to 75°C.
4. Heat 420 g of item 14 to 90°C in mixer.
5. Dissolve items 8 and 9 by stirring.
6. Mix for 15 minutes at 10 to 12 rpm.
7. Cool to 65°C to 70°C.
8. Dissolve items 11 and 12 in 71.86 g of item 14 at 40°C to 45°C in a stainless steel drum.
9. Check the pH (limit: 6.3–7.0 at 25°C).
10. Dissolve item 2 into 79.08 g of phosphate solution. The solution should be clear.
11. Disperse item 1 in the neomycin/phosphate solution.
12. Homogenize two times with homogenizer (gap setting 1) to make smooth dispersion.
13. Dispersion should be smooth with no lumps.
14. Add 50 g of item 10 in a separate stainless steel container, and heat to 40°C to 45°C; then, dissolve item 3 by using a homogenizer. The solution should be clear.
15. Disperse item 4 in the clear solution of gramicidin/propylene glycol by using a homogenizer.

16. Homogenize until no lumps are present.
17. Maintain temperature at 40°C to 45°C.
18. Transfer the melt from previous step to the mixer through a stainless steel sieve while mixing at 1012 rpm (manual mode) at a temperature of 65°C.
19. Homogenize at high speed for 10 to 12 minutes at a temperature of 60°C to 65°C and a vacuum of 0.6 bar. Scrape the sides and blade.
20. Cool down to 50°C.
21. Transfer the homogenized dispersion to the mixer.
22. Rinse the container with 10 g of item 10.
23. Add the rinsings to the mixer, and mix for 10 minutes.
24. Transfer the dispersion to the mixer.
25. Rinse the container with 40 g of item 14.
26. Add to the mixer, and mix for 10 minutes.
27. Homogenize at high speed for 20 minutes at a temperature of 45°C, mixer speed of 10 to 12 rpm, and vacuum of 0.6 bar.
28. Cool down to 25°C to 30°C while mixing.
29. Transfer the cream to a stainless steel drum.

NYSTATIN, NEOMYCIN SULFATE, GRAMICIDIN, AND TRIAMCINOLONE ACETONIDE OINTMENT

Bill of Materials

Scale (mg/g)	Item	Material Name	Qty/kg (g)
22.96	1	Nystatin microfine ^a	22.96
4.43	2	Neomycin sulfate ^a	4.43
0.28	3	Gramicidin ^a	0.28
1.00	4	Triamcinolone acetonide (micronized)	1.00
100.00	5	Mineral oil (liquid paraffin)	100.00
10.00	6	Syncrowax	10.00
861.33	7	Petrolatum (soft white paraffin)	861.33

^a Actual quantity to be calculated per actual potency. Difference in quantity to be adjusted by use of soft white paraffin.

MANUFACTURING DIRECTIONS

1. Melt item 7 at 70°C in fat-melting vessel.
2. Add item 6 to the melt while mixing.
3. Transfer the melt to the mixer through filters, and cool to 40°C while mixing.
4. Add 60 g of item 5 in a stainless steel container, and disperse item 1 manually by using a spatula.
5. Homogenize two times with homogenizer (gap setting 1) to make a smooth dispersion, and then transfer to the mixer.
6. Add 20 g of item 5 in a stainless steel container, and disperse items 2, 3, and 4 by using the homogenizer to make a smooth dispersion.
7. Homogenize until no lumps are present.
8. Transfer the dispersion to the mixer.

9. Rinse the homogenizer and stainless steel container with 20 g of item 5, and transfer the rinsings to the mixer.
10. Mix for 10 minutes at a mixer speed of 10 rpm and vacuum of 0.4 to 0.6 bar.
11. Set thermostat at 28°C to 30°C.
12. Homogenize at high speed for 20 minutes with recirculation.
13. Mix until the temperature of ointment reaches 28°C to 30°C.
14. Transfer the ointment to a stainless steel drum.
15. Keep drum tightly closed.

OMEGA FATTY ACIDS TABLETS

Bill of Materials

Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
140.00	1	Omega fatty acids dry N-3	140.00
140.00	2	Avicel™ PH101	140.00
8.40	3	Kollidon® VA 64	8.40
2.00	4	Magnesium stearate	2.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with high compression force.
2. Compress 289 mg in 9 mm biconvex punches.
3. The dry powder omega fatty acids dry N-3 contains 25% fish oil; this fish oil consists of approximately 30% eicosapentaenoic acid (EPA) + docosahexaenoic acid (DHA).
4. These tablet cores could be coated with an enteric coating of Kollicoat MAE 30 D.
5. See Appendix for more choices.

ORAL REHYDRATION SALT (45 MEQ)

Bill of Materials

Scale (mg/g)	Item	Material Name	Qty/kg (g)
811.90	1	Cerelose powder	811.90
66.57	2	Sodium chloride	66.57
31.82	3	Sodium citrate dihydrate, USP	31.82
70.14	4	Potassium citrate monohydrate (food grade)	70.14
19.57	5	Povidone (PVP K-29-32), USP/BP	19.57
–	6	Alcohol SD 3A (200 proof/190 proof), USP	500.00 mL
–	7	Purified water, USP	50.00 mL

MANUFACTURING DIRECTIONS

1. Mill the dextrose through a 1.2 mm aperture screen or similar on a comminuting mill (knives forward, medium speed).
2. Individually mill the sodium chloride, sodium citrate, and potassium citrate through a 1.2 mm aperture screen on a comminuting mill (knives forward, medium speed).
3. *Note:* Do not mix the milled items until ready to add them to the dextrose.
4. Charge the powders from steps 1 and 2 into a suitable mass mixer, and mix for 10 minutes.
5. Screen the povidone through a 1.2 mm aperture screen, and transfer to the mixer.
6. Mix all the powders for 5 minutes.
7. Mix 500 mL of alcohol with 50 mL of water, and slowly add to the mixer while mixing.
8. Continue to mix for 5 to 10 minutes. Do not overwet the mass.
9. Granulate the wet mass through a 4.76 mm screen using an oscillating granulator, and spread on stainless steel trays.
10. Dry the granules at 45°C for approximately 16 hours, or until LOD is less than 0.8%.
11. Turn the granules over after 3 to 4 hours of drying.
12. Screen dry granules through an 840 µm screen.
13. Transfer the fines to a suitable blender.
14. Pass coarse granules through 840 µm screen using an oscillating granulator, and transfer to the blender.
15. Blend for 5 to 10 minutes.
16. Discharge into polyethylene-lined drums.
17. Fill 3.08 g for 100 mL, 7.70 g for 250 mL, and 30.80 g for 1000 mL of reconstituted solution. Prorate weights for different volumes.

ORLISTAT CHEWABLE TABLETS**MANUFACTURING DIRECTIONS**

1. Melt orlistat (60 g) and myristic acid (30 g) together at 50°C.
2. Add mannitol (400 g) and lactose (400 g), and cool the mixture to room temperature under continuous stirring.
3. Add talcum (10 g) and homogeneously distribute.
4. Press the powder into tablets of 960 mg weight (= orlistat content of 120 mg).

ORLISTAT CHEWABLE TABLETS**MANUFACTURING DIRECTIONS**

1. Melt orlistat (120 g) and myristic acid (30 g) together at 50°C.

2. Add sucrose palmitate (PEG-40 stearate, 12 g) and lactose (15 g), and cool the mixture to room temperature under continuous stirring.
3. Press the powder into tablets of 960 mg weight (= orlistat content of 120 mg).

ORLISTAT CHEWABLE TABLETS**MANUFACTURING DIRECTIONS**

1. Mix together orlistat, 120 g; sodium laurate, 30 g; mannitol, 80 g; and HPMC 3 cp, 60 g, with stepwise addition of a (50:50% m/m) ethanol/water mixture (0.2 mL/g).
2. The formed granules are dried in vacuum at 30° C to constant weight and pressed into tablets (each containing 120 mg orlistat).

PANCREATIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
30.00	1	Pancreatin	30.00
308.00	2	Ludipress®	308.00
10.00	3	Kollidon® CL	10.00
2.00	4	Magnesium stearate	2.00

MANUFACTURING DIRECTIONS

1. Mix the components, pass through a 0.8 mm sieve, and press with low compression force.
2. Compress 355 mg using 8 mm biconvex punches.
3. Coat by enteric coating. (See Appendix in Volume 1.)

PANCREATIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
300.00	1	Pancreatin	300.00
290.00	2	Ludipress®	290.00
25.00	3	Kollidon® CL	25.00
3.00	4	Magnesium stearate	3.00

MANUFACTURING DIRECTIONS

1. Mix the components, pass through a 0.8 mm sieve, and press to tablets with low compression force.
2. Compress 615 mg in 11 mm biconvex punches.
3. Coat by enteric coating. (See Volume 1.)

PANCREATIN AND CHOLIC ACID TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
130.00	1	Pancreatin	130.00
2.00	2	Cholic acid	2.00
127.00	3	Avicel™ PH101	127.00
56.00	4	Lactose monohydrate	56.00
2.00	5	Magnesium stearate	2.00
3.00	6	Aerosil® 200	3.00

MANUFACTURING DIRECTIONS

1. Mix the components, and press with high compression force.
2. Compress 324 mg in 9 mm biconvex punches.
3. Coat by enteric coating. (See Volume 1.)

PANTHENOL LOTION

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L Tablets (g)
26.25	1	D-Panthenol (2.5%) ^a	26.25
2.50	2	DL-Lactone (pure)	2.50
1.00	3	Sequestrene disodium	1.00
3.00	4	Chlorhexidine hydrochloride (micropowder)	3.00
5.00	5	POEG 300-stearate ^b	5.00
50.00	6	Paraffin oil (low viscosity)	50.00
5.00	7	Polydimethylsiloxane M 350	5.00
3.00	8	Perfume PCV 1155/8	3.00
—	9	Purified water	QS to 1 L

^a Based on 100% content; adjust for assay.

^b POEG 300 is a mixture of monoesters and diesters of polyoxyethylene glycol 300 with palmitic and stearic acids and free polyoxyethylene glycol 300.

MANUFACTURING DIRECTIONS

1. Aqueous phase: Prepare a solution of DL-lactone (previously liquefied at approximately 100 °C) in water.
2. Add the DL-lactone solution to the main part of water at 70°C.
3. Incorporate the D-panthenol (previously liquefied at approximately 45°C).
4. Admix and dissolve sequestrene disodium.

5. Fatty phase: Melt at approximately 65°C under stirring POEG 300-stearate, paraffin oil, and polydimethylsiloxane M 350.
6. Emulsion: Add the fatty phase at 65°C to the aqueous phase at approximately 45°C.
7. Cool to approximately 36°C while stirring and homogenizing.
8. Chlorhexidine suspension: Suspend chlorhexidine in water.
9. Lotion: Add the chlorhexidine suspension to the emulsion at approximately 36°C.
10. Stir, homogenize, and deaerate.
11. Finally, add the perfume, homogenize again, and filter.

PANTHENOL OINTMENT

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
50.00	1	Protegin X	50.00
18.00	2	Cetyl alcohol	18.00
12.00	3	Stearyl alcohol	12.00
40.00	4	Wax (white)	40.00
250.00	5	Wool fat (deodorized)	250.00
130.00	6	Vaseline® (white)	130.00
50.00	7	Almond oil	50.00
150.00	8	Paraffin oil	150.00
50.00	9	D-Panthenol	50.00
250.00	10	Deionized water	250.00

MANUFACTURING DIRECTIONS

1. Place in a heating vessel wool fat, Vaseline, almond oil, and paraffin.
2. Heat and melt the fats together at 80°C with stirring to keep the fatty phase at this temperature until further processing.
3. In a separate container, add Protegin X, cetyl alcohol, stearyl alcohol, and white wax. Melt these fats with stirring at 80°C.
4. Add to step 2.
5. The final temperature in the melt should be approximately 70°C.
6. Keep this temperature until further processing.
7. Transfer D-panthenol into a 10 L container by pouring; then, rinse it with hot deionized water.
8. Continue to mix for another 5 minutes, check the final weight, and make up for evaporated water (5.67 kg).
9. Place in kettle, and heat to 70°C while stirring. Transfer the melted fatty mass under vacuum (−0.3 atm) through the inline sieve (0.150 mm mesh).
10. After the addition, evacuate again to −0.3 atm.

11. Then, stir for another 15 minutes, and homogenize for 5 minutes under the same conditions.
12. Cool to 30°C (the cooling should occur within 4 hours).
13. When this temperature is reached, continue stirring until the ointment has reached 24°C to 26°C.
14. Stop cooling; then, evacuate quickly to -0.3 atm, and stir for 5 minutes.
15. Transfer the ointment in a storage vessel, and mix for 5 minutes with electric mixer.
16. Fill the ointment.

PAPAIN CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
1.00	1	Papain	1.00
150.00	2	Lycasin	150.00
17.40	3	Hydrogenated vegetable oil	17.40
9.60	4	Water	9.60
5.80	5	Gelatin (40% solution)	5.80
17.40	6	Starch coated dicalcium phosphate	17.40
1.60	7	Mono- and diglyceride mixture	1.60
0.60	8	Lecithin	0.60
0.10	9	Aspartame	0.10
0.10	10	Vanillin	0.10
0.20	11	Glycerin	0.20
0.20	12	Sodium bicarbonate	0.20
0.38	13	Mint flavor	0.38

MANUFACTURING DIRECTIONS

1. Boil lycasin, water, fat, mono- and diglyceride mixture, glycerin, and lecithin to 131°C.
2. Glycerin is added to the mixture and cooled to 60°C.
3. Thereafter, sodium bicarbonate, papain, dicalcium phosphate, and the remaining ingredients are added.
4. Thereafter, the mixture cooled to room temperature is ground into powder and compressed into 205 mg tablets using a tablet press.

PAPAIN CHEWING GUM

FORMULATION

Gum base, 31.20%; sorbitol, 28.08%; mannitol, 5.23%; papain, 1.00%; acesulfame K, 0.16%; aspartame, 0.16%; menthol powder, 1.00%; liquid flavor, 0.47%; isomalt PF, 11.70%; isomalt DC, 16.00%; anticaking agents (magnesium stearate, talc, or silica gel), 4.00%; flavor, 2.00%.

PEPPERMINT RUB CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
25.00	1	Sorbitol stearate	25.00
15.00	2	Polysorbate 60	15.00
300.00	3	Peppermint oil	300.00
20.00	4	Cetyl alcohol	20.00
40.00	5	Stearic acid	40.00
10.00	6	Triethanolamine (99%)	10.00
2.00	7	Carbopol 980	2.00
QS	8	Deionized water	QS
QS	9	Preservative, color	QS

MANUFACTURING DIRECTIONS

1. Hydrate Carbopol in water at 60°C to 65°C.
2. Add remaining water-phase ingredients.
3. Heat oil and water phases separately to 70°C to 75°C.
4. Add water phase to oil phase while stirring.
5. Stir to cool, neutralizing at 65°C with triethanolamine.

PEPTIDE SUBLINGUAL TABLET

FORMULATION

The individual component peptides, each having a molecular weight of less than 20,000 Da. Thymosin fraction, 5%; water, 5.0%; sucrose/lactose, 69.5%; propylene glycol, 0.5%; silicon dioxide, 15.0%; methyl nicotinate, 0.5%.

MANUFACTURING DIRECTIONS

1. Form the wetted mixture into tablets of the desired weight, and dry the tablets at 30°C for 36 hours.

PEPTIDE TOPICAL LIQUID

FORMULATION

Peptide such as thymic fraction, 5; glycerin, 44.5; propylene glycol, 44.9; methyl nicotinate, 0.1; water, 50; polysorbate 80, 0.5% by weight.

PHENINDIONE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
50.00	1	Phenindione	50.00
165.00	2	Ludipress®	165.00
2.00	3	Magnesium stearate	2.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with low compression force.
2. Compress 230 mg in 8 mm biplanar punches.

PHENOLPHTHALEIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
200.00	1	Phenolphthalein	200.00
150.00	2	Dibasic calcium phosphate	150.00
11.00	3	Kollidon® 30	11.00
—	4	Isopropanol or ethanol (96%)	QS
19.00	5	Kollidon® CL	19.00
3.00	6	Magnesium stearate	3.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 and 2 with solution of items 3 and 4, mix with items 5 and 6, pass through a 0.8 mm sieve, and press with low compression force.
2. Compress 385 mg using 9 mm biconvex punches.

PHENOLPHTHALEIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
90.00	1	Yellow phenolphthalein	90.00
64.80	2	Microcrystalline cellulose	64.80
187.20	3	Dicalcium phosphate	187.20
3.60	4	Croscarmellose sodium	3.60
3.60	5	Fumed silica	3.60
7.20	6	Stearic acid	7.20
3.60	7	Magnesium stearate	3.60

MANUFACTURING DIRECTIONS

1. Screen items 6 and 7 through a 40 mesh sieve.
2. Blend items 1 and 5 in a V-blender for 3 minutes.

3. Add items 2 and 4 to the blender, and mix for 5 minutes.
4. Add item 3 to the blender, and mix for 12 minutes.
5. Add item 6, and blend for 3 minutes.
6. Add item 7, and mix for another 5 minutes.
7. Compress using 3/8 in, flat, bevel-edged punches to hardness of 10 kg; average tablet weight is 360 mg.

PHENYLPROPANOLAMINE AND BROMPHENIRAMINE FAST-DISSOLVING TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
6.25	1	Phenylpropanolamine hydrochloride	6.25
1.00	2	Brompheniramine maleate	1.00
6.00	3	Citric acid	6.00
1.80	4	Magnasweet 135	1.80
4.50	5	Aspartame	4.50
3.60	6	Cherry flavor	3.60
21.00	7	Croscarmellose sodium	21.00
3.00	8	Lecithin	3.00
30.00	9	Cornstarch	30.00
3.00	10	Silicon dioxide	3.00
2.10	11	Magnesium stearate	2.10
219.25	12	Fast-dissolving granulation (see following)	219.25

MANUFACTURING DIRECTIONS

1. Make a fast-dissolving granulation by combining 400 g of melted PEG-900 with fructose powder (100 g) in a planetary mixer (low-shear mixer) and mixing until the granules form.
2. Allow the granulations to cool, and then screen.
3. Mix all ingredients in a V-blender.
4. Compress tablets (301.5 mg) at approximately 3 kN.
5. Tablet hardness should be 0.2 to 0.5 kp, and disintegration time is 10 seconds.

**PHENYLPROPANOLAMINE,
CHLORPHENIRAMINE, DEXTROMETHORPHAN,
VITAMIN C SYRUP**

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
150.00	1	PEG-400 (low color), NF	150.00
21.66	2	Acetaminophen, USP	21.66
0.075 mL	3	Glycerin, USP (96%)	75.00 mL
0.35 mL	4	Sorbitol; use sorbitol solution, USP	350.00 mL
1.00	5	Benzoic acid, USP	1.00
1.75	6	Saccharin sodium (dihydrate powder), USP	1.75
0.91	7	Phenylpropanolamine hydrochloride, USP	916.70 mg
0.06	8	Chlorpheniramine maleate, USP (plus 10% manufacturing)	73.30 mg
0.66	9	Dextromethorphan hydrobromide, USP	667.00 mg
20.00	10	Sodium CMC (premium low viscosity)	20.00
70.00 mcg	11	Dye	70.00 mg
6.00 mcg	12	Dye	6.00 mg
5.00	13	Ascorbic acid; use sodium ascorbate (fine powder)	5.62
0.50	14	Flavor, orange	500.00 mg
0.25	15	Flavor, orange	250.00 mg
QS	16	Carbon dioxide gas	QS
QS	17	Purified water, USP	QS to 1 L

MANUFACTURING DIRECTIONS

Manufacture under complete CO₂ protection. Bubble the CO₂ gas through the solution from the bottom of the tank.

If excessive foaming occurs, change CO₂ gas protection from the bottom to the top of the tank. Minimize vortex formation while mixing to prevent aeration of the product.

1. In a covered stainless steel container, heat 500 mL of water to boiling. Boil for 30 minutes.
2. Turn off the heat. While keeping the container covered, cool the water to 30°C while purging the water with CO₂.
3. Keep this water in a covered container blanketed with CO₂ gas, and use where indicated.
4. Transfer the PEG-400 to the main stainless steel mixing tank, and cover.
5. Start bubbling CO₂ gas. While mixing, slowly heat to 60°C to 65°C. Maintain at this temperature.
6. While mixing, add and dissolve the acetaminophen. Maintain the temperature and CO₂ protection.

7. When all the acetaminophen has dissolved, add, while mixing, the glycerin and sorbitol.
8. Continue mixing while maintaining the temperature and CO₂ gas protection until mixture is used later.
9. Do not allow the temperature to go to more than 65°C.
10. During this mixing period, remove samples through the bottom valve of the mixing tank, and inspect for clarity. Return samples to the mixing tank. Continue mixing and sampling until absolutely clear.
11. In a separate stainless steel mixing tank, heat 300 mL of water covered to 90°C.
12. While maintaining at this temperature, start bubbling CO₂ gas.
13. While mixing, add and dissolve successively the benzoic acid, saccharin sodium, and phenylpropanolamine hydrochloride. Continue mixing until all have dissolved.
14. Reduce the temperature to 60°C to 65°C while mixing. Do not force cool.
15. Add the solution from previous step to the solution in the main mixing tank while mixing and bubbling CO₂ gas.
16. Rinse the container with two lots of 5 mL of CO₂-saturated water, and add the rinsings to the batch while mixing.
17. Continue mixing for 15 minutes while maintaining the temperature at 60°C to 65°C and under CO₂ gas protection.
18. While mixing the batch, sprinkle on the sodium CMC.
19. Continue mixing until all the sodium CMC has been dispersed.
20. Check on the absence of any undissolved lumps.
21. Add CO₂-saturated water from step 3 to 900 mL, and mix while cooling the batch to 30°C.
22. Dissolve the dyes in 10 mL of CO₂-saturated water; then, add to the batch with mixing.
23. Rinse the container with two lots of 5 mL of the same water, and add the rinsings to the batch.
24. Mix until a homogeneously colored batch is formed.
25. Stop bubbling in CO₂ gas, but maintain CO₂ protection of the tank headspace.
26. In a stainless steel container, dissolve the sodium ascorbate in 25 mL of CO₂-saturated water, taking care to minimize exposure of the solution to air or light.
27. Mix all solutions, add rinsings where necessary, and continue mixing for 15 minutes.
28. Add the flavors, complete the batch to 1 L with CO₂-saturated water, and mix well for 1 hour.
29. Stop mixing, saturate the headspace with CO₂, and leave overnight to release any entrapped air.

PHENYLPROPANOLAMINE HYDROCHLORIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
60.00	1	Phenylpropanolamine hydrochloride, USP	60.00
180.00	2	Calcium sulfate dihydrate	180.00
—	3	Starch paste 10%	QS
12.00	4	Starch 1500 (StarX)	12.00
6.00	5	Magnesium stearate	6.00

MANUFACTURING DIRECTIONS

1. Add starch to cold water in 1:10 ratio. Heat to boil with constant stirring until a thick, translucent white paste is formed.
2. Keep it for use in following granulation.
3. Mix the phenylpropanolamine hydrochloride with the calcium sulfate in a Sigma blade mixer for 15 minutes.
4. Add starch paste in sufficient quantity to form a suitable wet mass of desirable consistency.
5. Allow to mix for 30 minutes.
6. Pass the wet mass through a No.14 screen, and distribute on drying trays.
7. Dry in a forced-air oven at 49 °C to 54 °C or in a fluid-bed dryer.
8. Pass the dried granules through a No. 18 mesh screen.
9. Transfer granules to a twin-shell blender, add items 4 and 5, and blend for 6 to 8 minutes.
10. Compress the granulation in a rotary press using 3/8 in. standard punches. Tablet weight is 260 mg.

PLACEBO TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
299.70	1	Ludipress®	299.70
0.30	2	Magnesium stearate	0.30

MANUFACTURING DIRECTIONS

1. Mix the components, sieve, and press.
2. For this formulation, compress 300 mg.
3. The compression force determines hardness and friability.
4. At 7 kN, the hardness is 45 N; at 22 kN, the hardness is 160 N.
5. The disintegration time increases from 1 minute to 4 minutes.

POLIDOCANOL WOUND SPRAY

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
5.00	1	Polidocanol	5.00
50.00	2	Kollidon® VA 64	50.00
50.00	3	Ethocel™ 20	50.00
20.00	4	Lutrol E 400	20.00
675.00	5	Ethyl acetate	675.00
200.00	6	Isopropanol	200.00

MANUFACTURING DIRECTIONS

1. Dissolve items 1 to 4 in the solvent mixture of items 5 and 6.
2. Fill the solution into spray cans with the necessary quantity of propellant (e.g., propane/butane) or in a mechanical pump bottle.

POTASSIUM BICARBONATE–COATED TABLET

MANUFACTURING DIRECTIONS

1. Preparation of the potassium bicarbonate crystals: U.S. Patent 5,445,805 describes how to prepare crystals of size within the range of 800 to 900 µm, a Brunauer–Emmett–Teller (BET) surface area of 0.004 to 0.01 m²/g, and particle distributions such that greater than 90% by weight of the crystals are within the range of 700 to 1000 µm. (At least 90% of the crystals are retained on a 25 mesh screen [707 µm], and fewer than 10% are retained on an 18 mesh screen [1000 µm]).
2. Preparation and application of controlled-release coating lacquers: Coating lacquer composition: Cutina HR, 23.45 g; Ethocel™, 163.45 g; acetyl tributyl citrate, 8.75 g; isopropyl alcohol, 3304.35 g; total, 3500.00 g.
3. Coating conditions: process air flow (m³/h), 100–171; spray period (minutes), 135; spray temperature, 60.1°C to 68.1°C; spray pressure (bar), 2; liquid flow rate, 26–28 g/min; product temperature, 46°C to 52°C; coated crystals: theoretical yield (g), 3191.1; actual yield approximately 98% giving w/w dry matter of 6.37% (coated/uncoated crystals).
4. Dissolve hydrogenated castor oil (Cutina HR), ethyl cellulose (Ethocel™ Standard 100 premium), and acetyl tributyl citrate in isopropyl alcohol to provide the controlled-release coating lacquers.
5. Dissolve Cutina HR, Ethocel™, and acetyl tributyl citrate in the isopropyl alcohol solvent by heating in a mixer equipped with a heating jacket set at 60°C to 70°C with vigorous agitation. Continue the agitation for approximately 1 hour. When dissolved, the mixture should be clear to translucent.

- Maintain the coating lacquer composition at temperatures of 60°C to 70°C.
- Coat the lacquers on the potassium bicarbonate particles by cocurrent flow through a fluidized bed in which the moisture content is controlled. Spray the coating lacquer from a spray nozzle positioned at the bottom of a Glatt fluidized-bed apparatus equipped with a Wurster tube.
- Fluidize the potassium bicarbonate crystals, and spray the warm coating lacquer on the crystals in multiple coating cycles.
- Adjust the process air-flow rate as necessary to provide adequate movement of the crystals through the fluidized bed as they are coated. During the coating process, flash evaporate the isopropyl alcohol solvent from the crystals as they cycle through the fluidized bed.
- After completing the application of the coating lacquer to the crystals, remove any trace residual solvent remaining on the coated crystals by cycling in the fluidized bed without lacquer spray for 10 minutes.
- Following the residual solvent removal, cool the coated crystals in the bed.
- The amount of coating lacquer applied on the crystals is calculated as the % w/w of the dry matter of the respective coatings relative to the uncoated potassium bicarbonate crystals.
- Compression: potassium, 85.00%; bicarbonate-coated crystals, Cutina HR, 1.50%; Avicel™ PH, 7.68%; cornstarch, 5.12%; Syloid, 0.40%; Lubritab, 0.30%. Compress tablets of 1500 mg of potassium bicarbonate.

POVIDONE–IODINE AND LIDOCAINE GEL

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100.00	1	PVP–iodine 30/06	100.00
10.00	2	Lidocaine hydrochloride	10.00
10.00	3	Sodium chloride	10.00
200.00	4	Lutrol F 127	200.00
79.00	5	Sodium hydroxide (1 M solution)	79.00
61.10	6	Water	61.10

MANUFACTURING DIRECTIONS

- Dissolve items 1 to 3 in item 6, cool to approximately 6°C, dissolve item 4, and adjust the pH to a value of 4.5 to 5.0 with item 5.
- Maintain the cool temperature until the air bubbles escape.
- Viscosity (Brookfield, 23°C) is 54,000 mPa.

POVIDONE–IODINE BAR SOAP

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
50.00	1	PVP–iodine 30/06	50.00
10.00	2	Fragrance	10.00
75.00	3	Water	75.00
940.00	4	Syndet base	940.00

MANUFACTURING DIRECTIONS

- Dissolve PVP–iodine in water, and mix the solution with the fragrance and the syndet base.
- Pass the blend four times through a three-roller mill.
- Blend three times through a plodder with a narrow-sieve hole disk.
- Pass the blended material through a wide-sieve hole disk combined with a mouth hole disk.
- Heat the area of the two disks to 50°C using a heating collar.
- Cut the bar in pieces on a laboratory stamper.
- Composition of the syndet base (in sequence of concentration): disodium lauryl sulfosuccinate, sodium lauryl sulfate, cetyl stearyl alcohol, paraffin, glycerol stearate, water, titanium dioxide.

POVIDONE–IODINE BAR SOAP

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
50.00	1	PVP–iodine 30/06	50.00
75.00	2	Water	75.00
241.5	3	Texapon® K 12	241.5
241.5	4	Setacin® F special paste	241.5
241.5	5	Emcol® 4400.1	241.5
145.00	6	Cetylstearyl alcohol	145.00
96.50	7	Paraffin	96.50
226.00	8	Glycerol monostearate	226.00

MANUFACTURING DIRECTIONS

- Heat mixture of items 3 to 8 to 75°C to 80°C, and cool to approximately 50°C, stirring well.
- Add solution of items 1 and 2, and let cool to room temperature, stirring continuously.
- Pass the blend four times through a three-roller mill, and let dry overnight at room temperature.
- Cut the bar into pieces on a laboratory stamper.

POVIDONE–IODINE BAR SOAP

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
50.00	1	PVP-iodine 30/06	50.00
75.00	2	Water	75.00
241.50	3	Texapon® K 12	241.50
145.00	4	Cetylstearyl alcohol	145.00
96.50	5	Paraffin	96.50
226.00	6	Glycerol monostearate	226.00

MANUFACTURING DIRECTIONS

1. Heat mixture of items 3 to 6 to 75°C to 80°C, and cool to approximately 50°C, stirring well.
2. Add solution of item 1, and let cool to room temperature, stirring continuously.
3. Pass the blend four times through a three-roller mill, and let dry overnight at room temperature.
4. Cut the bar into pieces on a laboratory stamper.

POVIDONE–IODINE CONCENTRATES FOR BROILERS AND CATTLE

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
200.00	1	PVP-iodine 30/06	200.00
50.00	2	Texapon® K 12	50.00
50.00	3	Cremophor NP 14	50.00
73.00	4	Tartaric acid	73.00
43.00	5	Sulfuric acid, diluted	43.00
100.00	6	Ethanol 96%	100.00
QS	7	Water	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Dissolve surfactant items 2 and 3 in solution of items 4 to 7, and slowly add PVP-iodine.
2. Brown transparent liquid having a pH of approximately 1 is obtained.
3. Dilute approximately 3 mL of the concentrate with 1 L of water prior to use.

POVIDONE–IODINE CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100.00	1	PVP-iodine 30/06	100.00
241.00	2	Citric acid (0.1 M solution)	241.00
369.00	3	Na ₂ HPO ₄ (0.2 M solution)	369.00
20.00	4	Cremophor A 6	20.00
20.00	5	Cremophor A 25	20.00
100.00	6	Cetylstearyl alcohol	100.00
100.00	7	Liquid paraffin	100.00
50.00	8	Glycerol	50.00

MANUFACTURING DIRECTIONS

1. Prepare a basic cream from the emulsifying agents and the fatty substances (items 4–8).
2. Stir in the PVP-iodine dissolved in the buffer solutions made from items 2 and 3.
3. A brown cream having a pH of 4.5 should be obtained.

POVIDONE–IODINE EFFERVESCENT VAGINAL TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
350.00	1	PVP-iodine 30/06, with excess	360.00
1450.00	2	Ludipress®	1450.00
360.00	3	Tartaric acid	360.00
265.00	4	Sodium bicarbonate	265.00
19.00	5	Talc	19.00
2.00	6	Calcium arachinate	2.00
2.00	7	Aerosil® 200	2.00

MANUFACTURING DIRECTIONS

1. Dry the mixture of items 2 to 4 for 4 hours at 60°C, mix with item 1 and items 5 to 7, and press to tablets.
2. Compress 2.5 g in 20 mm biplanar punches.
3. The tablet can be dissolved in water to obtain a vaginal douche solution.

POVIDONE–IODINE FOAM SPRAY

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100.00	1	PVP–iodine 30/06	100.00
0.10	2	Cremophor A 25	0.10
QS	3	Water	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Dissolve PVP–iodine in the solution of Cremophor A 25 in water.
2. Fill the aerosol cans with 90 parts of this solution and 10 parts propane:1 part butane.

POVIDONE–IODINE GARGLE

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
10.00	1	Polyvinylpyrrolidone–iodine (powder) (35% excess)	13.50
10.00	2	Glycerin, USP (96%)	10.00
–	3	Purified water, USP	QS to 1 L

MANUFACTURING DIRECTIONS

Wear gloves and mask during all phases of manufacturing and filling. Do not keep the lid of the manufacturing or storage tank open unless necessary, as iodine may be liberated.

1. Add 600 mL purified water to a suitable stainless steel manufacturing tank.
2. Slowly add povidone–iodine powder to the water (with continuous stirring).
3. Stir for 30 minutes or until a clear, brown solution is obtained.
4. Add glycerin to the manufacturing tank.
5. Stir until uniform solution is obtained.
6. Make up volume to 1 L with purified water, and mix well for 5 minutes.
7. Check pH (range: 2–4).
8. Filter the solution through a 100 mesh nylon cloth, and transfer to a stainless steel storage tank.
9. Keep the storage tank tightly closed.

POVIDONE–IODINE GARGLE SOLUTION CONCENTRATE

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
100.00	1	PVP–iodine 30/06	100.00
10.00	2	Propylene glycol	10.00
90.00	3	Ethanol (96%)	90.00
800.00	4	Water	800.00

MANUFACTURING DIRECTIONS

1. Dissolve the PVP–iodine in the solvent mixture to produce a brown transparent liquid.
2. Dilute 10 mL of the concentrate with approximately 100 mL of water prior to use.

POVIDONE–IODINE GEL CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100.00	1	PVP–iodine 30/06	100.00
359.00	2	Citric acid (0.1 M solution)	359.00
181.00	3	NA ₂ HPO ₄ ·12H ₂ O (0.2 M solution)	181.00
50.00	4	Lutrol E 400	50.00
100.00	5	Liquid paraffin	100.00
150.00	6	Lutrol F 127	150.00
70.00	7	Lutrol F 127	70.00

MANUFACTURING DIRECTIONS

1. Dissolve item 1 in solution of items 2 to 4, mix with item 5, and dissolve item 6 at approximately 20°C.
2. Cool to 5°C to 8°C, and dissolve item 7.
3. Maintain cool temperature until all air bubbles have disappeared.
4. A brown, turbid gel should be obtained.

POVIDONE–IODINE GELS

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100.00	1	PVP–iodine 30/06	100.00
10.00	2	Sodium chloride	10.00
200.00	3	Lutrol F 127	200.00
79.00	4	Sodium hydroxide (1 M solution)	79.00
610.00	5	Water	610.00

MANUFACTURING DIRECTIONS

1. Dissolve items 1 and 2 in item 5, and cool to approximately 6°C.
2. Dissolve Lutrol F 127 and item 2, and adjust the pH value with item 4.
3. Maintain cool until all air bubbles escape.
4. Viscosity (Brookfield, 23°C) is 61,000 to 54,000 mPa; pH value (20% in water) is 2.2 to 4.6.

POVIDONE–IODINE GLUCOSE OINTMENT

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
20.00	1	PVP–iodine 30/06, with excess	26.00
45.00	2	Ethanol (96%)	45.00
849.00	3	Glucose	849.00
34.00	4	Lutrol E 4000	34.00
6.00	5	Glycerol	6.00
6.00	6	Water	6.00

MANUFACTURING DIRECTIONS

1. Dissolve Lutrol E 4000 in the hot mixture of glycerol and water, and add the glucose warmed to 60°C to 80°C.
2. Incorporate item 4 to obtain a brown, viscous, and turbid paste.

POVIDONE–IODINE LIQUID SPRAY

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100.00	1	PVP–iodine 30/06	100.00
150.00	2	Kollidon® VA 64	150.00
750.00	3	<i>N</i> -Propanol	750.00
750.00	4	Ethanol	750.00

MANUFACTURING DIRECTIONS

1. Dissolve Kollidon® VA 64 in the mixture of solvents, and slowly add PVP–iodine to the well-stirred solution.
2. Fill in aerosol cans with propellants such as propane and butane or with manual valves.

POVIDONE–IODINE LOZENGES

Bill of Materials			
Scale (mg/lozenge)	Item	Material Name	Qty/1000 Lozenges (g)
5.00	1	PVP–iodine 30/06	5.00
150.00	2	Sorbitol (crystallized)	150.00
4.00–5.00	3	Menthol (crystalline)	4.00–5.00
4.00–5.00	4	Eucalyptol (crystalline)	4.00–5.00
1.00	5	Aspartame, potassium	1.00
0.10	6	Saccharin sodium	0.10
1.00	7	Aerosil® 200	1.00
1.00	8	Magnesium stearate	1.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with medium compression force.
2. Compress 176 mg in 8 mm biplanar punches.

POVIDONE–IODINE MASTITIS CREAM FOR CATTLE

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100.00	1	PVP–iodine 30/06	100.00
100.00	2	Liquid paraffin	100.00
100.00	3	Vaseline®	100.00
50.00–80.00	4	Cetylstearyl alcohol	50–80
20.00	5	Cremophor A 6	20.00
20.00	6	Cremophor A 25	20.00
50.00	7	Propylene glycol	50.00
QS	8	Water	530.00–560.00

MANUFACTURING DIRECTIONS

1. Dissolve PVP–iodine in the solvents (items 7 and 8).
2. Mix items 2 to 6 by heating, stir the solution in the previous mixture, and cool by stirring.

POVIDONE–IODINE MOUTHWASH AND GARGLE SOLUTION CONCENTRATE

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
75.00	1	PVP–iodine 30/06	75.00
5.00	2	Saccharin sodium	5.00
150.00	3	Water	150.00
2.00	4	Menthol	2.00
1.00	5	Anise oil + eucalyptus oil (1+1)	1.00
150.00	6	Lutrol E 400	150.00
500.00	7	Ethanol (96%)	500.00

MANUFACTURING DIRECTIONS

1. Dissolve PVP–iodine and saccharin in water, and mix with solution of items 4 to 7.
2. Brown transparent liquid has a fresh odor.
3. Dilute 10 to 20 mL with a glass of water.
4. A brown liquid with a fresh taste should be obtained.

POVIDONE–IODINE POWDER SPRAY

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
250.00	1	PVP–iodine 30/06	250.00
250.00	2	Maize PO ₄ aerosol	250.00
15.00	3	Isopropyl myristate	15.00
100.00	4	Dow Corning® 344 fluid	100.00
500.00	5	Pentane	500.00
220.00	6	Propane + butane (1+3)	220.00

MANUFACTURING DIRECTIONS

1. Suspend PVP–iodine and maize PO₄ aerosol in the liquid mixture of items 3 to 5.
2. Fill in aerosol cans with the propellants.

POVIDONE–IODINE PUMP SPRAY

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
10.00	1	PVP–iodine 30/06	10.00
100.00	2	Water	100.00
1.00	3	Potassium iodide	1.00
100.00	4	Xylitol	100.00
787.50	5	Propylene glycol	787.50
1.00	6	Menthol (crystalline)	1.00
0.50	7	Peppermint oil (double rectified)	0.50

MANUFACTURING DIRECTIONS

1. Dissolve potassium iodide in water, warm up to 40°C, and dissolve xylitol.
2. At room temperature, dilute with propylene glycol, dissolve PVP–iodine, and add flavors to produce a clear, brown liquid with a sweet, refreshing taste.

POVIDONE–IODINE SHAMPOO

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
75.00	1	PVP–iodine 30/06	75.00
250.00	2	Neutronyx® S 60	250.00
40.00	3	Super Amide® L 9	40.00
5.00–7.00	4	Natrosol™ HR 250	5.00–7.00
–	5	Water	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Dissolve Super Amide® and Natrosol™ in hot water (approximately 60°C); then, dissolve PVP–iodine.
2. After cooling, incorporate Neutronyx®.
3. A brown, clear solution should be obtained.
4. The viscosity can be changed by modification of the amount of Natrosol™ 250 HR.

POVIDONE–IODINE SOFT GEL

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
10.00	1	PVP–iodine 30/06	10.00
25.00	2	Natrosol™ HR 250	25.00
QS	3	Water	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Dissolve PVP–iodine and Natrosol™ HR 250 in the water, and stir well to produce a clear, brown gel.
2. Viscosity (Brookfield, 23°C) is 31,500 mPa.

POVIDONE–IODINE SOLUTION

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
100.00	1	Povidone–iodine powder (35% excess)	135.00
9.318	2	Anhydrous citric acid (powder)	9.318
14.62	3	Anhydrous sodium phosphate (dibasic)	14.62
QS	4	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

Wear gloves and mask during all phases of manufacturing and filling. Do not keep the lid of the manufacturing or storage tank open unless necessary, as iodine may be liberated.

1. Citric acid–phosphate buffer solution (pH 5): Add 600 mL purified water to a suitable stainless steel manufacturing tank.
2. With gentle stirring, add citric acid to the purified water in the manufacturing tank.
3. Stir for 10 minutes or until completely dissolved.
4. During this mixing period, remove samples from the bottom valve of the manufacturing tank, and inspect for clarity.
5. Return samples to the manufacturing tank.
6. Continue mixing and sampling until the solution is completely clear.
7. With gentle stirring, add dibasic sodium phosphate to the solution.
8. Stir for 10 minutes or until completely dissolved.
9. During this mixing period, remove samples from the bottom valve of the manufacturing tank, and inspect for clarity.
10. Return samples to the manufacturing tank.
11. Continue mixing and sampling until the solution is completely clear.
12. Make up volume to 1 L with purified water, and mix well for 5 minutes.
13. Check and record pH (range: 4.8–5.2).
14. Filter the solution through a 100 mesh nylon cloth.
15. Transfer into a suitable stainless steel storage tank, and keep tightly closed.
16. This solution should be freshly prepared, and should not be stored for more than 24 hours.
17. Preparation of solution: Dissolve povidone–iodine in approximately 600 mL of citric acid/phosphate buffer (pH 5) solution in a suitable stainless steel mixing tank.
18. Stir evenly for 10 minutes or until a clear, brown solution is obtained.
19. Make up volume to 1 L with citric acid/phosphate buffer solution.

20. Mix well for 10 minutes.
21. Check and record pH (range: 3.0–4.5).
22. Filter the solution through a 100 mesh nylon cloth.
23. Transfer into a suitable stainless steel storage tank, and keep it tightly closed.

POVIDONE–IODINE SCRUB

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
75.00	1	PVP–iodine (powder) (40% excess)	105.00
250.00	2	Sodium lauryl sulfate	250.00
35.00	3	Lauric diethanolamide	35.00
–	4	Distilled purified water, USP	QS to 1 L

MANUFACTURING DIRECTIONS

1. Add 600 mL purified water to a suitable stainless steel manufacturing tank.
2. Add, by sprinkling, the sodium lauryl sulfate to the manufacturing tank.
3. Continue to mix slowly under vacuum, and begin to heat until product temperature is 70°C.
4. Continue to mix vigorously under vacuum at 65°C to 70°C for 15 minutes or until completely dissolved.
5. (*Note:* Do not add detergent quickly, as a gel may form that is difficult to dissolve.) Stop mixer, release vacuum, and open tank.
6. Add and disperse the previously broken lauric diethanolamide in the warmed solution from the previous step.
7. Maintain vacuum, and mix vigorously for 30 minutes at 65°C to 70°C or until completely dissolved.
8. Slowly cool under vacuum to room temperature with slow mixing. (*Note:* Do not force cool with cold water; otherwise the mixture will adhere to the walls of the manufacturing tank.) When temperature reaches 30°C, release vacuum, and open tank.
9. While mixing slowly, add povidone–iodine in small portions.
10. Rinse the container of povidone–iodine with 150 mL purified water, and add to the main tank. (*Note:* Do not keep the lid of the manufacturing or storage tank open unless necessary, as iodine may be liberated.) Mix under vacuum until a clear reddish-brown solution is obtained.
11. Make volume up to 1 L with purified water, and mix well under vacuum for at least 15 minutes to ensure product uniformity and to deaerate the product.
12. Stop mixing, release the vacuum, and then open the tank.
13. Check and record pH (range: 3–6).
14. Filter the solution through 100 mesh nylon cloth.

POVIDONE–IODINE SOLUTION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100.00	1	PVP–iodine 30/06	100.00
3.00	2	Lutrol F 127	3.00
5.00	3	Lutrol E 400	5.00
432.00	4	Citric acid (0.1 M solution)	432.00
460.00	5	Na ₂ HPO ₄ ·12H ₂ O (0.2 M solution)	460.00

MANUFACTURING DIRECTIONS

1. Dissolve the PVP–iodine (and Lutrol F 127) in the mixture of buffer solutions (and Lutrol E 400).
2. Brown clear solutions having a low viscosity and pH of approximately 4.5.
3. Items 2 and 3 can be deleted and compensated with item 5.

POVIDONE–IODINE SOLUTION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100.00	1	PVP–iodine 30/06	100.00
0.23	2	Texapon® K 12	0.23
1.40	3	Sodium biphosphate	1.40
0.30	4	Sodium citrate	0.30
20.80	5	Sodium hydroxide (1 M solution)	20.80
10.00	6	Glycerol	10.00
QS	7	Water	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Dissolve Texapon® K 12 in solution of items 3 to 7, and slowly add PVP–iodine to the well-stirred solution.
2. The brown transparent liquid has a pH of 4.5.

POVIDONE–IODINE SOLUTION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100.00	1	PVP–iodine 30/06	100.00
10.00	2	Natrosol™ HR 250	10.00
2.00	3	Lutrol F 127	2.00
32.00	4	Sodium hydroxide (1 M solution)	32.00
QS	5	Water	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Dissolve Lutrol F 127 and then Natrosol™ in the water.
2. As soon as both are dissolved, slowly add the PVP–iodine to the well-stirred solution.
3. Adjust the pH with the sodium hydroxide solution to approximately 3.5.

POVIDONE–IODINE SOLUTION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
20.00	1	Tylose® M 300	20.00
2.00	2	Texapon® K 12	2.00
595.00	3	Citric acid (0.1 M solution)	595.00
283.00	4	Sodium biphosphate (0.2 M solution)	283.00

MANUFACTURING DIRECTIONS

1. Dissolve Tylose® M 300 in the mixture of the citric acid and sodium biphosphate solutions.
2. Add Texapon®, and slowly dissolve the PVP–iodine.
3. The brown, clear solution will have a pH of 3 to 4.

POVIDONE–IODINE SURGICAL SCRUB

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
75.00	1	PVP–iodine 30/06	75.00
250.00	2	Neutronyx® S 60	250.00
40.00	3	Super Amide L 9	40.00
QS	4	Floral bouquet	QS
QS	5	Water	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Dissolve Super Amide in hot water, cool, dissolve PVP–iodine, and add Neutronyx® to produce a brown, clear viscous solution with pH of approximately 3.4.

POVIDONE–IODINE SURGICAL SCRUB

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
75.00	1	PVP–iodine 30/06	75.00
250.00	2	Lutensit® AES	250.00
40.00	3	Monoamide® 150 MAW	40.00
QS	4	Floral bouquet	QS
QS	5	Water	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Dissolve monoamide in hot water, cool, dissolve PVP–iodine, and add Lutensit to produce a brown, clear, viscous solution.

POVIDONE–IODINE TRANSPARENT OINTMENT

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100.00	1	PVP-iodine 30/06	100.00
600.00	2	Lutrol E 400	600.00
46.00	3	Sodium hydroxide (1 M solution)	46.00
4.00	4	Water	4.00
250.00	5	Lutrol E 4000	250.00

MANUFACTURING DIRECTIONS

1. Prepare solution of items 1 to 4, heat to approximately 60°C, incorporate item 5 (stirring well), and cool to room temperature.
2. The transparent ointment, similar to a gel, will have a pH of 4 and be miscible and washable with water.

POVIDONE–IODINE VAGINAL DOUCHE CONCENTRATE

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100.00	1	PVP–iodine 30/06	100.00
5.00	2	Lutrol E 400	5.00
3.00	3	Lutrol F 127	3.00
432.00	4	Citric acid (0.1 M solution)	432.00
460.00	5	Na ₂ HPO ₄ ·12H ₂ O (0.2 M solution)	460.00

MANUFACTURING DIRECTIONS

1. Dissolve PVP–iodine and Lutrol F 127 in the mixture of buffer solutions with Lutrol E 400.
2. The brown, clear solution will have a low viscosity and pH of approximately 4.3.

POVIDONE–IODINE VAGINAL OVULE

Bill of Materials			
Scale (mg/Ovule)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	PVP–iodine 30/06	5.00
200.00	2	Lutrol E 400	10.00
170.00	3	Lutrol E 4000	85.00

MANUFACTURING DIRECTIONS

1. Melt the Lutrol E grades by gentle heating.
2. Stir in the micronized PVP–iodine product in small portions into the melt.
3. After a uniform suspension has been obtained, pour it into polyethylene molds.
4. The homogeneous, brown-colored ovule has a weight of 2 g.

POVIDONE–IODINE VAGINAL OVULE

Bill of Materials			
Scale (mg/Ovule)	Item	Material Name	Qty/kg (g)
200.00	1	PVP–iodine 30/06	200.00
100.00	2	Lutrol E 400	100.00
100.00	3	Lutrol E 1500	100.00
700.00	4	Lutrol E 4000	700.00

MANUFACTURING DIRECTIONS

1. Melt the Lutrol E grades by gentle heating.
2. Stir in the micronized PVP–iodine product in small portions into the melt.
3. After a uniform suspension has been obtained, pour it into polyethylene molds.
4. The homogeneous, brown-colored ovule has a weight of 2 g.

POVIDONE–IODINE VISCOUS SOLUTION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
10.00	1	PVP–iodine 30/06	10.00
15.00	2	Natrosol™ HR 250	15.00
QS	3	Buffer	QS
QS	4	Water	975.00

MANUFACTURING DIRECTIONS

1. Dissolve PVP–iodine and Natrosol™ in the well-stirred buffered solution in water to produce a clear, brown, viscous liquid.
2. Viscosity (Brookfield) should be 7500 mPa.

PROMETHAZINE HYDROCHLORIDE SYRUP

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
1.00	1	Promethazine HCl (5% excess)	1.05
675.00	2	Sucrose	675.00
1.00	3	Citric acid (monohydrate)	1.00
2.40	4	Sodium citrate	2.40
0.50	5	Ascorbic acid	0.50
0.25	6	Sodium metabisulfite (sodium disulfite)	0.25
0.25	7	Anhydrous sodium sulfite	0.25
50.00	8	Alcohol (ethanol, 95%)	50.00
0.15	9	Flavor	0.15
0.30	10	Flavor	0.30
0.50	11	Polysorbate 80 (Tween 80)	0.50
0.15	12	Caramel color	0.15
QS	13	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

Promethazine HCl undergoes thermal and photochemical oxidation. Protect from light, heat, and oxygen as practicable. Avoid vortex or overmixing to avoid air entrapment. Use nitrogen gas whenever necessary to expel air.

1. Add 400 g of item 13 to the manufacturing vessel, and heat to 90°C to 95°C.
2. Add item 2 while mixing at slow speed.
3. After addition of item 2, mix for 30 minutes at high speed and a temperature of 90°C to 95°C.
4. Cool down to 30°C to 35°C while mixing at low speed.
5. Add items 3 and 4 to the manufacturing vessel while mixing, and mix until dissolved.
6. Add items 6 and 7 to the manufacturing vessel while mixing, and mix until dissolved.
7. Add item 5 to the manufacturing vessel while mixing, and mix until dissolved.
8. Mix items 9 and 10 with items 8 and 11 in a separate container by using stirrer.
9. Mix for 10 minutes, and add to the manufacturing vessel while mixing.
10. Add 8 g of cold purified water (25–30°C) to a separate container, and dissolve item 12 by using stirrer.
11. Mix for 10 minutes, and add to the manufacturing vessel while mixing.

12. Start flushing the syrup with nitrogen gas pressure at 20 to 40 psi.
13. Add 10 g of cold purified water (cooled and flushed with N₂ gas) in a separate container with lid.
14. Pass nitrogen gas at 20 to 40 psi pressure for 15 minutes.
15. Dissolve item 1 in nitrogen-flushed, cold purified water (25–30°C) by using stirrer.
16. Mix for 10 minutes and add to the manufacturing vessel while mixing. Do not produce vortex.
17. Bring volume up to 1 L with nitrogen-flushed purified water.
18. Continue flushing nitrogen gas at 20 to 40 psi pressure for 30 minutes while mixing at slow speed.
19. Check and record the pH (limit: 4.5–5.5). If required, adjust pH with 10% citric acid or 10% sodium citrate solution.
20. Filter the syrup at 1.5 bar.
21. Recirculate approximately 20 to 30 mL syrup.
22. Transfer the filtered syrup to the storage vessel.
23. Flush with nitrogen gas and seal the tank.

PROMETHAZINE HYDROCHLORIDE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
10.00	1	Promethazine HCl, with excess	10.50
41.95	2	Lactose monohydrate	41.95
20.00	3	Maize starch	20.00
0.05	4	Sodium metabisulfite (sodium disulfite)	0.05
2.00	5	Povidone (PVP K-30)	2.00
5.00	6	Maize starch (dried)	5.00
0.50	7	Magnesium stearate	0.50
–	8	Alcohol (ethanol, 95%)	6.07
–	9	Purified water	8.67

MANUFACTURING DIRECTIONS

Avoid overmixing of lubricants; otherwise, hardness will be reduced.

1. Mix items 8 and 9 in a stainless steel container.
2. Dissolve items 4 and 5 by slow stirring with stirrer until mixture becomes clear.
3. Sift items 1, 2, and 3 through a stainless steel 500 µm sieve in sifter.
4. Load into mixer, and mix for 5 minutes at low speed.
5. Add binding solution at a rate of 5 to 7 g/min to the dry powders while mixing at low speed.
6. After addition is complete, scrape sides and blades.
7. Mix further for 2 minutes using a mixer and chopper at low speed.
8. Scrape sides and blades.

9. Check for the end point of granulation, which is the point where the granulation consists of few or no lumps.
10. If required, add purified water.
11. Dry the wet granules with the air circulation heater to expel alcohol for 2 hours.
12. Then, dry at 55°C for 14 hours.
13. After 4 hours of drying, scrape the semidried granules to break up the lumps to promote uniform drying.
14. Check the LOD (limit: 1.0–1.5%).
15. If required, dry further at 55°C for 2 hours.
16. Grind the dried granules through a 1.25 mm sieve using a granulator at medium speed.
17. Collect in stainless steel drums.
18. Load granules into the blender.
19. Sift item 6 material through a 500 µm sieve using a sifter, and add it into blender.
20. Mix for 3 minutes.
21. Sift item 7 through a 500 µm sieve, and add 1 to 2 g of granules.
22. Mix in polyethylene bag for 1 minute.
23. Add to blender.
24. Mix for 30 seconds.
25. Compress 0.80 g.
26. Coat using one of the HPMC coatings in the Appendix.

PROMETHAZINE HYDROCHLORIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
25.00	1	Promethazine HCl, with excess	26.00
103.75	2	Lactose monohydrate	103.75
50.00	3	Maize starch	52.50
1.50	4	Sodium metabisulfite (sodium disulfite)	1.50
5.00	5	Povidone (PVP K-30)	5.00
12.50	6	Maize starch (dried)	12.50
1.25	7	Magnesium stearate	1.25
—	8	Alcohol (ethanol, 95%)	15.00
—	9	Purified water	21.67

MANUFACTURING DIRECTIONS

Avoid overmixing of lubricants; otherwise, hardness will be reduced.

1. Mix items 8 and 9 in a stainless steel container.
2. Dissolve items 4 and 5 by slow stirring with stirrer until mixture becomes clear.
3. Sift items 1, 2, and 3 through a stainless steel 500 µm sieve in sifter.
4. Load into mixer, and mix for 5 minutes at low speed.

5. Add binding solution at a rate of 5 to 7 g/min to the dry powders while mixing at low speed.
6. After addition is complete, scrape sides and blades.
7. Mix further for 2 minutes using a mixer and chopper at low speed.
8. Scrape sides and blades.
9. Check for the end point of granulation, which is the point where the granulation consists of few or no lumps.
10. If required, add purified water.
11. Dry the wet granules with the air circulation heater to expel alcohol for 2 hours.
12. Then, dry at 55°C for 14 hours.
13. After 4 hours of drying, scrape the semidried granules to break up the lumps to promote uniform drying.
14. Check the LOD (limit: 1.0–1.5%).
15. If required, dry further at 55°C for 2 hours.
16. Grind the dried granules through a 1.25 mm sieve using a granulator at medium speed.
17. Collect in stainless steel drums.
18. Load granules into the blender.
19. Sift item 6 material through a 500 µm sieve using a sifter, and add it into blender.
20. Mix for 3 minutes.
21. Sift item 7 through a 500 µm sieve, and add 1 to 2 g of granules.
22. Mix in polyethylene bag for 1 minute.
23. Add to blender.
24. Mix for 30 seconds.
25. Compress 0.80 g.
26. Coat using one of the HPMC coatings in the Appendix.

PSEUDOEPHEDRINE HYDROCHLORIDE CAPSULES

Bill of Materials			
Scale (mg/ capsule)	Item	Material Name	Qty/1000 Capsules (g)
24.00	1	Pseudoephedrine hydrochloride	24.00
15.00	2	Hydroxyethylcellulose, NF	15.00
60.00	3	Anhydrous lactose	60.00
1.00	4	Magnesium stearate	1.00

MANUFACTURING DIRECTIONS

1. Blend all the ingredients in a twin-shell blender for 10 minutes.
2. Fill No. 0 capsules with fill weight of 500 mg using a tamping force of 200 N.

PSEUDOEPHEDRINE HYDROCHLORIDE, CARBINOXAMINE MALEATE ORAL DROPS

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
500.00	1	Sucrose	500.00
300.00	2	Glucose liquid	300.00
150.00	3	Glycerin (96%)	150.00
30.00	4	D-Pseudoephedrine hydrochloride	30.00
1.00	5	Carbinoxamine maleate	1.00
4.00	6	Saccharin sodium (powder)	4.00
2.50	7	Sodium benzoate (powder)	2.50
1.25	8	Flavor	1.25
0.03	9	Dye	0.03
0.03	10	Dye	0.03
QS	11	Hydrochloric acid reagent-grade bottles	QS
QS	12	HyFlo filter aid	1.32
QS	13	Purified water	455.00
QS	14	Sodium hydroxide for pH adjustment	QS

MANUFACTURING DIRECTIONS

- Charge 315 mL of deionized water into a suitable tank.
- Begin heating water to 60°C to 70°C while adding sucrose with stirring.
- Stir until sugar is dissolved.
- Remove heat.
- Add glucose liquid and 125 g of glycerin in this step.
- Add and dissolve D-pseudoephedrine HCl, carbinoxamine maleate, saccharin sodium, and sodium benzoate with mixing.
- Cool solution to 30°C to 35°C.
- Mix flavor with 25 g of glycerin.
- (Note: Temperature of syrup must not be higher than 35°C.) Dissolve dyes, if used, in 5 mL of deionized water, and add to syrup with mixing.
- Adjust to pH 4.25 (range: 4.0–4.5), if necessary, with hydrochloric acid or sodium hydroxide.
- QS to 1 L with deionized water, and mix well.
- Allow product to stand overnight to let entrapped air escape.
- Readjust volume to 1 L with deionized water.
- Add and mix 1.320 g of HyFlo filter aid to the product.
- Circulate through a press.
- Filter into tank for filling.

PSEUDOEPHEDRINE HYDROCHLORIDE FAST-DISINTEGRATING TABLETS

- To the vortex of a rapidly stirred vessel containing 345 g of deionized water add 30 g of croscarmellose sodium.

- Mix this slurry for 10 minutes.
- Concurrently, place 300 g of pseudoephedrine hydrochloride and 300 g of microcrystalline cellulose (Avicel™ PH-101) in the bowl of a mixer.
- Stir this mixture for 10 minutes.
- At the conclusion of the mixing time, slowly add the slurry to the contents of the mixing bowl, forming a granulation; place this in trays and dry in a 65°C oven for 3 hours.
- Pass the dried granulation through a U.S. standard 16 mesh screen (1190 µm).
- Place the dried granulation in a twin-shell blender, and to it add 300 g of Avicel™ AC-815 (85% microcrystalline cellulose coprocessed with 15% of a calcium, sodium alginate complex) and 300 g of microcrystalline cellulose (Avicel™ PH-102).
- Thoroughly blend for 10 minutes, after which add 10.05 g of magnesium stearate and mix for an additional 5 minutes.
- Prior to being added to the blender, pass the magnesium stearate through a U.S. standard 30 mesh screen.
- Compress the resulting blend into tablets using 6.35 mm (0.25 in.) round standard concave tooling to give average weight of 0.1299 g and an average thickness of 4.864 mm (0.1915 in.).
- The hardness of these tablets should average 1.38 kp.
- Friability should measure at 0.077% after 4 minutes.
- The average disintegration time should be 15 seconds in 10 mL of deionized water, forming a suspension with minimal shaking.

PSEUDOEPHEDRINE HYDROCHLORIDE SYRUP

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
6.00	1	Pseudoephedrine HCl (3% excess)	6.18
600.00	2	Sucrose	600.00
100.00	3	Glycerin (glycerol)	100.00
100.00	4	Sorbitol (70% solution)	100.00
15.00	5	Propylene glycol	15.00
1.00	6	Methylparaben	1.00
0.30	7	Propylparaben	0.30
0.50	8	Saccharin sodium	0.50
0.02	9	Dye (if needed)	0.02
0.05	10	Menthol	0.05
0.13	11	Citric acid	0.13
1.15	12	Sodium citrate	1.15
QS	13	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

- Add 390 g of purified water to the manufacturing vessel, and heat to 90°C to 95°C.

- Add items 6 and 7 while mixing to dissolve at high speed.
- Add item 2 while mixing at slow speed at a temperature of 90°C to 95°C.
- Mix for 1 hour at high speed.
- Cool down to 50°C while mixing at slow speed.
- Dissolve items 8 and 12 in 10 g of item 13, and add to the manufacturing vessel while mixing at high speed.
- Dissolve item 11 in 10 g of purified water, and add to the manufacturing vessel while mixing at high speed.
- Load items 4 and 3 into the manufacturing vessel using a transfer pump while mixing at high speed.
- Mix for 5 minutes.
- Cool down to 30°C while mixing at slow speed.
- Add 20 g of item 13 (30°C) in a separate container, and dissolve item 1 by using stirrer.
- Mix for 10 minutes, and add to the manufacturing vessel while mixing at high speed.
- Add 6 g of item 13 in a separate container, and dissolve item 9 manually.
- Add color to the manufacturing vessel while mixing at high speed.
- Dissolve item 10 in item 5.
- Add this flavor mixture to the manufacturing vessel while mixing at high speed.
- Bring the volume up to 1 L with item 13, and finally, mix for 15 to 20 minutes at high speed.
- Check and record the pH (limit: 5.5–6.5 at 25°C).
- If required, adjust pH with 20% citric acid or 20% sodium citrate solution.
- Filter the syrup at 1.5 bar.
- Recirculate approximately 100 to 150 mL syrup.

PSEUDOEPHEDRINE HYDROCHLORIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
60.00	1	Pseudoephedrine HCl ^a	63.00
120.20	2	Lactose monohydrate	120.20
25.00	3	Maize starch	25.00
1.00	4	Povidone (PVP K-30)	1.00
4.00	5	Povidone (PVP K-30)	4.00
1.80	6	Magnesium stearate	1.80
–	7	Alcohol (ethanol, 95%)	29.00

^a Pseudoephedrine HCl 3 mg/tablet can be added in excess to compensate for moisture and handling loss.

MANUFACTURING DIRECTIONS

Avoid overmixing of lubricants; otherwise, hardness is reduced.

- Dissolve item 5 in item 7 while mixing at slow speed using a stirrer.
- Sift items 1 to 4 through a 500 µm sieve.
- Load into mixer, and mix for 5 minutes at low speed.
- Add binding solution to the dry powders while mixing at low speed for 2 minutes.
- After addition is complete, mix further for 1 minute using mixer and chopper at low speed.
- Scrape sides and blade.
- Check for the end point of granulation, which is when the granulation consists of wet granules with few or no lumps.
- If required, add ethanol 95% to achieve desired granules.
- Record extra quantity of ethanol 95% used.
- Dry the wet mass at 55°C for 7 hours.
- After 4 hours of drying, scrape the semidried granules to break the lumps to promote uniform drying.
- Check the moisture content (limit: 1.5–2.5%).
- Sift the dried granules through a 1.25 mm sieve using a granulator at medium speed.
- Collect in stainless steel drums.
- Load granules into the drum blender.
- Sift item 6 through a stainless steel 250 µm sieve in sifter.
- Add 8 to 12 g granules in mixer to sieved item 6.
- Mix manually for 1 minute.
- Add to drum blender, and blend for 1 minute.
- Compress 215 mg in 8 mm round punches.

PSEUDOEPHEDRINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
60.00	1	(+) Pseudoephedrine hydrochloride	60.00
95.00	2	Dicalcium phosphate (Di-Tab)	95.00
5.00	3	Kollidon® 30	5.00
–	4	Water	QS
20.00	5	PEG-6000 (powder)	20.00
2.00	6	Aerosil® 200	2.00

MANUFACTURING DIRECTIONS

- Granulate dicalcium phosphate with solution of items 3 and 4, dry, pass through a 0.8 mm sieve, and mix with item 1.
- Add items 5 and 6, and press with low compression force.
- Compress 192 mg using 8 mm biplanar punches.

PSORIASIS CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
40.00	1	Lanolin alcohol	40.00
50.00	2	White petroleum jelly	50.00
120.00	3	Paraffin wax 140F	120.00
300.00	4	Mineral oil (70 cS)	300.00
20.00	5	Coal tar	20.00
2.50	6	Allantoin	2.50
QS	7	Deionized water	QS to 1 kg
QS	8	Preservative	QS

MANUFACTURING DIRECTIONS

1. Heat oil and water phases separately to 70°C.
2. Slowly add water phase in increments to the oil phase.
3. Allow each addition time to be fully incorporated.
4. Stir to cool.
5. Fill just above melting point.
6. Further homogenization may improve stability prior to filling.

PSORIASIS CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
16,000	1	Stearic acid	1600
6.00	2	Oleyl alcohol	6.00
2.00	3	Lanolin	2.00
2.00	4	Coal tar	2.00
0.600	5	Triethanolamine (99%)	0.60
0.250	6	Allantoin	0.25
QS	7	Deionized water	QS to 1 kg
—	8	Preservative	QS

MANUFACTURING DIRECTIONS

1. Heat water and oil phases separately to 80°C.
2. Add water phase to oil phase while stirring.
3. Stir to cool.
4. Pass through homogenizer.
5. Fill at 40°C.

PSYLLIUM AND DIOCTYL SODIUM SULFOSUCCINATE POWDER**MANUFACTURING DIRECTIONS**

1. Psyllium husk, 5.1 g; dioctyl sodium sulfosuccinate, 240 mg.

2. The psyllium husk is milled to a small particle size: NMT 4% on 100 mesh and between 25% and 50% through 200 mesh.
3. These psyllium particles are then agglomerated with maltodextrin, and citric acid is sprayed on.
4. Dioctyl calcium sulfosuccinate or dioctyl potassium sulfosuccinate, can be substituted for the dioctyl sodium sulfosuccinate, or two or three of these can be combined.
5. Methyl cellulose, polycarbophil, calcium polycarbophil, bran, malt soup extract, karaya, guar gum, or mixtures of these can be substituted for the psyllium.
6. The amounts of psyllium and/or dioctyl sulfosuccinate can be varied within the ranges specified herein.

PSYLLIUM AND DOCUSATE SODIUM TABLETS**FORMULATION**

Psyllium, 71.0%; ethylcellulose, 4.8%; isopropyl alcohol, QS; microcrystalline cellulose, 16.7%; PVP cross-linked, 1.9%; carnauba wax, 2.3%; docusate sodium, 3.3%.

MANUFACTURING DIRECTIONS

1. Soak ethylcellulose in isopropyl alcohol overnight.
2. Granulate psyllium with isopropyl/ethylcellulose mixture in mixer.
3. Dry at 49°C for 3 hours.
4. Mill through 12 mesh screen.
5. Mix in a mixer the following: psyllium, microcrystalline cellulose, and carnauba wax.
6. Compress the tablet per granulation specifications using a tableting press.
7. Coat the core tablets.

Methylcellulose, polycarbophil, calcium polycarbophil, bran, malt soup extract, karaya, guar gum, or mixtures of these can be substituted for the psyllium. The amounts of psyllium and/or dioctyl sulfosuccinate can be varied. Dioctyl calcium sulfosuccinate or dioctyl potassium sulfosuccinate can be substituted for the dioctyl sodium sulfosuccinate, or two or three of these can be combined.

PSYLLIUM AND DOCUSATE SODIUM WAFER**FORMULATION**

Ascorbic acid, 0.15%; natural and artificial flavors, 1.54%; corn oil, 14.80%; cornstarch, 1.97%; fructose crystalline, 6.82%; lecithin oil, 0.99%; molasses granular light, 0.39%; oat hull fiber, 6.42%; psyllium husk, 13.32%; sodium bicarbonate, 0.20%; sucrose white granulated, 17.40%; table oats, 8.89%; water purified USP, QS; wheat flour, 19.21%; docusate sodium, 0.63%; sorbitan tristearin, 0.20%.

MANUFACTURING DIRECTIONS

1. In an appropriate mixer, add corn oil and lecithin, and mix for 1 minute using low speed.
2. *Note:* Preheat (microwave) lecithin, if necessary.
3. Add psyllium and docusate (which has been coated with the sorbitan tristearin), and mix for 1 minute using low speed.
4. Into a separate bowl, add part of the sucrose, fructose, molasses, and half of the water.
5. Mix for 1 minute using low speed.
6. Add psyllium/oil/lecithin premix and oat fiber.
7. Mix for 1 minute. Add rest of water, soda, flavors, ascorbic acid, and starch.
8. Mix for 1 minute at low speed.
9. Add flour to the mixer, and mix for 1 minute at low speed.
10. Roll dough into sheets approximately 0.1 in. thick.
11. Cut dough into rectangles of approximately 2.5 in. $\times$ 1.6 in.
12. Place bars on baking trays, and bake at 375°C for 10 to 12 minutes.
13. Ethylcellulose, polycarbophil, calcium polycarbophil, bran, malt soup extract, karaya, guar gum, or mixtures of these can be substituted for the psyllium. The amounts of psyllium and/or dioctyl sulfosuccinate can be varied within the ranges specified herein. Dioctyl calcium sulfosuccinate or dioctyl potassium sulfosuccinate can be substituted for the dioctyl sodium sulfosuccinate, or two or three of these can be combined.

PSYLLIUM HUSK GRANULES

1. Stir raw, unmilled psyllium seed husk (2 g) with 0.2 N sodium hydroxide (400 mL) containing sodium borohydride (400 mg) in a nitrogen atmosphere at ambient temperature for 90 minutes.
2. The pH of the solution should be from 10 to 11.
3. Pass the solution through a pasteurizer at a temperature of 100°C for a period of 50 seconds.
4. Once pasteurized, centrifuge the mixture for 20 minutes at 23,500 g.
5. Decant the supernatant from an insoluble fraction that settles out in the centrifuge bottle.
6. Mix the insoluble fraction with fresh sodium hydroxide/sodium borohydride solution (100 mL) and recentrifuge for 15 minutes to increase yield of the soluble fraction.
7. Adjust the pH of the supernatant to 5.5 by the addition of acetic acid at ambient temperature with stirring, forming a gel.
8. Desiccate the gel with isopropanol added with high-shear mixing.
9. Decant the isopropanol solution from the gel.
10. The solids content of the gel should be 30%.

11. Pass the gel material through an extruder and extrude into individual particles with an average particle size of 500 μ m.
12. Introduce the extruded particles to a fluidized-bed dryer fitted with a cyclonic airflow screen, such as a Conidur screen.
13. Maintain the air temperature at 80°C.
14. The gel temperature should remain below 70°C throughout the drying process.
15. Dry the particles to a powder, with 90% of the water being removed.
16. The yield of the gel-forming polysaccharide will be 85%.
17. The final compositions comprise the following components by weight: gel-forming, 50.0%; polysaccharide sorbitol Neosorb P20, 48.16%; magnesium stearate, 0.5%; flavorant, 0.4%; colorant, 0.14%; citric acid, 0.8%.
18. The granules can be coated using the coating formulation: isopropanol, 94.5%; Eudragit® RD100, 5%; polyethylene glycol, 0.5%.
19. Dry and combine the coated gel-forming polysaccharide particles with the excipients as described previously.

PSYLLIUM HUSK TABLETS**MANUFACTURING DIRECTIONS**

1. Stir raw, unmilled psyllium seed husk (2 g) with 0.2 N sodium hydroxide (400 mL) containing sodium borohydride (400 mg) in a nitrogen atmosphere at ambient temperature for 90 minutes.
2. The pH of the solution should be from 10 to 11.
3. Pass the solution through a pasteurizer at a temperature of 100°C for a period of 50 seconds.
4. Once pasteurized, centrifuge the mixture for 20 minutes at 23,500 g.
5. Decant the supernatant from an insoluble fraction that settles out in the centrifuge bottle.
6. Mix the insoluble fraction with fresh sodium hydroxide/sodium borohydride solution (100 mL) and recentrifuge for 15 minutes to increase yield of the soluble fraction.
7. Adjust the pH of the supernatant to 5.5 by the addition of acetic acid at ambient temperature with stirring, forming a gel.
8. Desiccate the gel with isopropanol added with high-shear mixing.
9. Decant the isopropanol solution from the gel.
10. The solids content of the gel should be 30%.
11. Pass the gel material through an extruder and extruded into individual particles with an average particle size of 500 μ m.
12. Introduce the extruded particles to a fluidized-bed dryer fitted with a cyclonic airflow screen, such as a Conidur screen.

13. Maintain the air temperature at 80°C.
14. The gel temperature should remain below 70°C throughout the drying process.
15. Dry the particles to a powder with 90% of the water being removed.
16. The yield of the gel-forming polysaccharide will be 85%.
17. Manufacture chewable tablets, total weight 2.5 g, while dry blending step 8 with sorbitol for 10 minutes, each component having an average particle size of approximately 500 µm.
18. Add the premix, if desired, and blend the mixture for an additional 10 minutes.
19. Add magnesium stearate, and blend the composition for another 5 minutes.
20. Directly compress the mixture into tablets using pressure from 2000 to 4000 psi.
21. The final compositions comprise the following components by weight: gel-forming, 50.0%; polysaccharide sorbitol Neosorb P20, 48.16%; magnesium stearate, 0.5%; flavorant, 0.4%; colorant, 0.14%; citric acid, 0.8%.
22. Optionally, the coating can be applied directly to a chewable tablet containing the gel-forming polysaccharide.
23. Additionally, it may be desired to include a flavorant within the coating composition: ethanol, 94%; polyethylene glycol, 5%; flavorant, 1%.

PVP–IODINE MOUTHWASH

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100.00	1	PVP–iodine	100.00
5.00	2	Saccharin sodium	5.00
2.00	3	Menthol	2.00
0.50	4	Aniseed oil	0.50
0.50	5	Eucalyptus oil	0.50
160.00	6	PEG-400	160.00
300.00	7	Ethanol	300.00
QS	8	Purified water	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Dissolve PVP–iodine powder and saccharin sodium in 440 g of water to obtain a clear solution.
2. In a separate container, add alcohol.
3. Mix and dissolve aniseed oil, eucalyptus oil, menthol, and PEG-400 to obtain a clear solution.
4. QS with water.
5. Add solution from previous step and mix with stirring.
6. Package in HDPE plastic bottles.

PYRIDOXINE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
40.00	1	Pyridoxine hydrochloride	40.00
150.00	2	Lactose monohydrate	150.00
150.00	3	Avicel™ PH101	150.00
15.00	4	Kollidon® VA 64	15.00
10.00	5	Kollidon® CL	10.00
1.00	6	Magnesium stearate	1.00
1.00	7	Aerosil® 200	1.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.5 mm sieve, mix, and press with high compression force.
2. Compress 361 mg in 12 mm biplanar punches.

PYRIDOXINE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
40.00	1	Pyridoxine hydrochloride	40.00
300.00	2	Cornstarch	300.00
15.00	3	Kollidon® 30	15.00
80.00	4	Water + isopropanol	80.00
1.00	5	Magnesium stearate	1.00
2.00	6	Aerosil® 200	2.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 and 2 with solution of items 3 and 4, dry, pass through a 0.8 mm sieve, mix with items 5 and 6, and press with high compression force.
2. Compress 354 mg in 12 mm biplanar punches.

PYRIDOXINE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Pyridoxine hydrochloride	100.00
200.00	2	Tablettose®	200.00
10.00	3	Kollidon® VA 64	10.00
3.00	4	Kollidon® CL	3.00
1.00	5	Magnesium stearate	1.00
1.00	6	Aerosil® 200	1.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with medium compression force.
2. Compress 363 mg in 12 mm biplanar punches.

PYRIDOXINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Pyridoxine hydrochloride	100.00
150.00	2	Lactose monohydrate	150.00
83.00	3	Avicel™ PH101	83.00
10.00	4	Kollidon® VA 64	10.00
3.00	5	Kollidon® CL	3.00
1.00	6	Magnesium stearate	1.00
1.00	7	Aerosil® 200	1.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with medium compression force.
2. Compress 360 mg in 12 mm biplanar punches.

PYRIDOXINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
250.00	1	Pyridoxine hydrochloride	250.00
100.00	2	Avicel™ PH101	100.00
12.00	3	Kollidon® VA 64	12.00
5.00	4	Magnesium stearate	5.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with high compression force.
2. Compress 361 mg in 12 mm biplanar punches.

PYRIDOXINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
300.00	1	Pyridoxine hydrochloride	300.00
100.00	2	Lactose monohydrate D 20	100.00
20.00	3	Kollidon® 30	20.00
QS	4	Isopropanol + water (1+1)	60.00
10.00	5	Kollidon® CL	10.00
2.00	6	Aerosil® 200	2.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 and 2 with solution of items 3 to 6, dry, and sieve through a 0.8 mm screen.
2. Press with medium compression force.
3. Compress 440 mg using 12 mm biplanar punches.

RANITIDINE HYDROCHLORIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
75.00	1	Ranitidine; use Ranitidine HCl	88.88
65.00	2	Microcrystalline cellulose, NF	65.00
1.12	3	Magnesium stearate, NF	1.12

MANUFACTURING DIRECTIONS

1. Pass ranitidine and microcrystalline cellulose through a 595 µm screen, and transfer to a suitable mixer.
2. Mix for 10 minutes.
3. Screen the magnesium stearate through a 400 µm screen, and add to the blender.
4. Blend for 2 minutes.
5. Compress using slightly convex round punches at hardness 8 ppi and disintegration time NMT 15 minutes in water.
6. Coat using a Methocel™–Ethocel™ coating solution (see Appendix).

RANITIDINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Quantity/1000 Tablets (g)
167.39	1	Ranitidine HCl USP (Orchev Pharma)	167.39
78.28	2	Microcrystalline cellulose NF (Avicel™ PH-102, FMC)	78.28
62.00	3	Pregelatinized starch NF (Starch 1500, Colorcon)	62.00
1.55	4	Fumed silica NF (Aerosil® 200, Degussa AG)	1.55
0.78	5	Magnesium stearate NF (Peter Greven)	0.78

MANUFACTURING DIRECTIONS

1. Blend all materials, with the exception of magnesium stearate, for 10 minutes in a blender.
2. Add magnesium stearate and blend for an additional 2 minutes.
3. Compress tablets at 310 mg.

RANITIDINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
75.00	1	Ranitidine; use Ranitidine HCl ^a	85.00
95.00	2	Microcrystalline cellulose (Avicel™ PH102)	95.00
7.00	3	Croscarmellose sodium (Ac-Di-Sol)	7.00
6.60	4	Microcrystalline cellulose (Avicel™ PH102)	6.60
1.40	5	Magnesium stearate	1.40

^a Ranitidine HCl (1.5%) is added to compensate LOD and process loss.

MANUFACTURING DIRECTIONS

1. Process the product in an area where the RH is 40% to 45% and temperature does not exceed 25°C.
2. Store the bulk tablets in polyethylene-lined stainless steel containers at a controlled RH of 45% to 50% and temperature not exceeding 25°C.
3. Pass items 1, 2, and 3 through a sifter using a 900 µm sieve.
4. Load into a blender, and mix for 3 minutes.
5. Manually mix items 4 and 5 in a polyethylene bag for 1 minute.
6. Pass through a sifter using a 500 µm sieve.
7. Collect in a polyethylene bag.
8. Add to blender, and blend for 1 minute.
9. Check temperature and humidity before start of slugging (at a temperature not exceeding 25°C and a RH of 40–45%).
10. Slug 240 g of mixed powder in a rotary tableting machine.
11. Grind the slugs in a granulator using a 3 mm sieve followed by a 1 mm sieve.
12. Compress 195 mg using oblong biconvex punches.
13. Check temperature and humidity before start of compression (limit: temperature not exceeding 25°C and RH of 40–45%).
14. Coat using a hydroalcoholic HPMC coating.

RIBOFLAVIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
3.00	1	Riboflavin	3.00
195.00	2	Ludipress®	195.00
2.00	3	Magnesium stearate	2.00
1.00	4	Aerosil® 200	1.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with very low compression force (4 kN).
2. Compress 202 mg using 8 mm biplanar punches.
3. This is a very low-active ingredient formulation (3 mg).
4. If content uniformity is a problem, prepare a pre-mix of the active ingredient with a small part of the Ludipress® or with lactose monohydrate before mixing with the other components of the formulation.

RIBOFLAVIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
10.00	1	Riboflavin	10.00
75.00	2	Lactose monohydrate	75.00
20.00	3	Cornstarch	20.00
15.00	4	Avicel™ PH101	15.00
5.00	5	Kollidon® 30	5.00
25.00	6	Water	25.00
0.80	7	Aerosil® 200	0.80
2.50	8	Talc	2.50
1.70	9	Hydrogenated castor oil	1.70

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 4 with solution of items 5 and 6, dry, pass through a 0.8 mm sieve, mix with items 7 to 9, and press with low compressive force.
2. Compress 134 mg in 8 mm biplanar punches.

RIBOFLAVIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
75.00	1	Riboflavin	75.00
375.00	2	Sorbitol (crystalline)	375.00
23.00	3	Kollidon® VA 64	23.00
4.00	4	Magnesium stearate	4.00
12.00	5	Aerosil® 200	12.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with low compressive force.
2. Compress 493 mg using 12 mm biplanar punches.

RIBOFLAVIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Riboflavin	100.00
250.00	2	Sorbitol (crystalline)	250.00
19.00	3	Kollidon® VA 64	19.00
5.00	4	Magnesium stearate	5.00
10.00	5	Aerosil® 200	10.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with medium compression force.
2. Compress 384 mg using 12 mm biplanar punches.

RIBOFLAVIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
150.00	1	Riboflavin, with excess	156.00
150.00	2	Ludipress®	150.00
4.00	3	Magnesium stearate	4.00
2.00	4	Aerosil® 200	2.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with low compressive force.
2. Compress 308 mg using 8 mm biplanar punches.

RUBEFACIENT ANALGESIC OINTMENT

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
150.00	1	Polawax, NF	150.00
100.00	2	Methyl salicylate	100.00
50.00	3	Menthol	50.00
100.00	4	Mineral oil (70 cS)	100.00
QS	5	Deionized water	QS to 1 kg
QS	6	Preservative, color	QS

MANUFACTURING DIRECTIONS

1. Heat oil and water phases separately to 70°C.
2. Add water phase to oil phase while stirring. Stir to cool.
3. Fill at 30°C.

SACCHARIN EFFERVESCENT TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
15.00	1	Saccharin sodium	15.00
10.00	2	Tartaric acid	10.00
14.00	3	Sodium bicarbonate	14.00
2.00	4	Kollidon® VA 64	2.00
2.00	5	PEG-6000 (powder)	2.00

MANUFACTURING DIRECTIONS

1. Dry saccharin sodium and tartaric acid for 1 hour at 100°C.
2. Mix all components, pass through a 0.8 mm sieve, and press with low compressive force.
3. Compress 42 mg in 5 mm biplanar punches.

SACCHARIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
37.50	1	Sodium cyclamate	37.50
17.00	2	Mannitol	17.00
6.35	3	Soda ash (light-milled powder, 58% Na ₂ O)	6.35
3.75	4	Saccharin sodium (dehydrated powder)	3.75
1.40	5	Povidone (PVP K-29-32)	1.40
8.00	6	Purified water	8.00
11.00	7	Tartaric acid	11.00
0.80	8	Soda ash (light-milled powder, 58% Na ₂ O)	0.80
1.00	9	Anhydrous sodium citrate	1.00
1.00	10	Sodium benzoate	1.00
0.20	11	PEG-8000	0.20

MANUFACTURING DIRECTIONS

1. This product is hygroscopic and should be processed in a low-humidity area not exceeding 50% RH at 24°C.
2. Maintain at 35 to 40% RH at 24°C if possible.
3. If necessary, pass sodium cyclamate and mannitol (if used) through a Fitz mill or similar type using a 420 µm or similar screen, and then charge into a suitable mixer.
4. To this mixture, add soda ash (item 3) and blend for 30 minutes or until uniform.
5. Dissolve povidone in 4 mL of warm purified water.
6. Dissolve saccharin sodium in 3 mL of warm purified water.

- Add solutions from previous steps together plus sufficient purified water.
- Mass with blended powders.
- Blend for 1 hour or until uniform.
- Pass the wet mass through a 4.76 mm or similar screen in an oscillating granulator, and spread onto trays.
- Oven dry at 50°C to 55°C for 16 to 24 hours using a full oven load of trays (LOD NMT 0.9%).
- Pass dried granulation through a 1.19 mm or similar screen in an oscillating granulator or through a 1.68 mm or similar screen using a comminuting mill (knives forward, slow speed).
- Lubricants must meet LOD/moisture content before proceeding.
- If lubricants fail, dry them at 80°C for 8 hours.
- Use 60°C for tartaric acid.
- Mill lubricants (except tartaric acid and granulated lactose, if used) through a 600 µm or similar screen in a comminuting mill (hammers forward, medium speed).
- Load dried granulation, coated tartaric acid, lactose (if used), and milled lubricants into a suitable mixer, and blend for 30 to 40 minutes.
- Compress 80 mg per tablet in 7/32 in. punches.

SACCHARIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
15.00	1	Saccharin sodium	15.00
31.00	2	Ludipress®	31.00
2.00	3	Kollidon® CL	2.00
0.30	4	Magnesium stearate	0.30
2.00	5	PEG-6000 (powder)	2.00
2.00	6	Lutrol F 68	2.00

MANUFACTURING DIRECTIONS

- Mix all components, pass through a 0.8 mm sieve, and press with medium compression force.
- Compress 51 mg (or 50 mg if items 5 and 6 are omitted) using 5 mm punches.

SALICYLIC ACID CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
150.00	1	Glyceryl stearate and PEG-75 stearate	150.00
5.00	2	Stearic acid	5.00
80.00	3	Mineral oil	80.00
665.00	4	Deionized water	665.00
100.00	5	Salicylic acid	100.00

MANUFACTURING DIRECTIONS

- Mix and heat items 1 to 4 to 75°C.
- Allow to cool with gentle stirring.
- At 30°C, add item 5. Homogenize if necessary.

SCOPOLAMINE TABLETS

MANUFACTURING DIRECTIONS

- To 0.2 g of scopolamine hydrobromide, add 29.4 g of calcium hydrogen phosphate (anhydrous) in small portions and mix well in a mortar to form a triturate.
- Mix the triturate (29.6 g) well with fumaric acid (60 g) and calcium stearate (0.4 g) in a polyethylene bag to form a mixed powder A.
- Mix 25 g of fumaric acid, 9.8 g of potassium hydrogen phosphate (anhydrous), and 0.2 g of calcium stearate in a polyethylene bag to make a mixed powder B.
- To 0.1 g of scopolamine hydrobromide, add 10 g of crystalline cellulose in small portions and mix well in a mortar to make a triturate.
- Mix this triturate (10.1 g) well with 24.7 g of lactose and 0.2 g of calcium stearate in a polyethylene bag to make a mixed powder C.
- Perform multilayer tableting on a single-punch machine equipped with a die (8 mm) and flat-faced punches: First, place 90 mg of the mixed powder A in the die and precompress lightly; place 35 mg of the mixed powder B on the first fill and lightly precompress; thereafter, place 35 mg of the mixed powder C on the second fill and compress with a total pressure of approximately 1.2 tonnes.

SELEGILINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
5.00	1	Selegiline	5.00
94.00	2	Ludipress®	94.00
1.00	3	Magnesium stearate	1.00

MANUFACTURING DIRECTIONS

- Mix all components intensively, pass through a 0.8 mm sieve, and press with low compressive force.
- Compress 99 mg in 6 mm biplanar punches.

SELENIUM SULFIDE SHAMPOO WITH CONDITIONER

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
10.00	1	Selenium sulfide	10.00
2.00	2	Methylparaben	2.00
10.00	3	Magnesium aluminum silicate type IIA	10.00
20.00	4	Titanium	20.00
0.17	5	Dye	0.17
230.00	6	Sodium alkyl ether sulfate/ sulfonate	230.00
30.00	7	Cocamide DEA surfactant	30.00
40.00	8	Cocoamphocarboxyglycinate	40.00
10.00	9	Hydrolyzed protein	10.00
4.00	10	Perfume	4.00
QS	11	Citric acid	QS
QS	12	Sodium chloride	QS
QS	13	Deionized purified water	QS to 1 L

Note: Item 11 is used for pH adjustment, if necessary, and item 12 is used for viscosity adjustment, if necessary.

MANUFACTURING DIRECTIONS

1. Selenium sulfide is toxic. Handle carefully, and use approved respiratory protection.
2. Add 7 mL of purified water to an appropriate mill containing full-charge alumina grinding cylinder media.
3. Add selenium sulfide.
4. Seal the mill, and agitate for approximately 10 minutes to wet down the powdered material.
5. Recycle for approximately 5 minutes with the pump set at 1040 mmHg.
6. Stop agitation.
7. If necessary, add purified water (25–30°C) to nearly cover the grinding media.
8. Seal the mill, and recirculate the slurry for 1 to 2 hours with the pump set to obtain the required particle size specifications for the selenium sulfide.
9. Load 250 mL of purified water into a suitable jacketed mixing tank, and heat to 60°C to 70°C.
10. With good stirring, add and dissolve methylparaben.
11. Slowly add and disperse the magnesium aluminum silicate. Continue mixing until fairly smooth.
12. Stop mixing, and allow to hydrate for 1 hour.
13. Add and disperse titanium dioxide.
14. Mix for 30 minutes.
15. With good stirring, add the selenium sulfide slurry, and rinse the mill with purified water.
16. Mix for 30 minutes.
17. Stop mixing, and add sodium lauryl ether sulfate/sulfonate.
18. Mix slowly for 5 minutes.
19. Add cocamide DEA.

20. Mix slowly for approximately 3 minutes.
21. Add cocoamphocarboxyglycinate.
22. Mix slowly for 30 minutes.
23. Separately dissolve hydrolyzed protein (hydrogel) in 4 mL of purified water, and mix until uniform.
24. Add solution to the tank, and mix until uniform.
25. Add perfume, and mix for 1 minute.
26. Dissolve dye in 2 mL of warm purified water (50–60°C), and add to mixing tank.
27. Mix until uniform.
28. Check and record pH. Adjust to 4.5 to 5.0, if necessary, using citric acid. Record amount of citric acid used and the adjusted pH.
29. Add purified water QS to 980 mL, and mix for 30 minutes.
30. Check and record viscosity.
31. If necessary, adjust by adding sodium chloride.
32. Deaerate by slow stirring under vacuum or use of a suitable deaerator.
33. Mix for 1 hour.

SERRATIOPEPTIDASE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
10.00	1	Serratiopeptidase	10.00
228.00	2	Ludipress®	228.00
2.00	3	Magnesium stearate	2.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix intensively, and press with low compressive force (6 kN).
2. Compress 238 mg in 8 mm biplanar punches.

SERTRALINE L-LACTATE OSMOTIC TABLETS

MANUFACTURING DIRECTIONS

1. Blend tablet cores comprising sertraline L-lactate (13.8 wt%), L-aspartic acid (11 wt%), calcium acetate (5 wt%), microcrystalline cellulose (29.5 wt%), and fructose (38.2 wt%) and then run through a roller compactor and mill.
2. Blend this milled material with 2.5 wt% magnesium stearate to form the final blended material; use this to make tablets having a total weight of 470 mg on a conventional tablet press.
3. Semipermeable asymmetric membrane coatings comprise 10 wt% cellulose acetate 398-10, 2.5 wt% polyethylene glycol 3350, 15 wt% water, and 72.5 wt% acetone.
4. The coating solution is spray-coated onto the tablets at a rate of 20 g/min until a 10 wt% coating level on the tablets has been achieved.

SILICONE PROTECTIVE CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
150.00	1	Polawax, NF	150.00
40.00	2	Oleyl alcohol	40.00
50.00	3	PEG-75 lanolin	50.00
150.00	4	Mineral oil (70 cS)	150.00
50.00–100.00	5	Dimethicone	50.00– 100.00
QS	6	Deionized water	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Heat water and oil phase separately to 60°C to 65°C.
2. Add the water phase to the oil phase while stirring.
3. Stir to cool to 30°C.
4. May add perfume or color as desired.

SILYMARIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
35.50	1	Silymarin	35.50
410.50	2	Ludipress®	410.50
4.50	3	Magnesium stearate	4.50

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with low compressive force (approximately 10 kN).
2. Compress 458 mg in 12 mm biplanar punches.

SIMETHICONE AND MAGNESIUM CARBONATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
16.00	1	Dextrose monohydrate, USP 25.0 kg	16.00
0.16	2	D&C Yellow No.10 Lake 250 g	0.16
0.06	3	FD&C Blue No.1 Lake 90.0 g	0.06
80.00	4	Simethicone powder GS (30%) 417 kg	266.40
64.00	5	Magnesium carbonate 100 kg	64.00
128.00	6	Microcrystalline cellulose 200 kg	128.00
175.68	7	Dextrates 275 kg	175.68
5.00	8	Stearic acid 8.00 kg	5.00

MANUFACTURING DIRECTIONS

1. Process the simethicone mix by preblending magnesium carbonate and simethicone powder GS 30% in a V-blender.
2. Dry granulate this preblended mix and place in a V-shell blender.
3. Add dextrates and microcrystalline cellulose to the preblended mix in the V-shell blender, and blend the preblended mix, dextrates, and microcrystalline cellulose for approximately 10 minutes.
4. Combine FD&C Blue No. 1 Lake, D&C Yellow No. 10 Lake, and dextrose in a drum roller, dry granulate, and then place in the V-shell blender with the preblended mix, dextrates, and microcrystalline cellulose.
5. Dry granulate an additional amount of dextrose in the same granulator that the colorants are granulated in for the purpose of rinsing the granulator after the dry granulation of the colorants.
6. Add this amount of dextrose to the V-shell blender.
7. Pass an amount of stearic acid through a 30 mesh screen and add to the V-shell blender.
8. Blend the preblended mix, dextrates, microcrystalline cellulose, colorants, dextrose, and stearic acid in the V-shell blender for 3 minutes.
9. Measure a sample of the V-shell blender mix to test blend uniformity.
10. Upon meeting satisfactory blend uniformity requirements, transfer the simethicone layer mix to tote bins and then compress into 650 mg tablets.

SIMETHICONE CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
70.00	1	Simethicone dry powder 25%	280.00
158.00	2	Sucrose, powder	158.00
7.00	3	Kollidon® 90 F	7.00
3.50	4	Kollidon® 90 F	3.50
QS	5	Isopropanol	QS
2.80	6	Aerosil® 200	2.80

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 3 with solution of items 4 and 5, dry, pass through a 0.8 mm sieve, add item 6, mix thoroughly, and press with high compressive force.
2. Compress 442 mg in 12 mm biplanar punches.

SIMETHICONE CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
80.00	1	Simethicone (Wacker silicon oil, S184)	80.00
400.00	2	Sorbitol (crystalline)	400.00
20.00	3	Aerosil® 200	20.00
390.00	4	Ludipress®	390.00
2.00	5	Menthol (powder)	2.00
8.00	6	Magnesium stearate	8.00

MANUFACTURING DIRECTIONS

1. Mix items 2 and 3 with item 1, pass through a 0.8 mm sieve, add mixture of items 4 to 6, mix thoroughly, pass again through a 0.8 mm sieve, and press with high compressive force.
2. Compress 870 mg using 16 mm biplanar punches.

SIMETHICONE INSTANT GRANULES
(60 MG AND 120 MG)

FORMULATION

- I. Simethicone (Abil® 200, Goldschmidt), 10.0 g; Cremophor RH 40, 5.0 g.
- II. Kollidon® VA 64, 3.0 g; ethanol, 40.0 g.
- III. Sorbitol, crystalline, 50.0 g; fructose, 50.0 g; Kollidon® CL-M, 50.0 g; orange flavor (Dragoco), 0.5 g.

MANUFACTURING DIRECTIONS

1. Introduce solution II into mixture I.
2. Granulate the powder mixture III with the well-stirred mixture I/II, dry, and pass through a 1 mm sieve.
3. Fill 1 or 2 g in sachets.

SIMETHICONE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
70.00	1	Simethicone	70.00
71.40	2	Microcrystalline cellulose	71.40
71.40	3	Magnesium hydroxide	71.40
265.00	4	Mannitol	265.00
100.00	5	Lactose	100.00
395.10	6	Granular sugar	395.10
0.70	7	Menthol	0.70
10.00	8	Fumed silica	10.00
5.00	9	Fumed silica	5.00
10.00	10	Magnesium stearate	10.00

MANUFACTURING DIRECTIONS

1. Blend item 2 and item 3 in a V-blender for 10 minutes.
2. Transfer to planetary mixer.
3. Slowly add weighted amount of item 1 to the mix, and mix slowly using a “B” flat beater blade. After thorough mixing, pass through a No. 20 mesh screen.
4. Add the balance of the ingredients, mix, and compress.

SODIUM FLUORIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
0.50	1	Sodium fluoride	0.55
56.25	2	Sorbitol, crystalline	56.25
56.25	3	Dicalcium phosphate	56.25
2.20	4	Kollidon® VA 64	2.20
0.50	5	Magnesium stearate	0.50

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with high compressive force.
2. Compress 116 mg using 6 mm biplanar punches.
3. If the content uniformity is not sufficient, a premix of sodium fluoride and sorbitol or dicalcium phosphate should be prepared separately before mixing with the rest of the excipients.

SODIUM FLUORIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
1.30	1	Sodium fluoride	1.30
76.70	2	Ludipress®	76.70
0.40	3	Magnesium stearate	0.40

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with low compressive force.
2. Compress 78 mg using 5 mm biplanar punches.
3. If the content uniformity does not meet the requirements, prepare a premix of the active ingredient with a small part of the Ludipress® or with lactose monohydrate before mixing with the other components of the formulation.

SPIRULINA EXTRACT CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
250.00	1	Spirulina extract (powder)	250.00
245.00	2	Ludipress®	245.00
25.00	3	PEG-6000 (powder)	25.00
5.00	4	Aerosil® 200	5.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with medium compressive force.
2. Compress 495 mg using 12 mm biplanar punches.

SUCRALFATE AND SODIUM ALGINATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Sucralfate	500.00
20.00	2	Sodium alginate	20.00
70.00	3	Cornstarch	70.00
20.00	4	Kollidon® 30	20.00
—	5	Ethanol (95%)	80.00 mL
30.00	6	Kollidon® CL	30.00
3.00	7	Magnesium stearate	3.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 3 with solution of items 4 and 5, pass through a sieve, mix the dry granules with items 6 and 7, and press with low compressive force.
2. Compress 660 mg using 12 mm biplanar punches.

SULFUR ANTISEPTIC OINTMENT

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/1000 Tablets (g)
15.00	1	Sulfur (precipitated)	15.00
85.00	2	Kaolin	85.00
QS	3	White petroleum jelly	QS to 1 kg
60.00	4	Isopropyl palmitate	60.00
13.00	5	Camphor	13.00
13.00	6	Methyl salicylate	13.00
20.00	7	Lanolin	20.00
50.00	8	Tribehenin	50.00
50.00	9	Ozokerite	50.00
35.00	10	Sorbitan oleate	35.00
15.00	11	Deionized water	15.00
4.00	12	Salicylic acid	4.00
24.00	13	Glycerin	24.00
QS	14	Preservative	QS

MANUFACTURING DIRECTIONS

1. Heat oils, except sulfur and lanolin, to 70°C.
2. Disperse sulfur and kaolin in the oil phase.
3. Heat water, glycerin, and salicylic acid gently.
4. Add to oil phase while stirring.
5. Stir to 55°C.
6. Mill to disperse sulfur.

TANNIN–CROSPVIDONE COMPLEX TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
55.00	1	Tannic acid	55.00
230.00	2	Water	230.00
230.00	3	Kollidon® CL	230.00
33.00	4	Avicel™ PH101	33.00
2.60	5	Talc	2.60
0.30	6	Aerosil® 200	0.30
0.30	7	Calcium arachinate	0.30

MANUFACTURING DIRECTIONS

1. Prepare solution of items 1 and 2, suspend item 3, and filter the formed insoluble tannin–crospovidone complex.
2. Wash with water until the water is clear, pass the solids through a 0.8 mm sieve, and dry.
3. Add items 4 to 7, and press with low compressive force.
4. Compress 323 mg using 12 mm biplanar punches.

TETRAHYDROZOLINE EYE DROPS

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
17.20	1	Acid boric	17.20
1.50	2	Hydroxypropylmethylcellulose 2910 (4000 cps)	1.50
0.40	3	Borax	0.40
1.00	4	Disodium edetate	1.00
0.50	5	Tetrahydrozoline hydrochloride	0.50
0.63 mL	6	Benzalkonium chloride solution (17%)	0.63 mL
QS	7	Water purified	QS to 1 L

MANUFACTURING DIRECTIONS

1. Use thoroughly cleaned and rinsed steam-jacketed, glass-lined, or stainless steel tank (No. 304 or better) equipped with a speed-controlled agitator. The tank should have a cover. Foaming occurs because of the benzalkonium chloride, which concentrates in the foam. Processing and filling systems should be designed to minimize foaming and allow rapid dissipation of foaming.
2. Place 80% of the final volume of water into the mixing tank.
3. If using methyl cellulose, heat deionized water to 90°C.
4. While agitating, add and disperse methylcellulose by slowly sprinkling it on the surface of solution. Mix to avoid excessive foaming.
5. Allow 15 minutes for hydration of the methylcellulose before discontinuing heating, and allow to cool to 40°C.
6. While agitating, add and dissolve disodium edetate, benzalkonium chloride, boric acid, sodium borate, and tetrahydrozoline. Continue cooling to 25°C.
7. Discontinue agitation, and QS to 1 L with deionized water. (*Note:* Methylcellulose solutions filter at a slow rate.) Use inline Pall and Sartorius cartridges, and recirculate solution until clear. Transfer to holding or sterilization.
8. Use either heat sterilization or sterile filtration.
9. Heat sterilization: Sterilize at 112°C to 115°C for 60 minutes, cool solution to 25°C to 30°C, and aseptically add the sterile tetrahydrozoline solution. Mix well.
10. Set up a previously sterilized filter and transfer line with 10 µm stainless steel FulFlo filter or equivalent.
11. Aseptically fill sterile solution into sterilized containers, and apply sterile closure components.
12. Sterile filtration: Use Pall cartridge with Sartorius cartridge. Prepare and steam-sterilize the recommended filter units.
13. Aseptically fill the sterilize solution into each sterilized container, and apply sterile closure.

THIAMINE AND CAFFEINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Thiamine hydrochloride	500.00
100.00	2	Caffeine	100.00
30.00	3	Cornstarch	30.00
20.00	4	Kollidon® VA 64	20.00
15.00	5	Kollidon® VA 64	15.00
QS	6	Ethanol (96%)	QS
35.00	7	PEG-6000 (powder)	35.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 4 with solution of item 5 and 6, dry, sieve, mix with item 7, and press with low compressive force.
2. Compress 698 mg using 16 mm biplanar punches

THIAMINE HYDROCHLORIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Thiamine HCl with excess	110.00
43.50	2	Lactose monohydrate	43.50
4.00	3	Crospovidone (Kollidon® CL)	4.00
5.50	4	Povidone (PVP K-90)	5.50
5.50	5	Crospovidone (Kollidon® CL)	5.50
32.00	6	Microcrystalline cellulose (Avicel™ PH112)	32.00
5.60	7	Talc (fine powder)	5.60
3.70	8	Glyceryl behenate (glyceryl monostearate)	3.70
0.20	9	Magnesium stearate	0.20
–	10	Alcohol (ethanol, 95%)	50.67

MANUFACTURING DIRECTIONS

1. Sift items 1, 2, and 3 through a stainless steel 630 µm sieve.
2. Load into mixer.
3. Mix for 5 minutes at high speed.
4. Dissolve item 4 in item 10 under slow stirring by stirrer.
5. Add the binding solution while mixing at high speed over a period of 2 minutes. Scrape sides and blades.
6. Mix and chop at high speed for 2 minutes.
7. Check the end point of granulation.
8. If required, add additional item 10 to obtain the end point. (The end point of granulation occurs when the wet mass consists of few or no lumps.) Dry wet granules in oven at 55°C for 8 hours.

9. After 2 hours of drying, scrape the semidried granules to break up the lumps to promote uniform drying.
10. Check the LOD (limit: 1.0–1.5%).
11. If required, dry at 55°C for an additional hour.
12. Check the LOD again.
13. Grind the dried granules through a 1.25 mm sieve with the granulator set at medium speed.
14. Collect in stainless steel drums.
15. Load the granules into blender.
16. Sift items 5 and 6 through a 500 µm sieve and add to blender.
17. Mix for 2 minutes (do not overmix).
18. Sift items 8 and 9 through a 500 µm sieve.
19. Add 1.33 g to 2.67 g of granules.
20. Mix in a polyethylene bag for 1 minute.
21. Add to blender.
22. Blend for 1 minute.
23. Check temperature and humidity before start of compression (limit: temperature should not exceed 25°C; RH, 45–50%).
24. Compress using 8 mm round, beveled, concave punches.

THIAMINE HYDROCHLORIDE TABLETS (SUGAR-COATED)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Thiamine hydrochloride monohydrate (with excess)	110.00
110.00	2	Lactose	110.00
5.00	3	Luviskol® K-98	5.00
1.00	4	Magnesium stearate	1.00
40.00	5	Ethyl alcohol (denatured)	40.00
251.44	6	Sugar (crystalline)	251.44
1.40	7	Sugar powder	1.40
14.50	8	Maize starch	14.50
14.81	9	Talcum	14.81
21.00	10	Copolymer lacquer	21.00
0.40	11	Paraffin (solid)	0.40
0.16	12	Gum acacia	0.16
0.228	13	Ethyl alcohol (denatured)	0.228
0.01	14	Paraffin (liquid)	0.01
QS	15	Purified water	QS

MANUFACTURING DIRECTIONS

1. In a suitable stainless steel vessel, add denatured ethyl alcohol and Luviskol®. Mix until homogeneous mixture is obtained. Set aside.
2. Pass lactose through a No. 2 mesh sieve, add thiamine, and mix for 10 minutes in an appropriate mixer.
3. Slowly add to this mixture the solution made earlier, and stir until slightly lumpy mass is obtained.
4. If required, add ethyl alcohol to the mixture.
5. Pass the wet mass through an oscillating granulator with a 7 mm perforated sieve.
6. Spread the granules over paper-lined trays, and dry at 40°C for 5 hours in a drying oven.
7. The RH of the granules should be 15% to 25%.
8. Pass magnesium stearate and talcum through a 1 mm hand sieve.
9. Compress on a rotary tablet machine at approximately 4 to 5 tonnes of pressure. The weight of each tablet should be approximately 230 mg.
10. In a suitable container, add purified water and acacia gum. Pass the resulting solution through a 0.8 mm sieve.
11. Charge the compressed tablets into a coating pan, and apply the copolymer lacquer in 10 portions. After the last application, apply neutral spray (crystalline sugar in demineralized water).
12. Dry the insulated tablets in a drying oven overnight at 45°C (minimum 14 hours). The tablet weight should be approximately 236 mg each.
13. In an electric-jacketed kettle, put demineralized water, crystalline sugar, maize starch, and talcum. Mix by stirring until homogeneous.
14. Pass through a sieve of mesh size 0.8 mm (pH: 6–8, density: 1.335–1.356).
15. Coat the tablets to 400 mg weight using the coating solution and a sugar-coating pan. Set pans at slow speed, open air inlets, and set air inflow at 80°C and maximum contact temperature at 42°C.
16. Roll tablets to reach this temperature.
17. Turn pan to fast speed, close the inlet air flap, and make first application of syrup.
18. When all tablets are wet, and distribution of syrup is uniform, open the air inlet flap, and allow 80°C air to blow (tablet temperature falls 1–2°C for a short time and then slowly rises to 42°C).
19. The next application of the syrup cycle begins.
20. Coat the tablets with color solution as described earlier to 495 mg weight.
21. Set the air inflow temperature at 25°C, and reduce the size of application with the falling temperature, whereby tablets are evenly and lightly moistened after each application. The temperature drops from 42°C to 32°C.
22. Turn the coating pans slowly during the drying phase. For the last three applications, keep the pan lids closed, as well as the air intake and outflow during this phase.
23. Drying only with outlet air may be extended for the last three applications up to 10 to 15 minutes.
24. Immediately after the last application of syrup has dried slightly, begin the polishing step.

25. The polishing paste is prepared in a suitable boiling vessel by adding stock gum solution, crystalline sugar, and demineralized water.
26. Boil until temperature reaches 106°C with stirring.
27. In a steam kettle, melt solid and liquid paraffin, and pour melted paraffins into the mixture of gum. Make up the weight with demineralized water.
28. Polishing paste ready for use contains 0.75 kg of paste and 0.113 kg of ethyl alcohol.
29. Tablet temperature is 28°C to 32°C.
30. Shut off the inlet flaps and outlet flaps, set the pans at the fast speed, and add polishing paste (approximately 0.3% of tablet weight).
31. Close the pans with inner lids, and allow them to rotate at fast speed for 90 seconds for even distribution.
32. Remove the inner lid of the pan, and set it on slow speed.
33. Open the outlet air for 3 minutes, and blow the inlet air at 40°C for 6 to 8 minutes until a good sheen appears.
34. Set the pans on automatic system for overnight with intermission time of 5 minutes off and 10 seconds on.

THIAMINE, PYRIDOXINE, AND CYANOCOBALAMIN TABLETS

Bill of Materials

Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
110.00	1	Thiamine mononitrate	110.00
210.00	2	Pyridoxine hydrochloride	210.00
76.82	3	Lactose monohydrate	76.82
10.00	4	Crospovidone (Kollidon® CL)	10.00
18.50	5	Povidone (PVP K-90)	18.50
0.30	6	Cyanocobalamin	0.30
85.00	7	Microcrystalline cellulose (Avicel™ PH102)	85.00
14.00	8	Crospovidone (Kollidon® CL)	14.00
10.00	9	Glyceryl behenate (glyceryl monostearate)	10.00
0.49	10	Magnesium stearate	0.49
15.00	11	Talc (fine powder)	15.00
—	12	Alcohol (ethanol, 95%)	88.90

MANUFACTURING DIRECTIONS

1. Dissolve item 5 in item 12 by using a stirrer to make a clear solution.
2. Dissolve item 6 carefully in the solution.
3. Sift items 1 to 4 through a 630 µm sieve.
4. Load the material into a mixer.
5. Mix and chop at high speed for 5 minutes.
6. Add binding solution from previous step to the dry powder in the mixer while mixing and chopping at high speed for 2 minutes.
7. Check for satisfactory wet mass.
8. Add additional item 12, if required, to obtain a satisfactory wet mass.
9. Do not allow big lumps.
10. Record the additional quantity of ethanol 95%.
11. Spread the granules onto stainless steel trays to a thickness of one-fourth of the tray thickness, and load the trays onto a trolley.
12. Load the trolley into an oven.
13. Keep the door open and switch on the oven with air circulation and heater turned off for 2 hours.
14. Dry the granules at 55°C for 12 hours.
15. Check the LOD of dried granules (limit: NMT 0.7%).
16. Grind the dried granules through a 1.25 mm sieve using a granulator.
17. Collect in a stainless steel drum.
18. Load into the blender.
19. Sift items 7, 8, and 9 through a 500 µm sieve.
20. Collect in stainless steel container.
21. Load the sieved powder into the blender.
22. Blend for 3 minutes.
23. Sift items 11 and 10 through a 500 µm sieve.
24. Collect in a polyethylene bag.
25. Add 4.44 g to 6.67 g of granules from earlier step, and mix manually for 1 minute.
26. Add this mixture to the blender, and mix for 1 minute.
27. Compress the granules using a rotary tableting machine.
28. Compress 550 mg using round, biconvex punches at 9 to 16 kp.
29. Coat tablets using an HPMC coating (see Appendix).

THIAMINE, PYRIDOXINE, AND CYANOCOBALAMIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Thiamine mononitrate (powder), with excess	115.00
50.00	2	Pyridoxine hydrochloride	50.00
9.75	3	Anhydrous citric acid (powder)	9.75
20.10	4	Monohydrate lactose (powder, regular)	20.10
1.67	5	Saccharin sodium	1.67
0.24	6	Dye	0.24
0.009	7	Dye	0.009
0.02	8	Dye	0.02
2.00	9	Cornstarch	2.00
QS	10	Purified water	18.00 mL
50.00 µg	11	Vitamin B ₁₂ ; use vitamin B ₁₂ oral powder cobalamin conc.	62.50
12.50	12	Monohydrate lactose (powder, regular)	12.50
1.50	13	Oil orange terpeneless	1.50
3.50	14	Magnesium stearate	3.50
1.50	15	Talc (powder)	1.50
17.70	16	Cornstarch, light coral red 6 LA	17.70

MANUFACTURING DIRECTIONS

1. Pass thiamine mononitrate, pyridoxine HCl, citric acid, lactose (item 4), and saccharin sodium through a No. 30-mesh (595 µm or similar) screen.
2. Charge into mixer, and dry mix.
3. Dissolve the dyes in purified water.
4. Add the starch (item 9) to this dye solution with stirring.
5. Heat, and continue stirring until a thick paste is formed.
6. Cool to room temperature before using.
7. (Note: Use 7.5 g of colored starch paste for the vitamins B₁ and B₆ blend and 12.5 g of colored starch paste for the vitamin B₁₂ blend.) Add 7.5 g of colored starch paste to powder blend, and mix until mass is formed.
8. Pass through a No. 6 mesh (3.36 mm or similar) screen, and air dry for 3 to 4 hours.
9. Screen vitamin B₁₂ oral powder and lactose (item 12) through a No. 30 mesh (595 µm or similar) screen.
10. Charge into mixer, and dry mix.
11. Add 12.5 g colored starch paste to powder blend, and mix until mass is formed.
12. Pass through No. 6 mesh (3.36 mm or similar) screen, and air dry for 3 to 4 hours.
13. Dry granulations from the two steps separately at 49°C overnight or until LOD is less than 1%.

14. Mill the two dried granulations through a No. 16 mesh (1.2 mm or similar) screen (knives forward, medium speed), and combine.
15. Sift a small quantity of granulation from the previous steps over a No. 30 mesh (595 µm or similar) screen, and add the orange oil to the fines.
16. Add magnesium stearate, talc powder, and light coral red starch to mixture, and pass through a No. 30 mesh (595 µm or similar) screen.
17. Charge base granulation and lubricants into a blender, and blend thoroughly.
18. Compress using 11/32 in. concave punches.

THIAMINE, PYRIDOXINE, AND CYANOCOBALAMIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Thiamine hydrochloride	100.00
10.00	2	Pyridoxine hydrochloride	10.00
0.10	3	Cyanocobalamin (gelatin-coated, 1%)	10.00
277.00	4	Ludipress®	277.00
3.00	5	Magnesium stearate	3.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with low compressive force.
2. Compress 394 mg in 12 mm biplanar punches.

THIAMINE, PYRIDOXINE, AND CYANOCOBALAMIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Thiamine mononitrate	100.00
200.00	2	Pyridoxine hydrochloride	200.00
0.10	3	Cyanocobalamin (gelatin-coated, 1%)	10.00
250.00	4	Ludipress®	250.00
45.00	5	PEG-6000 (powder)	45.00
5.00	6	Aerosil® 200	5.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with low compressive force.
2. Compress 609 mg using 12 mm biplanar punches.

THIAMINE, PYRIDOXINE, AND CYANOCOBALAMIN TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
250.00	1	Thiamine mononitrate	250.00
250.00	2	Pyridoxine hydrochloride	250.00
75.00	3	Lactose monohydrate	75.00
25.00	4	Kollidon® 30	25.00
QS	5	Isopropanol	QS
1.00	6	Cyanocobalamin (gelatin-coated, 1%)	100.00
25.00	7	Kollidon® CL	25.00
2.00	8	Magnesium stearate	2.00
2.00	9	Talc	5.00

MANUFACTURING DIRECTIONS

1. Granulate mixture items 1 to 3 with solution of items 4 and 5, dry, pass through a 0.8 mm sieve, mix with items 6 to 9, and press with low compressive force, applying a vibrating hopper.
2. Compress 730 mg using 12 mm biplanar punches.

THIAMINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
50.00	1	Thiamine hydrochloride or thiamine mononitrate	50.00
293.00	2	Ludipress®	293.00
5.00	3	Magnesium stearate	5.00
2.00	4	Aerosil® 200	2.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.5 mm sieve, mix, and press with medium compressive force.
2. Compress 357 mg, if hydrochloride salt is used, or 347 mg, if mononitrate salt is used, with 12 mm biplanar punches.

THIAMINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
50.00	1	Thiamine hydrochloride or thiamine mononitrate	50.00
150.00	2	Lactose monohydrate	150.00
150.00	3	Avicel™ PH101	150.00
15.00	4	Kollidon® CL	15.00
2.00	5	Aerosil® 200	2.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.5 mm sieve, mix, and press with high compressive force.
2. Compress 344 mg, if hydrochloride salt is used, or 373 mg, if mononitrate salt is used, with 12 mm biplanar punches.

THIAMINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Thiamine hydrochloride or thiamine mononitrate	110.00 (or 100.00)
190.00	2	Ludipress®	190.00
100.00	3	Lactose monohydrate	100.00
100.00	4	Avicel™ PH101	100.00
9.00	5	Kollidon® CL	9.00
3.00	6	Aerosil® 200	3.00
2.00	7	Magnesium stearate	2.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.5 mm sieve, mix, and press with medium compressive force.
2. Compress 302 mg, if hydrochloride salt is used, or 320 mg, if mononitrate salt is used, with 8 mm biplanar punches.

THIAMINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Thiamine hydrochloride	100.00
200.00	2	Lactose monohydrate	200.00
10.00	3	Kollidon® 30	10.00
60.00	4	Isopropanol	60.00
10.00	5	Kollidon® CL	10.00
2.00	6	Magnesium stearate	2.00
1.00	7	Aerosil® 200	1.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 and 2 with solution of items 3 and 4, dry, sieve through a 0.8 mm screen, mix with items 5 to 7, and press to tablets.
2. Compress 330 mg using 8 mm biplanar punches.

THIAMINE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
300.00	1	Thiamine mononitrate	300.00
100.00	2	Dicalcium phosphate (Di-Tab)	100.00
15.00	3	Kollidon® 30	15.00
QS	4	Isopropanol	~50.00
10.00	5	Kollidon® CL	10.00
4.00	6	Magnesium stearate	4.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 and 2 with solution of items 3 and 4, dry, and sieve through a 0.8 mm screen.
2. Mix with items 5 and 6, and compress 430 mg into tablets using 12 mm biplanar punches.

TOLNAFTATE AND UNDECYLENATE
FOOT CARE CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
150.00	1	Glyceryl stearate and PEG-75 stearate	150.00
20.00	2	Hydrogenated palm/Palm kernel oil PEG-6 esters	20.00
60.00	3	Mineral oil	60.00
0.50	4	Sorbic acid	0.50
0.50	5	Sodium methylparaben	0.50
509.00	6	Deionized water	509.00
50.00	7	Undecylenic acid	50.00
200.00	8	Zinc undecylenate	200.00
10.00	9	Tolnaftate	10.00

MANUFACTURING DIRECTIONS

1. Mix and heat items 1 to 7 to 75°C.
2. Allow to cool with gentle stirring.
3. At 30°C, add items 8 and 9.
4. Homogenize if necessary.

TOLNAFTATE FOOT CARE MICROEMULSION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
155.00	1	Ethoxydiglycol	155.00
130.00	2	Polyglyceryl-6-dioleate	130.00
450.00	3	PEG-8 caprylic/capric glycerides	450.00
10.00	4	Tolnaftate	10.00
100.00	5	Deionized water	100.00
50.00	6	Apricot kernel oil PEG-6 esters	50.00
100.00	7	Caprylic/Capric triglycerides	100.00
5.00	8	Chlorocresol	5.00

MANUFACTURING DIRECTIONS

1. Mix items 1 to 3, and dissolve item 4 in this mixture.
2. Add items 5 to 8, and mix until uniform.

TOLU BALSAM COUGH SYRUP

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
11.03	1	Tolu balsam tincture	11.03
2.50	2	Magnesium carbonate (powder)	2.50
15.00	3	Sucrose (granulated sugar)	15.00
QS	4	Purified water	90.00 mL
0.77	5	Methylparaben	0.77
0.086	6	Propylparaben	0.86
514.36	7	Sucrose (granulated sugar)	514.36
129.24	8	Glycerin (96%)	129.24
2.00	9	Dextromethorphan hydrobromide	2.00
1.00	10	Ephedrine HCl (powder)	1.00
8.00	11	Ammonium chloride	8.00
0.40	12	Chlorpheniramine maleate	0.40
1.00	13	Phenylephrine HCl	1.00
333.32	14	Glucose (liquid)	333.32
0.35	15	Flavor	0.35
0.15	16	Flavor	0.15
1.01	17	Ipecac (fluid extract)	1.01
8.57	18	Alcohol (ethanol, 190 proof)	8.57
0.037	19	Dye	0.037
QS	20	Hydrochloric acid (reagent-grade bottles)	QS
QS	21	Purified water	212.00 mL

MANUFACTURING DIRECTIONS

1. Load tolu balsam tincture into mixing tank, and add magnesium carbonate.
2. Mix well to suspend.
3. Add sugar (item 3) with mixing.
4. Add 90 mL purified water (item 4), and mix thoroughly.

5. Allow to set for 1 hour.
6. Mix periodically while circulating through Shriver filter (or equivalent).
7. Solution must be brilliantly clear.
8. Filter, and save for next part.
9. Place 210.5 mL purified water (item 21) into suitable tank.
10. Add and dissolve parabens with heat (90–95°C) and mixing.
11. Add and dissolve sugar (item 7) with mixing; heat if necessary.
12. Add glycerin, continue agitation, and cool to room temperature.
13. To cooled syrup, add filtrate from previous step.
14. Add and dissolve the following ingredients with mixing: dextromethorphan hydrobromide, ephedrine HCl, ammonium chloride, chlorpheniramine maleate, and phenylephrine HCl.
15. Add glucose. Mix well.
16. Add and dissolve flavors and Ipecac fluid extract in 190 proof alcohol.
17. To the tank or in a separate container, add flavors and Ipecac extract to 10 mL of glucose liquid, and mix.
18. Add this mixture to the main mixture.
19. Rinse the container with a further 5 mL of liquid glucose, and add the rinsings to the mixture.
20. Add the remaining liquid glucose. Mix well.
21. Dissolve in 1.75 mL purified water, and add.
22. Check pH (range: 4–5).
23. Use hydrochloric acid to adjust pH to 4 to 5, with 4.5 being optimum (approximately 0.3 mL HCl per liter of syrup).
24. QS to 1 L with purified water.
25. Filter until sparkling clear.
26. Add a suitable filter aid, and mix until uniform.
27. Filter into tank for filling.

TRICLOSAN AND ZINC FOOT DEODORANT POWDER

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/1000 Tablets (g)
3.00	1	Triclosan (Irgasan® DP300)	3.00
2.00	2	Zinc undecylenate, USP	2.00
0.20	3	Menthol (crystals), USP	0.20
926.80	4	Talc (powder), USP	926.80
30.00	5	Magnesium stearate	30.00
30.00	6	Cornstarch, NF	30.00
8.00	7	Perfume	8.00

MANUFACTURING DIRECTIONS

1. Pass the following ingredients through a 250 µm screen or similar: Irgasan® DP300, zinc undecylenate, magnesium stearate, cornstarch, menthol, and approximately 10% of the total amount of talc.
2. Place materials from first step into a suitable mixer.
3. Mix until uniform.
4. Discharge powder from second step into another suitable mixer.
5. Add and disperse perfume.
6. Mix until uniform.
7. Pass mixture from previous step through a 250 µm screen or similar.
8. Place mixture from previous step into a V-mixer or similar, and add balance of talc powder.
9. Mix for 30 minutes or until homogeneous.

TRICLOSAN FOOT CARE CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
50.00	1	Glyceryl stearate (Gelol)	50.00
50.00	2	Propylene glycol stearate	50.00
100.00	3	Octyldodecyl myristate	100.00
50.00	4	Isostearyl isostearate	50.00
20.00	5	Dimethicone (100 cS)	20.00
651.00	6	Deionized water	651.00
50.00	7	Sucrose distearate	50.00
4.00	8	Phenoxyethanol, methylparaben, ethylparaben, and propylparaben	4.00
20.00	9	Propylene glycol	20.00
3.00	10	Triclosan	3.00
2.00	11	Fragrance	2.00

MANUFACTURING DIRECTIONS

1. Heat items 1 to 5 and items 6 to 7 separately to 75°C. Mix the two parts with turbine mixing for 1 minute.
2. Cool with gentle stirring.
3. Add items 9 and 10 and then item 11 with mixing at 30°C to 35°C.

TRIPROLIDINE AND PSEUDOEPHEDRINE HYDROCHLORIDE SYRUP

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
0.25	1	Triprolidine HCl (4.8% excess)	0.26
6.00	2	Pseudoephedrine HCl (3.0% excess)	6.18
600.00	3	Sucrose	600.00
100.00	4	Glycerin (glycerol)	100.00
100.00	5	Sorbitol (70% solution)	100.00
15.00	6	Propylene glycol	15.00
1.00	7	Methylparaben	1.00
0.30	8	Propylparaben	0.30
0.50	9	Saccharin sodium	0.50
0.04	10	Quinoline yellow	0.04
0.05	11	Menthol	0.05
0.25	12	Raspberry flavor	0.25
1.15	13	Sodium citrate	1.15
QS	14	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Add 400 g of purified water to the manufacturing vessel and heat to 90°C to 95°C.
2. Add items 7 and 8 while mixing to dissolve at high speed.
3. Add item 3 while mixing at slow speed (temperature: 90–95°C).
4. Mix for 1 hour at high speed.
5. Cool down to 50°C while mixing at slow speed.
6. Add items 9 and 13 to the manufacturing vessel while mixing at high speed.
7. Load items 4 and 5 into the manufacturing vessel using a transfer pump while mixing at high speed.
8. Add 20 g of cold purified water (30°C) in a separate container, and dissolve items 1 and 2 by using stirrer.
9. Mix for 10 minutes, and add to the manufacturing vessel while mixing at high speed.
10. Add 1 g of purified water in a separate container, and manually dissolve item 10.
11. Add color to the manufacturing vessel while mixing at high speed.
12. Dissolve item 11 in item 12; then, add item 6.
13. Add this flavor mixture to the manufacturing vessel while mixing at high speed.
14. Bring the volume up to 1 L with item 14, and finally, mix for 15 to 20 minutes at high speed.
15. Check and record the pH (limit: 5.8–6.8 at 25°C).
16. If required, adjust pH with 20% citric acid or 20% sodium citrate solution.
17. Filter the syrup at 1.5 bar.
18. Recirculate approximately 20 to 30 mL syrup.

TRIPROLIDINE AND PSEUDOEPHEDRINE HYDROCHLORIDE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
2.60	1	Triprolidine HCl (4% excess)	2.70
60.00	2	Pseudoephedrine HCl (5% excess)	63.00
122.40	3	Lactose monohydrate	122.40
25.50	4	Maize starch	25.500
1.00	5	Povidone (PVP K-30)	1.00
4.00	6	Povidone (PVP K-30)	4.00
—	7	Alcohol (ethanol, 95%)	28.00
1.50	8	Magnesium stearate	1.50

MANUFACTURING DIRECTIONS

1. Dissolve item 6 in item 7 using a stirrer.
2. Avoid loss of ethanol by evaporation.
3. Pass items 1 to 5 through a 630 µm sieve using sifter.
4. Collect in a stainless steel drum.
5. Load the sieved powders into a mixer.
6. Mix and chop for 5 minutes at low speed.
7. Add PVP solution to the mixer at medium rate while mixing.
8. Start the chopper at low speed when half of the solution is added.
9. Mix and chop at low speed until the satisfactory mass is obtained.
10. Spread the wet granules onto the trays.
11. Keep the trolleys in the open air for approximately 1 hour.
12. Load the trolleys into the oven, and start the air circulation at room temperature for 2 hours.
13. Dry the granules at 55°C with air circulation for 5 hours.
14. Scoop the granules after 2 hours of drying. Move the upper trays down and the lower trays up for uniform drying.
15. Check the moisture content (limit: NMT 1.5%).
16. Pass the dried granules through a 1 mm sieve using a granulator.
17. Collect in a stainless steel drum, and load into the blender.
18. Pass item 8 through a 250 µm sieve using a sifter.
19. Collect in a polyethylene bag.
20. Mix 2 g of granules with this mixture, and add to the blender.
21. Mix for 1 minute.
22. Unload the lubricated granules in a stainless steel drum.
23. Compress 220 mg in 8.5 mm round, concave punches.

TROLAMINE SALICYLATE CREAM

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/kg (g)
50.00	1	Glyceryl stearate	5.00
25.00	2	Cetyl alcohol	2.50
30.00	3	Cetyl phosphate and DEA cetyl phosphate	3.00
40.00	4	Stearyl stearoyl stearate	4.00
40.00	5	Cococaprylate/Caprates	4.00
40.00	6	Cetyl palmitate	4.00
5.00	7	Dimethicone	0.50
502.00	8	Deionized water	50.20
10.00	9	Propylene glycol, diazolidinyl urea, methylparaben, and propylparaben	1.00
5.50	10	Magnesium aluminum silicate	0.55
2.50	11	Xanthan gum	0.25
100.00	12	Deionized water	10.00
100.00	13	Trolamine salicylate (TEA salicylate)	10.00
50.00	14	Propylene glycol	5.00

MANUFACTURING DIRECTIONS

1. Heat items 8 and 9 to 85°C, and add items 10 and 11.
2. Mix until well dispersed.
3. Add items 1 to 7, and mix well at 80°C to 85°C.
4. Continue mixing. While cooling to 65°C, add items 12 to 14, and continue mixing and cooling to 35°C.
5. The pH should be 5.5 to 5.6.

ULTRASONIC ADHESIVE GEL

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
5.00	1	Preservative (e.g., parabens)	5.00
754.00	2	Water	754.00
6.00	3	Carbopol 940 (Goodrich)	6.00
20.00	4	Sodium hydroxide solution 10%	20.00
15.00	5	Kollidon® 30	15.00
200.00	6	Water	200.00

MANUFACTURING DIRECTIONS

1. Prepare solution of item 1 in item 2 by heating to 70°C, and add item 3 slowly to obtain a homogeneous suspension.
2. Add items 4 to 6.
3. A clear, colorless adhesive gel is obtained.
4. Addition of sodium chloride changes consistency.

UREA PEROXIDE EAR DROPS

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
65.00	1	Urea peroxide (40% excess)	91.00
15.00	2	Sodium citrate (dihydrate, powder)	15.00
5.00	3	Polysorbate 20 (Tween 20)	5.00
2.50	4	Tartaric acid (12663)	2.50
QS	5	Anhydrous glycerin	QS
QS	6	Nitrogen	QS

MANUFACTURING DIRECTIONS

1. Add 500 mL of glycerin into a suitable tank.
2. Start mixing at slow speed, and heat the contents to 70°C to 75°C.
3. Flood tank with nitrogen, increase mixing speed, and slowly add sodium citrate.
4. Add tartaric acid.
5. Mix for at least 30 minutes or until dissolved.
6. Maintain the temperature at 70°C to 75°C.
7. When sodium citrate is completely dissolved, cool to 25°C to 30°C with constant mixing.
8. Prepare urea peroxide by breaking up lumps and screening to remove large particles.
9. Wear gloves.
10. Add an additional 250 to 300 mL of glycerin into tank.
11. Add urea peroxide slowly to prevent lumping while mixing constantly.
12. Mix at high speed after addition.
13. Add Polysorbate 20 with constant mixing, and QS to final volume with glycerin.
14. Mix for at least 30 minutes and until solution is clear.
15. Pass solution through an approximately No. 100 mesh (150 µm or similar) screen, and collect in clean, dry carboys. (The filter support screen in a Millipore holder may be used for filtering. The solution is too viscous to flow through a membrane or any cellulosic filter.)

VALERIANA AND PASSIFLORA EXTRACT TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
44.00	1	Valeriana extract, powder	44.00
33.00	2	Passiflora extract, powder (with excess)	36.00
120.00	3	Avicel™ PH101	120.00
11.00	4	Kollidon® CL	11.00
3.60	5	Aerosil® 200	3.60
7.30	6	Magnesium stearate	7.30

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with low compressive force.
2. Compress 231 mg using 9 mm biconvex punches.

VITAMIN A AND VITAMIN D INFANT DROPS

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
1500 IU	1	Vitamin A palmitate (1.7 MM IU/g) (50% excess)	1.323
400 IU	2	Vitamin D (40 MM IU/g) (Cholecalciferol) (25% excess)	0.012
10.00	3	Polysorbate 80 (Tween 80)	10.00
0.88	4	Vitamin E (oily; alpha-tocopheryl acetate)	0.88
0.50	5	Edetate disodium (sodium EDTA)	0.50
1.00	6	Ascorbic acid	1.00
0.10	7	Saccharin sodium	0.10
600.00	8	Glycerin (glycerol)	600.00
100.00	9	Sorbitol (70% solution)	100.00
50.00	10	Propylene glycol	50.00
1.00	11	Flavor	1.00
1.50	12	Flavor	1.50
QS	13	Dye	QS
QS	14	Dye	QS
–	15	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

1. This product is a microemulsion and thermolabile preparation. The temperature of solution must not exceed 25°C at the time of processing. Store bulk at a temperature of 15°C to 20°C under nitrogen protection. Period of storage should not exceed 48 hours prior to filling in the bottle.
2. Collect 200 g of purified water in a melting vessel.

3. Heat to 90°C to 95°C for 10 minutes, and then cool to 20°C to 25°C.
4. Bubble nitrogen gas into purified water for 20 minutes.
5. Load 100 g of purified water into the manufacturing vessel.
6. Bubble nitrogen gas during all stages of the processing.
7. Add items 5, 6, and 7 one by one to the manufacturing vessel while mixing.
8. Check that all materials are dissolved completely.
9. Add items 8 and 9 and 20 g of item 10 one by one to the manufacturing vessel while mixing at slow speed.
10. Mix for 5 minutes.
11. Avoid aeration.
12. Add item 3 in a stainless steel container.
13. Mix items 1, 2, and 4 one by one using a stirrer.
14. Mix for 1 hour at slow speed.
15. Avoid aeration.
16. Add the oil phase to the aqueous phase in the manufacturing vessel at a rate of 4 mL/min while mixing. Keep on bubbling nitrogen gas throughout the process.
17. Dissolve items 11 and 12 in 30 g of item 10 in a stainless steel container by slow stirring.
18. Add to manufacturing vessel while mixing.
19. Dissolve items 14 and 13 in 40 g of purified water (25–30°C) in a stainless steel container with slow stirring.
20. Add to manufacturing vessel while mixing.
21. Adjust the volume to 1 L with cooled purified water.
22. Check and record the volume and pH (limit: 2.5–4.8).
23. Filter the solution through a prefilter and 0.2 µm membrane filter into the receiving tank.
24. Bubble with nitrogen gas for 15 minutes.
25. Store the solution with a nitrogen blanket.

VITAMIN A AND VITAMIN D₃ DROPS

Bill of Materials			
Scale (mg/g)	Item	Material Name	Quantity/ L (g)
30,000 IU	1	Vitamin A palmitate (1.7 MM IU/g)	1.90
3000 IU	2	Vitamin D ₃ (40 MM IU/g)	7.50 mg
12.00	3	Cremophor (RH, 40%)	12.00
0.30	4	BHT	0.30
10.00	5	Lutrol E 400	10.00
0.80	6	Paraben	0.80
0.20	7	Sorbic acid	0.20
QS	8	Water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Heat mixture of items 1 to 5 and solution of items 6 to 8 to approximately 65°C, and add this slowly to the well-stirred mixture of items 1 to 5.
2. Clear or slightly opalescent yellow liquid is obtained.

VITAMIN A AND VITAMIN D₃ ORAL SOLUTION

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (mg)
1000 IU	1	Vitamin A palmitate (1.7 MM IU/g)	60.00
100 IU	2	Vitamin D ₃ (40 MM IU/g)	0.30
0.002	3	BHT	0.20
3.00	4	Cremophor EL or Cremophor (RH, 40%)	3.00 g
QS	5	Preservative	QS
QS	6	Flavor	QS
QS	7	Water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Heat mixture of items 1 to 4 to approximately 65°C, stir well, and slowly add the hot solution of item 5 (65°C).
2. Cool to room temperature, and add item 6 to obtain a clear, yellow liquid.

VITAMIN A AND VITAMIN D₃ SYRUP

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
30,000 IU	1	Vitamin A palmitate (1.7 MM IU/g)	19.00
10,000 IU	2	Vitamin D ₃ (40 MM IU/g)	0.25
70.00 mg	3	Cremophor (RH, 40%)	7.00
QS	4	Sugar syrup (50%)	QS to 1 L

MANUFACTURING DIRECTIONS

1. Heat mixture of items 1 to 3 to approximately 45°C, stir well, and slowly add item 4 to obtain a clear, yellow liquid (pH 6.2).

VITAMIN A AND VITAMIN E DROPS

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
5000 IU	1	Vitamin A palmitate (1.7 MM IU/g)	3.33
50.00	2	Vitamin E acetate, with excess	60.00
150.00	3	Cremophor (RH, 40%)	150.00
150.00	4	Ethanol (96%)	150.00
QS	5	Water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Heat mixture of items 1 to 3 to approximately 65°C, stir well, and slowly add the mixture of items 4 and 5.
2. Color is yellow. Clarity is clear (turbidity units, 25 FTU).
3. It must be determined whether or not the ethanol concentration has a sufficient preservative efficiency.
4. The addition of BHT as an antioxidant is recommended.

VITAMIN A AND VITAMIN E DROPS

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L
25,000 IU	1	Vitamin A palmitate (1.7 MIU/g)	1.50
50.00	2	Vitamin E acetate	5.00
210.00	3	Cremophor (RH, 40%) ^a	21.00
QS	4	Preservative	QS
QS	5	Water	71.50

^a The quantity is reduced by 1 g if 1 g of D,L-alpha-tocopherol is also added in the formulation.

MANUFACTURING DIRECTIONS

1. Mix the vitamins with Cremophor (and D,L-alpha-tocopherol, if used) at 60°C.
2. Add solution of preservatives (at 37°C) slowly, with stirring, to produce clear, yellow, viscous liquids.

VITAMIN A AND VITAMIN E TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
33,000 IU	1	Vitamin A acetate (dry powder, 500,000 IU/g)	69.00
70.00	2	Vitamin E acetate (dry powder)	70.00
146.00	3	Mannitol (granulated) with 10% of Kollidon® 30	146.00
17.00	4	Kollidon® CL	17.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with high compressive force.
2. Compress 300 mg in 12 mm biplanar punches.

VITAMIN A CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100,000 IU	1	Vitamin A acetate (dry powder, 325,000 IU/g)	350.00
350.00	2	Mannitol	350.00
25.00	3	Kollidon® VA 64	25.00
5.00	4	Magnesium stearate	5.00
3.00	5	Aerosil® 200	3.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with medium compressive force.
2. Compress 750 mg in 12 mm biplanar punches.

VITAMIN A CONCENTRATE (WATER-MISCIBLE)

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
100,000 IU	1	Vitamin A palmitate (1.7 MM IU/g)	6.50
0.200	2	BHT	0.20
21.00	3	Cremophor (RH, 40%)	21.00
QS	4	Preservative	QS
QS	5	Water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Heat the mixture of items 1 to 3 to approximately 65°C. Stir well.
2. Add slowly the warm solution of items 4 and 5 (65°C) to obtain a clear, yellow liquid that is miscible with water.

VITAMIN A DROPS

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/1000 Tablets (g)
50,000 IU	1	Vitamin A palmitate (1.7 Mio IU/g)	3.00
110.00	2	Cremophor (RH, 40%)	11.00
1.00	3	BHT	0.10
QS	4	Water	85.90

MANUFACTURING DIRECTIONS

1. Heat the mixture of items 1 to 3 to approximately 65°C. Stir well.
2. Slowly add the hot water (65°C) to obtain a clear or slightly opalescent yellow solution of low viscosity.
3. Lutrol E 400 can be added at a level of 5% (compensated for by item 4).

VITAMIN A SUPPOSITORIES

Bill of Materials			
Scale (mg/ suppository)	Item	Material Name	Qty/1000 Suppositories (g)
150,000 IU	1	Vitamin A palmitate (1.7 MM IU/g)	88.23
1.00	2	BHT	10.00
400.00	3	Cremophor (RH, 40%)	400.00
800.00	4	Lutrol E 1500	800.00
500.00	5	Lutrol E 4000	505000

MANUFACTURING DIRECTIONS

1. Dissolve BHT in warm vitamin A.
2. Add Cremophor, and mix with the molten Lutrol E grades.
3. Fill into molds of suppositories to obtain a weight of 2 g.

VITAMIN A TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
50,000 IU	1	Vitamin A acetate (dry powder, 500,000 IU/g)	110.00
100.00	2	Avicel™ PH102	100.00
10.00	3	Kollidon® VA 64	10.00
5.00	4	Kollidon® CL	5.00
1.00	5	Aerosil® 200	1.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with low compressive force.
2. Compress 231 mg using 9 mm biconvex punches.

VITAMIN A TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
5000	1	Vitamin A acetate (dry powder, 500,000 IU/g)	110.00
189.00	2	Ludipress®	189.00
1.00	3	Magnesium stearate	1.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with low compressive force.
2. Compress 306 mg in 8 mm punches.

VITAMIN A TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
50,000	1	Vitamin A acetate (dry powder, 500,000 IU/g)	120.00
120.00	2	Ludipress®	120.00
10.00	3	Avicel™ PH101	10.00
1.00	4	Magnesium stearate	1.00
1.00	5	Aerosil® 200	1.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with low compressive force.
2. Compress 277 mg in 8 mm punches.

VITAMIN A TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
50,000	1	Vitamin A acetate (dry powder, 500,000 IU/g)	110.00
154.00	2	Avicel™ PH101	154.00
10.00	3	Kollidon® VA 64	10.00
4.00	4	Kollidon® CL	4.00
1.00	5	Aerosil® 200	1.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press with low compressive force.
2. Compress 250 mg in 8 mm punches.

VITAMIN A TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
25,000 IU	1	Vitamin A acetate (dry powder, 500,000 IU/g)	55.00
572.00	2	Dicalcium phosphate (granulated) (Di-Tab) with 3% of Kollidon® 30	572.00
28.00	3	Polyethylene glycol, powder	28.00
19.40	4	Kollidon® CL	19.40
5.60	5	Aerosil® 200	5.60

MANUFACTURING DIRECTIONS

1. Granulate the dicalcium phosphate with Kollidon® 30, dissolved in isopropanol or water, and pass through a 0.5 to 12 mm screen sieve using a vibrating hopper.
2. Mix the obtained dried granules with the other components, sieve, and press with high compressive force.
3. Compress 680 mg in biplanar punches.

VITAMIN A, VITAMIN B₆, AND VITAMIN E TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
40,000 IU	1	Vitamin A acetate (dry powder, 500,000 IU/g)	80.00
40.00	2	Pyridoxine hydrochloride	40.00
35.00	3	Vitamin E acetate (dry powder, SD 50)	75.00
395.00	4	Ludipress®	395.00
4.00	5	Magnesium stearate	4.00
5.00	6	Aerosil® 200	5.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with high compressive force.
2. Compress 583 mg in 12 mm biplanar punches.

VITAMIN A, VITAMIN C, AND VITAMIN D₃ CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
2000/200 IU	1	Vitamin A and vitamin D ₃ (dry powder, 500,000 and 50,000 IU/g, respectively)	4.00
30.00	2	Ascorbic acid (powder), with excess	33.00
300.00	3	Sucrose (crystalline)	300.00
300.00	4	Sorbitol (crystalline)	300.00
300.00	5	Mannitol	300.00
300.00	6	Ludipress®	300.00
5.00	7	Stearic acid	5.00
0.10	8	Saccharin sodium	0.10
30.00	9	Cyclamate sodium	30.00
30.00	10	Flavor mixture (Firmenich)	30.00
20.00	11	PEG-6000, powder	20.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with high compressive force.
2. Compress 1290 mg in 16 mm biplanar punches.

VITAMIN A, VITAMIN C, AND VITAMIN E TABLETS (1200 IU, 60 MG, 30 MG)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
1200 IU	1	Vitamin A acetate (dry powder, 500,000 IU/g)	2.40
60.00	2	Ascorbic acid (powder)	60.00
30.00	3	Vitamin E acetate (dry powder, 50%)	60.00
105.00	4	Lactose monohydrate	105.00
30.00	5	Avicel™ PH101	30.00
20.00	6	Kollidon® 25	20.00
5.00	7	Talc	5.00
1.00	8	Aerosil® 200	1.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with medium compression force.
2. Compress 285 mg in 8 mm biplanar punches.

VITAMIN B COMPLEX, AMINO ACIDS, AND MAGNESIUM EFFERVESCENT GRANULES (SUGAR-FREE)

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
2.00	1	Thiamine hydrochloride	2.00
2.00	2	Pyridoxine hydrochloride	2.00
5.00	3	Cyanocobalamin (dry powder, 0.1%)	5.00
20.00	4	L-Glutamine	20.00
10.00	5	Inositol	10.00
10.00	6	Potassium L-aspartate	10.00
500.00	7	D,L-Carnitine hydrochloride	500.00
350.00	8	Magnesium L-aspartate	350.00
600.00	9	Anhydrous citric acid	600.00
500.00	10	Sodium bicarbonate	500.00
QS	11	Flavors	QS
50.00	12	Kollidon® VA 64	50.00
80.00	13	Isopropanol	80.00

MANUFACTURING DIRECTIONS

1. Mix items 1 to 6, add the mixture of items 7 to 12, granulate the mixture of these two combinations with item 13, pass through a 0.8 mm sieve, dry well, and mix.
2. Fill 2.1 g of the granules into sachets.

VITAMIN B COMPLEX + AMINO ACID + MAGNESIUM EFFERVESCENT GRANULES (SUGAR-FREE, 1 RDA OF VITAMINS + 500 MG CARNITINE + 20 MG GLUTAMINE)

FORMULATION

- I. Thiamine hydrochloride, 2 g; pyridoxine hydrochloride, 2 g; cyanocobalamin dry powder 0.1%, 5 g; L-glutamine, 20 g; inositol, 10 g; potassium L-aspartate, 10 g.
- II. DL-Carnitine hydrochloride, 500 g; magnesium L-aspartate, 350 g; citric acid, anhydrous, 600 g; sodium bicarbonate, 500 g; flavors, QS; Kollidon® VA 64, 50 g.
- III. Isopropanol, 80 g.

MANUFACTURING DIRECTIONS

1. Mix the components I, add the mixture II, granulate mixture I + II with the liquid III, pass through a 0.8 mm sieve, dry well, and mix with III.
2. Fill 2.1 g of the granules in sachets.

VITAMIN B COMPLEX AND CARNITINE TABLETS

Bill of Materials

Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
95.00	1	Thiamine mononitrate	95.00
20.00	2	Riboflavin	20.00
100.00	3	Nicotinamide	100.00
50.00	4	Calcium D-pantothenate	50.00
2.00	5	Folic acid	2.00
0.20	6	Biotin	0.20
0.5	7	Cyanocobalamin (gelatin coated, 1%)	0.50
50.00	8	Carnitine hydrochloride	50.00
100.00	9	Inositol	100.00
2.00	10	Adenosine phosphate	2.00
15.70	11	Kollidon® 30	15.70
70.00	12	Isopropanol	70.00
26.00	13	Kollidon® CL	26.00
122.00	14	Lactose monohydrate	122.00
14.00	15	PEG-6000, powder	14.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 10 with solution of items 11 and 12.
2. Dry, pass through a 0.8 mm sieve, mix with items 13 and 15, and press with low compressive force.
3. Compress 708 mg using 13 mm biplanar punches.

VITAMIN B COMPLEX AND FOLIC ACID DRAGÉES

Bill of Materials

Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
4.35	1	Calcium D-pantothenate (granulate, 67%)	6.50
2.60	2	Thiamine mononitrate (10.4%)	25.00
20.00	3	Magnesium oxide (light)	20.00
45.75	4	D-Mannitol (powder)	45.75
100.00	5	DL-Methionine	100.00
2.30	6	Riboflavin	2.30
6.30	7	Nicotinamide	6.30
2.40	8	Pyridoxine HCl	2.40
4.00	9	Magnesium stearate	4.00
0.1150	10	D-Biotin	0.1150
0.46	11	Folic acid	0.46
100.00	12	Choline tartrate	100.00
28.00	13	Silicic acid (precipitated)	28.00
0.87 µg	14	Vitamin B ₁₂ (as 0.1% water soluble form)	0.871
3.15	15	Vitamin E (50%)	6.30
30.00	16	Sodium carboxymethyl starch	30.00
116.66	17	Isopropyl alcohol	116.66
22.00	18	Povidone (PVK K-90) (Luviskol®)	22.00

MANUFACTURING DIRECTIONS

1. Incorporate in mixer PVP K-90 and isopropyl alcohol, and make a solution with continuous stirring.
2. Place in mixer choline tartrate, DL-methionine, D-mannitol powder, magnesium oxide (previously sieved), silicic acid, and sodium carboxymethyl starch, and mix for 15 minutes.
3. Add the solution of isopropyl alcohol and alcohol in first step for 10 minutes until moist mass is obtained.
4. Granulate the moist mass through a centrifugal granulator with a 10 mm screen.
5. Spread the granules on paper-lined trays, and dry overnight in a drying oven at 50°C.
6. Crush the granules through a 1.5 mm sieve.
7. Vitamin granulate: Tumble D-biotin, vitamin B₁₂, folic acid, riboflavin, and pyridoxine hydrochloride in mixer for 5 minutes.
8. Combine in the mixer the nicotinamide, vitamin E, thiamine mononitrate/gelatin/mannitol granulate, D-mannitol powder, and sodium carboxymethyl starch; then, add the vitamin mixture, and mix for 10 minutes.
9. Pass through a 1 mm sieve if lumpy.
10. In a mixer, make a separate solution of PVP K-90 and isopropyl alcohol.

11. Place in the mixer the solution of isopropyl alcohol and PVP; then, knead until an evenly moist homogeneous mass is obtained.
12. Add calcium D-pantothenate granules, and mix for 3 to 5 minutes.
13. Pass the granules through a centrifugal granulator with a 10 mm screen, and spread on paper-lined trays.
14. Keep overnight in a drying oven at 50°C. The RH of the granules should be 10% to 20%.
15. Crush the dried granules through an oscillator with a 1.5 mm sieve.
16. Put the granulate mixture in the mixing drum—the choline tartrate and the two lots of vitamin granules.
17. Mix, and then add the magnesium stearate.
18. Check to be sure that the RH of the mixture is 10% to 20%.
19. Compress and apply a sealer coat (lacquer), sugar coat, and finishing coating.

VITAMIN B COMPLEX AND IRON SYRUP

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
910.00	1	Sorbitol solution	910.00
0.019	2	Propylparaben	0.019
0.17	3	Methylparaben	0.17
1.50	4	Niacinamide (white powder)	1.50
0.30	5	Riboflavin	0.30
103.60	6	Propylene glycol	103.60
126.40	7	Glycerin	126.40
26.13	8	Iron sulfate (granular)	26.132
0.037	9	Dye	37.50 mg
0.25	10	Pyridoxine hydrochloride	0.25
1.20	11	Saccharin sodium (dihydrate powder)	1.20
22.00	12	Sodium cyclamate (powder)	22.00
30.00	13	Ascorbic acid (white powder)	30.00
0.80	14	Sodium bicarbonate (powder)	0.80
0.36	15	Thiamine hydrochloride (powder, regular)	0.36
0.625	16	D-Pantothenyl alcohol (dexpantenol)	0.62
0.002	17	Vitamin B ₁₂ (cyanocobalamin)	2.00 mg
0.007	18	Flavor	0.70 mL
QS	19	Deionized purified water	QS to 1 L
QS	20	HyFlo filter aid	QS
QS	21	Hydrochloric acid	QS
QS	22	Sodium hydroxide	QS

MANUFACTURING DIRECTIONS

1. Manufacture under complete carbon dioxide (CO₂) protection.
2. Load 780 g (portion of item 1) of sorbitol solution into a jacketed stainless steel tank. The remaining sorbitol will be used later.
3. Add parabens (unless added previously), niacinamide, and riboflavin to the sorbitol or glucose solution.
4. Heat solution to 85°C to 90°C, and mix until the ingredients are dissolved.
5. Remove heat.
6. While mixing, cool the main solution to 50°C to 60°C.
7. Hold at this temperature while bubbling CO₂ into it.
8. CO₂ protection must be continued for the remainder of the manufacturing procedure.
9. Heat 50 mL of purified water to boiling, and bubble CO₂ into it while cooling to 55°C.
10. Add and dissolve, with mixing, iron sulfate with 30 mL of purified water at 55°C.
11. Use CO₂ protection.
12. Warm the solution to 50°C to 55°C while mixing to dissolve; then, slowly add the solution, with good mixing, to the previous solution.
13. This addition should be made as soon as possible to prevent oxidation.
14. Add the pyridoxine, saccharin sodium, and sodium cyclamate, and mix until dissolved.
15. Cool the solution to 30°C.
16. Add the ascorbic acid, with good stirring, to 78 g of reserved sorbitol; make a slurry.
17. Use a container that has plenty of headspace.
18. Then, add the sodium bicarbonate slowly in small portions to the ascorbic acid slurry, with stirring, until all of the powder has been added and most of the foaming has stopped.
19. Add this slurry slowly to the solution from the previous step with vigorous mixing until a uniform solution results.
20. Rinse the mixing container with 22 g of the reserved sorbitol, and add to the product with stirring.
21. Add and dissolve thiamine hydrochloride with mixing.
22. If necessary, warm the D-pantothenyl alcohol until liquefied, and add it to the 0.5 mL CO₂-saturated purified water.
23. Use an additional 0.5 mL of CO₂-saturated purified water to thoroughly rinse the container of D-pantothenyl alcohol, and add this to the D-pantothenyl alcohol solution.
24. Mix the D-pantothenyl alcohol solution thoroughly until it is homogeneously dispersed.
25. Add the D-pantothenyl alcohol solution to the main solution with mixing.
26. Use an additional 0.5 mL of CO₂-saturated purified water to rinse out the container in which the D-pantothenyl alcohol solution is made, and add to the product with mixing.

27. Dissolve the vitamin B₁₂ in 0.5 mL of purified water to make a clear solution, and add this to the product with good mixing.
28. Dissolve the guarana flavor in the 10 g of propylene glycol reserved from earlier step with good stirring.
29. Add this solution to the product with good mixing.
30. Check pH (range: 3.00–3.30).
31. Adjust, if necessary, with a solution of 10% sodium hydroxide or 10% hydrochloric acid depending on the test results.
32. Adjust the volume of the product with the remaining 30 g of the sorbitol solution and if necessary, purified water to 1 L.
33. Mix for 1 hour.
34. Allow to stand overnight to eliminate entrapped CO₂ gas.
35. Readjust volume to 1 L with purified water.
36. Mix for 1 hour.
37. Filter by adding HyFlo filter aid and mixing it, followed by passing through a filter press.
38. Do not allow temperature to exceed 30°C.
39. Bubble CO₂ gas into clear filtrate for 5 minutes; then seal tank, and hold product under CO₂ protection.

VITAMIN B COMPLEX AND VITAMIN C EFFERVESCENT TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
33.00	1	Thiamine mononitrate	33.00
4.00	2	Riboflavin	4.00
10.00	3	Pyridoxine hydrochloride	10.00
66.00	4	Nicotinamide	66.00
17.00	5	Calcium D-pantothenate	17.00
350.00	6	Tartaric acid (powder)	350.00
450.00	7	Sodium bicarbonate	450.00
750.00	8	Sucrose, crystalline	750.00
30.00	9	Kollidon® 30	30.00
QS	10	Isopropanol	QS
500.00	11	Ascorbic acid (crystalline)	500.00
3.00	12	Riboflavin	3.00
10.00	13	Cyanocobalamin (gelatin-coated, 0.1%)	10.00
10.00	14	Orange flavor	10.00
2.00	15	Saccharin sodium	2.00
5.00	16	Cyclamate sodium	5.00
50.00	17	PEG-6000 (powder)	50.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 9 with solvent item 10, dry, pass through a 0.8 mm sieve, mix with items 13 to 17, and press with high compressive force at a maximum relative atmospheric humidity of 30%.
2. Compress 2315 mg in 20 mm biplanar punches.

VITAMIN B COMPLEX AND VITAMIN C INSTANT GRANULES

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
3.60	1	Thiamine hydrochloride	3.60
5.70	2	Riboflavin phosphate sodium	5.70
45.00	3	Nicotinamide	45.00
4.50	4	Pyridoxine hydrochloride	4.50
15.0	5	Cyanocobalamin (gelatin-coated, 0.1%)	15.00
150.0	6	Ascorbic acid (powder)	150.00
723.00	7	Sucrose	723.00
51.00	8	Kollidon® 30	51.00
QS	9	Ethanol	180 mL

MANUFACTURING DIRECTIONS

1. Mix items 1 to 7, granulate with solution of items 8 and 9, dry, and pass through a 0.8 mm sieve.
2. Fill 1 g of the granules in sachets (or 10 g in 100 mL flakes as dry syrup) to produce yellow, homogeneous granules dispersible in cold water.
3. Approximately 1 g of the granules (= 1 sachet) corresponds to two daily vitamin B and vitamin C requirements of adults.
4. Because of the high loss of riboflavin phosphate sodium, it should be substituted by riboflavin.

VITAMIN B COMPLEX AND VITAMIN C SYRUP

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
0.60	1	Thiamine hydrochloride	0.60
0.55	2	Riboflavin phosphate sodium	0.55
2.50	3	Nicotinamide	2.50
1.20	4	Dexpantenol	1.20
0.55	5	Pyridoxine hydrochloride	0.55
9.00	6	Ascorbic acid (crystalline)	9.00
0.25	7	Orange flavor	0.25
0.05	8	EDTA sodium	0.05
0.50	9	Propyl gallate	0.50
2.00	10	Sorbic acid	2.00
5.00	11	Kollidon® 25	5.00
10.00	12	Sorbitol (crystalline)	10.00
9.00	13	Glycerol	9.00
10.00	14	1,2-Propylene glycol (pharma)	10.00
5.00	15	Water	5.00
QS	16	Sugar syrup (64% sucrose in water)	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Mix solution of items 1 to 5 with sugar syrup, adjust the clear solution to approximately pH 4.2, and use nitrogen as an inert gas in the final packaging; 10 g provides 2 to 3 RDA.

VITAMIN B COMPLEX AND VITAMIN C SYRUP

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
0.15	1	Thiamine hydrochloride	0.15
0.15	2	Riboflavin phosphate sodium	0.15
0.70	3	Nicotinamide	0.70
0.035	4	Dexpanthenol	0.035
0.15	5	Pyridoxine hydrochloride	0.15
2.25	6	Ascorbic acid (crystalline)	2.25
0.28	7	Orange aroma	0.28
0.56	8	EDTA sodium	0.56
186.50	9	Propylene glycol (pharma) + water (2:1)	186.50
0.15	10	Paraben	0.15
84.30	11	Sorbitol (crystalline)	84.30
562.50	12	Sucrose (crystalline)	562.50
42.00	13	Water	42.00

MANUFACTURING DIRECTIONS

1. Dissolve items 1 to 8 in item 2.
2. Prepare a solution of items 10 to 13 by heating.
3. Cool, and mix with solution of the balance of the formulation.
4. Adjust to a pH of 4.2 to 4.5.
5. Adjust volume with water. Use more if necessary.
6. Use nitrogen as an inert gas during packaging.

VITAMIN B COMPLEX AND VITAMIN C TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
5.00	1	Thiamine mononitrate	5.00
5.00	2	Riboflavin	5.00
5.00	3	Pyridoxine hydrochloride	5.00
0.50	4	Folic acid	0.50
30.00	5	Niacin	30.00
0.10	6	Biotin	0.10
10.00	7	Calcium D-pantothenate	10.00
150.00	8	Ascorbic acid (crystalline/powder)	150.00
172.40	9	Ludipress®	172.40
20.00	10	Kollidon® VA 64	20.00
2.00	11	Magnesium stearate	2.00

MANUFACTURING DIRECTIONS

1. Mix all ingredients, pass through a 0.8 mm sieve, and mix.
2. Use medium to low compressive force to compress 400 mg in 10 mm biplanar punches.

VITAMIN B COMPLEX AND VITAMIN C TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
15.00	1	Thiamine hydrochloride	15.00
2.00	2	Riboflavin	2.00
5.00	3	Pyridoxine hydrochloride	5.00
25.00	4	Choline bitartrate	25.00
10.00	5	Nicotinamide	10.00
100.00	6	Ascorbic acid (crystalline/powder)	100.00
220.00	7	Ludipress®	220.00
8.00	8	Stearic acid	8.00

MANUFACTURING DIRECTIONS

1. Mix all ingredients, pass through a 0.8 mm sieve, and mix.
2. Use medium to low compressive force to compress 411 mg in 12 mm biplanar punches.
3. The thiamine mononitrate formulation is more stable compared with the thiamine hydrochloride formulation.

VITAMIN B COMPLEX, CHOLINE, AND BILE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
60.00	1	Acid dehydrochloric (powder)	60.00
100.00	2	Choline dihydrogen citrate	100.00
20.00	3	Niacinamide (white powder)	20.00
100.00	4	Inositol	100.00
2.50	5	Riboflavin (2% excess)	2.55
0.50	6	Pyridoxine hydrochloride	0.50
30.00	7	Povidone (K value, 29–32)	30.00
100.00	8	Racemethionine (crystals)	100.00
60.00	9	Ox bile extract (powder, No. 30 mesh) (Bilein)	60.00
—	10	Alcohol dehydrated (200 proof)	26.00
3.00 µg	11	Cyanocobalamin (oral powder in gelatin, 1000 µg/g)	3.30
3.00	12	Thiamine hydrochloride (powder, regular), with excess	3.60
8.40	13	Magnesium stearate (impalpable powder)	8.40
8.40	14	Stearic acid (fine powder)	8.40

MANUFACTURING DIRECTIONS

1. Mill dehydrochloric acid, choline dihydrogen citrate, nicotinamide, inositol, and methionine through a 600 μm screen.
2. Combine milled mixture from first step with riboflavin, pyridoxine hydrochloride, povidone, and ox bile extract in mass mixer.
3. Add alcohol QS (approximately 26 g or 32.7 mL) slowly to the mass.
4. Mass for approximately 45 minutes in mixer.
5. Scrape all material from the mass mixer as much as possible.
6. Rinse mass mixer between runs.
7. Granulate through a comminuting or similar mill or a 4.76 mm screen.
8. Dry at 49°C to less than 1% LOD.
9. Sift through an 840 μm screen in a shaker, and grind coarsely through a comminuting mill (knives forward, medium speed).
10. Pass one-half of the base granulation through a 1.68 mm screen into a blender if necessary.
11. Mix cyanocobalamin oral powder with an equal volume of base granulation, and charge into a blender through a 1.68 mm screen.
12. Blend thiamine hydrochloride, magnesium stearate, and stearic acid.
13. Then, hand-screen mixture through a 600 μm screen.
14. Load into a blender through a 1.68 mm screen with the remainder of the base granulation, and blend for 20 minutes.
15. Compress and coat tablets using an appropriate formulation to render required color and sealing of tablet.

VITAMIN B COMPLEX SYRUP

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
0.60	1	Thiamine hydrochloride	0.60
0.55	2	Riboflavin 5-phosphate sodium	0.55
2.50	3	Nicotinamide	2.50
1.20	4	Dexpanthenol	1.20
0.55	5	Pyridoxine hydrochloride	0.55
2.00	6	Sorbic acid	2.00
0.05	7	EDTA sodium	0.05
2.25	8	Vanillin	2.25
465.00	9	Sucrose	465.00
25.00	10	Kollidon® 25	25.00
90.00	11	Glycerol	90.00
100.00	12	Propylene glycol (pharma)	100.00
310.00	13	Water	310.00

MANUFACTURING DIRECTIONS

1. Dissolve the sucrose in the hot mixture of glycerol, propylene glycol, and water.
2. Cool to room temperature, and dissolve the other components to obtain a clear solution.

VITAMIN B COMPLEX SYRUP

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
0.66	1	Dexpanthenol	0.66
4.40	2	Nicotinamide	4.40
0.22	3	Pyridoxine hydrochloride	0.22
0.60	4	Riboflavin-5-phosphate sodium	0.60
1.50	5	Thiamine hydrochloride	1.50
350.00	6	Sorbitol (70% solution)	350.00
11.20	7	Propylene glycol	11.20
0.84	8	Methylparaben	0.84
0.168	9	Propylparaben	0.168
550.00	10	Maltitol solution (Lycasin 80/55)	550.00
0.15	11	Edetate disodium (sodium EDTA)	0.15
3.72	12	Citric acid (monohydrate)	3.72
3.72	13	Sodium citrate	3.72
2.50	14	Sodium benzoate	2.50
0.50	15	Saccharin sodium	0.50
150.00	16	Glycerin (glycerol)	150.00
1.50	17	Flavor	1.50
1.00	18	Flavor	1.00
–	19	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Load items 6, 10, and 16 in a manufacturing vessel, and mix for 5 minutes.
2. Dissolve items 8 and 9 in item 7 in a stainless steel container.
3. Put the entire container in hot water (60–70°C), and stir to dissolve the contents.
4. Add the clear solution to the mixer.
5. Dissolve items 11 and 12 in 40 g of purified water in a stainless steel container.
6. Add the clear solution to the mixer.
7. Dissolve items 13, 14, and 15 in 50 g of purified water in a stainless steel container.
8. Add the clear solution to mixer, and mix for 5 minutes.
9. Dissolve item 1 in 10 g of purified water in a stainless steel container.
10. Add the clear solution to mixer.
11. Dissolve items 3 and 5 in 10 g of purified water in a stainless steel container.
12. Add the clear solution to mixer.

13. Dissolve items 2 and 4 in 30 g of purified water in a stainless steel container.
14. Add the clear yellow solution to mixer, and mix for 5 minutes.
15. Add items 17 and 18 to mixer.
16. Bring the volume up to 1 L with purified water, and finally, mix for 15 to 20 minutes.
17. Check and record the pH (limit: 4.4–4.8 at 25°C).
18. If required, adjust pH with 20% citric acid or 20% sodium citrate solution.
19. Filter the syrup at 1.5 bar.
20. Recirculate approximately 200 to 300 mL syrup.
21. Transfer the filtered syrup to the storage vessel, flushing with nitrogen gas.
22. Store the syrup under a nitrogen blanket for NMT 2 days prior to filling.

VITAMIN B COMPLEX SYRUP (WITHOUT B₁₂)

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
570.00	1	Sucrose ^a	570.00
70.00	2	Glycerin (glycerol)	70.00
3.72	3	Citric acid (monohydrate)	3.72
1.00	4	Edetate disodium (sodium EDTA)	1.00
0.90	5	Calcium pantothenate (10% excess)	1.00
5.70	6	Sodium citrate	5.70
0.84	7	Methylparaben	0.84
0.168	8	Propylparaben	0.168
1.90	9	Benzoic acid	1.90
1.14	10	Strawberry flavor manefils	1.14
9.60	11	Alcohol (ethanol, 95%)	9.60
1.50	12	Thiamine hydrochloride (50% excess)	1.50
0.20	13	Pyridoxine hydrochloride (10% excess)	0.22
4.00	14	Nicotinamide (10% excess)	4.40
0.30	15	Riboflavin sodium phosphate (50% excess)	0.60
QS	16	Purified water	QS to 1 L

^a 513 mg for thiamine mononitrate and 504 mg for thiamine hydrochloride.

MANUFACTURING DIRECTIONS

1. Flush with nitrogen gas (purity 99.95%).
2. Add 400 g of purified water to the manufacturing vessel, and heat to 90°C to 95°C.
3. Add item 1 while mixing at low speed.
4. After addition of item 1, mix for 30 to 35 minutes at high speed (temperature: 90–95°C).
5. Cool to 40°C while mixing at low speed.

6. Disperse 1 g of filter aid in 10 g of cooled purified water (25–30°C) in a stainless steel container to prepare a slurry.
7. Add the slurry to the syrup in syrup vessel.
8. Mix for 15 minutes at high speed.
9. Filter the syrup at 1.5 bar.
10. Recirculate approximately 40 to 60 mL syrup.
11. Transfer the filtered syrup to the storage vessel.
12. Recharge the filtered syrup to the manufacturing vessel.
13. Start mixing.
14. Add item 2 to the syrup vessel while mixing at high speed.
15. Add item 3 to the syrup vessel while mixing to dissolve at high speed.
16. Dissolve item 4 in 6 g of cooled purified water (25–30°C), and add to the syrup vessel while mixing at high speed.
17. Dissolve item 5 in 6 g of cooled purified water, and add to the syrup vessel while mixing at high speed for 30 minutes.
18. Dissolve item 6 in 10 g of cooled purified water (25–30°C), and add to the syrup vessel while mixing at high speed.
19. Dissolve items 7 to 10 in item 11 in a stainless steel container, and add to the syrup vessel while mixing at high speed for 15 minutes.
20. Dissolve items 12 and 13 in 6 g of cooled purified water (25–30°C) in a separate stainless steel container, and add to the syrup vessel while mixing at high speed.
21. Rinse the container with 1 g of cooled, purified water (25–30°C), and add the rinsings to the syrup vessel while mixing at high speed.
22. Flush the vessel with nitrogen gas (purity 99.95%) for 15 minutes.
23. Dissolve item 14 in 9 g of cooled purified water in a separate stainless steel container, and add to the syrup vessel while mixing at high speed.
24. Rinse the container with 1 g of cooled purified water (25–30°C), and add the rinsings to the syrup vessel while mixing at high speed.
25. Dissolve item 15 in 4 g of cooled, purified water (25–30°C) in a separate stainless steel container, and add to the syrup vessel while mixing at high speed.
26. Rinse the container with 1 g of cooled, purified water, and add the rinsings to the syrup vessel while mixing at high speed.
27. Bring the volume up to 1 L with cooled, purified water (25–30°C), and finally, mix for 15 minutes at high speed.
28. Check and record the pH (limit: 4.3–4.7 at 25°C).
29. If required, adjust pH with 10% solution of citric acid or sodium citrate.
30. Flush the syrup with nitrogen gas (purity 99.95%) for 15 minutes.

31. Close the tank.
32. Hold the syrup for 12 hours.
33. Filter the syrup at 1.5 bar.
34. Recirculate approximately 40 to 60 mL syrup.
35. Transfer the filtered syrup to the storage vessel.

VITAMIN B COMPLEX TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
25.00	1	Thiamine mononitrate or hydrochloride	25.00
25.00	2	Riboflavin	25.00
80.00	3	Nicotinamide	80.00
40.00	4	Calcium D-pantothenate	40.00
16.00	5	Pyridoxine hydrochloride	16.00
0.16	6	Cyanocobalamin (gelatin coated, 0.1%)	16.00
282.00	7	Avicel™ PH101	282.00
16.00	8	Kollidon® 30	16.00
3.00	9	Aerosil® 200	3.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, and mix.
2. Compress in 12 mm biplanar punches with medium to high compressive force.
3. The mononitrate formulation is preferred for stability reasons.

VITAMIN B COMPLEX TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
2.30	1	Thiamine mononitrate	2.30
2.60	2	Riboflavin	2.60
2.30	3	Nicotinamide	2.30
2.20	4	Calcium D-pantothenate	2.20
2.70	5	Pyridoxine hydrochloride	2.70
0.024	6	Cyanocobalamin (gelatin coated, 0.1%)	2.40
280.00	7	Ludipress®	280.00
14.00	8	Flavor (Firmenich)	14.00
0.050	9	Saccharin sodium	0.05
4.00	10	Cyclamate sodium	4.00
5.00	11	Magnesium stearate	5.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, and mix.

2. Compress 314 mg using low compression force and 8 mm biplanar punches.
3. According to the European Commission, this formulation is classified as dietary food.

VITAMIN B COMPLEX TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
15.00	1	Microcrystalline cellulose (Avicel™ PH102)	15.00
0.20	2	Colloidal silicon dioxide (Aerosil® 200)	0.20
3.00	3	Calcium pantothenate	3.00
9.33	4	Powdered cellulose	9.33
35.60	5	Lactose (spray dried)	35.60
0.91	6	Magnesium stearate	0.91
20.00	7	Nicotinamide	20.00
2.10	8	Pyridoxine hydrochloride	2.10
2.00	9	Riboflavin base	2.00
0.80	10	Talc (fine powder)	0.80
2.10	11	Thiamine mononitrate	2.10

MANUFACTURING DIRECTIONS

1. Riboflavin base is a fine powder that tends to form globules while mixing.
2. Disperse the base carefully with Aerosil® and lactose.
3. Mix items 9 and 2 and 6.67 g of item 5 in the drum of a drum mixer for 10 minutes.
4. Pass the mix two times through a 500 µm sieve using a sifter.
5. Pass items 3, 8, and 11 and 6.67 g of item 5 through a granulator fitted with a 1.0 mm sieve.
6. Pass items 1, 4, and 7 and 22.27 g of item 5 through a granulator fitted with a 1.0 mm sieve.
7. Pass items 6 and 10 through a sifter fitted with a 500 µm sieve.
8. Load sieved material from previous step to the blender.
9. Load sieved material to the blender.
10. Blend the powders for 15 minutes.
11. Load lubricant powders into the blender, and mix for an additional 5 minutes.
12. Compress 91 mg at low RH (55–60%).
13. Coat tablets with a sealing coat, color coat, and polishing coat.

VITAMIN B COMPLEX, VITAMIN A, VITAMIN C, AND VITAMIN D SYRUP

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
60.00	1	Sucrose	600.00
1.00	2	Methylparaben	1.00
0.20	3	Propylparaben	0.20
1.00	4	Edetate disodium (sodium EDTA)	1.00
10.00	5	Ascorbic acid (50% excess)	15.00
0.80	6	Sodium hydroxide	0.80
4.00	7	Nicotinamide (5% excess)	4.20
0.40	8	Riboflavin sodium phosphate (8% excess)	0.43
1.00	9	Thiamine hydrochloride (50% excess)	1.50
1.20	10	Pyridoxine hydrochloride (10% excess)	1.32
0.50	11	Monosodium glutamate (sodium glutamate)	0.50
1.26 µg	12	Cyanocobalamin (50% excess)	0.0018
150.00	13	Propylene glycol	150.00
1000.0 IU	14	Vitamin A palmitate (1.75 MM IU/g) (54% excess)	0.88
100.0 IU	15	Cholecalciferol (40 MM IU/g) (52% excess)	0.0038
13.20	16	Polysorbate 80 (Tween 80)	13.20
2.50	17	Poloxyl 20 cetostearyl ether (Cetomacrogol 1000)	2.50
0.30	18	Lemon oil terpeneless	0.30
0.84	19	Strawberry oil (composed)	0.84
QS	20	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

- This product is an aqueous solution of water-soluble vitamins with oily vitamin A palmitate and cholecalciferol solubilized in water using the surfactant system of Tween 80 and Cetomacrogol.
- This syrup is a solubilized oil surfactant system and is affected by heat and rate of mixing.
- The temperature of the solution must not exceed 30°C at the time of final mixing.
- The final mixing must be continuous, without any interruption.
- For the preparation of oily phase, the container must be dry.
- Before start of batch, cool approximately 80 mL of purified water, and flush with nitrogen gas (purity, 99.95%).
- Use this water for making solutions and for adjusting the volume.
- Add 420 g of purified water to the manufacturing vessel, and heat to 90°C to 95°C.
- Add items 2 and 3 while mixing to dissolve.
- Add item 1 while mixing at slow speed.
- After addition of item 1, mix for 30 to 35 minutes at high speed and a temperature of 90°C to 95°C.
- Cool to 25°C to 30°C while mixing at low speed.
- Bubble nitrogen gas for 10 minutes.
- Add item 4 to the syrup while mixing at high speed to dissolve.
- Add item 5 to the syrup while mixing at high speed to dissolve.
- Add 4.00 g of purified water (25°C) in a separate container, and dissolve item 6 by using a stirrer.
- Transfer the cooled item 6 solution to the syrup tank while mixing at high speed.
- Mix for 15 minutes.
- Check the pH of the syrup (limit: 3.75–3.85).
- Add items 7 to 11 one by one to the syrup in the manufacturing vessel while mixing at high speed to dissolve.
- Mix for 10 minutes.
- Add 6 g of cold purified water (25°C) in a separate container, and dissolve item 12.
- Add to the manufacturing vessel while mixing at high speed.
- Rinse the container with cooled purified water (approximately 2 mL), and transfer the rinsing to the syrup-manufacturing vessel. Mix well at high speed.
- Add item 13 to the manufacturing vessel while mixing at high speed.
- Warm item 14 to 70°C in a separate stainless steel container in a water bath.
- Warm item 16 to 70°C, and mix well with item 14 under nitrogen atmosphere.
- Add item 15 while mixing.
- Melt item 17 in a stainless steel container, and add with stirring to mix well.
- Cool to 30°C while mixing under nitrogen atmosphere.
- Add items 18 and 19 to the oily phase solution, and mix for 15 minutes at high speed.
- Check and record the volume of the oily phase.
- Start mixing, and continue mixing (mixing must be continuous).
- Start the addition of the oily phase solution in a thin stream (do not stop mixing during addition of oily phase).
- After the addition is complete, mix for an additional 15 minutes at high speed.
- Rinse the oily phase vessel with a sufficient quantity of syrup from the syrup vessel.
- Transfer the rinsings to the syrup vessel.
- Bring the volume up to 1 L with cooled purified water (25°C), and finally, mix for 20 minutes at high speed.
- Check and record the pH (limit: 3.75–3.85 at 25°C).
- Filter the syrup at 1.5 bar.
- Recirculate approximately 40 to 60 mL syrup.

VITAMIN B COMPLEX, VITAMIN A, VITAMIN C, AND VITAMIN D TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
2.00	1	Thiamine mononitrate (20% excess)	2.40
1.00	2	Riboflavin (10% excess)	1.10
74.50	3	Lactose (spray dried)	74.50
15.00	4	Nicotinamide	15.00
300 IU	5	Vitamin D ₃ (dry powder, 100,000 IU/g)	3.60
3000 IU	6	Vitamin A palmitate (250,000 IU/g)	18.00
36.00	7	Cellulose (microcrystalline) (Avicel™ PH102)	36.00
20.00	8	Ascorbic acid (90%) (33% excess)	26.60
1.00	9	Silicon dioxide (colloidal) (Aerosil® 200)	1.00
1.80	10	Magnesium stearate	1.80

MANUFACTURING DIRECTIONS

- Mix items 1 and 2 and 13.33 g of item 3 in a drum using a drum mixer for 10 minutes.
- Pass the mix through a 250 μ m sieve using a sifter.
- Collect in a stainless steel drum, and load into the blender.
- Pass items 4 to 7 and 61.17 g of item 3 through a granulator fitted with a 1 mm sieve.
- Collect in a stainless steel drum, and load into the blender.
- Pass item 8 through a Fitz mill fitted with sieve number 24230.
- Collect in a stainless steel drum, and load into the blender.
- Mix for 10 minutes.
- Pass item 9 through a 500 μ m sieve using a sifter.
- Collect in a polyethylene bag.
- Pass item 10 through a 250 μ m sieve using a sifter.
- Collect in the same polyethylene bag.
- Mix, and add 0.53 to 1.33 g powder from the previous step.
- Mix gently.
- Add to the blender.
- Mix for 3 minutes.
- Unload lubricated granules in stainless steel drums.
- Compress 180 mg in 7 mm round concave punches.
- Apply a sealing coat, a color coat, and finishing coat (see Appendix).

VITAMIN B COMPLEX, VITAMIN A, VITAMIN C, VITAMIN D, AND CALCIUM DROPS

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
675.00	1	Glycerin (96%)	675.00
16.66	2	Niacinamide (white powder)	16.66
2.73	3	Riboflavin-5'-phosphate sodium (3% excess)	2.82
0.50	4	Methylparaben	0.50
1.00	5	Acid benzoic	1.00
105.00	6	Saccharin sodium (powder)	105.00
73.36	7	Calcium chloride (granules, dihydrate)	73.36
28.78	8	Ferrous gluconate	28.78
2.25	9	Thiamine hydrochloride (powder, regular) (35% excess)	3.375
1.00	10	Pyridoxine hydrochloride	1.00
83.33	11	Ascorbic acid (white powder) (35% excess)	112.50
0.25	12	Oil orange terpeneless	0.25
0.081	13	Alcohol (ethanol; 190 proof, nonbeverage)	0.081
80.00	14	Polysorbate 80	80.00
0.16	15	Butylated hydroxyanisole (BHA)	0.16
0.66	16	Viosterol in corn oil (syn., oleovitamin D; 1000 mD/g) (25% excess)	0.83
0.056	17	Vitamin A palmitate (1,500,000 IU/g)	0.056
10.00	18	Caramel (acid proof)	10.00
QS	19	Deionized purified water	QS to 1 L

MANUFACTURING DIRECTIONS

- Product must not stand more than 1 week before filling.
- Avoid unnecessary exposure of product to light, air, and heat.
- Manufacture and store product under complete CO₂ protection.
- Avoid vigorous mixing.
- Charge glycerin and 210 mL purified water into a stainless steel jacketed tank.
- Add, with mixing, in the following order: niacinamide, riboflavin-5'-phosphate sodium, methylparaben USP, benzoic acid, and saccharin sodium.
- Continue mixing, heat to 95°C to 100°C, and hold to completely dissolve the ingredients.
- Add in calcium chloride portions, and stir until complete solution is obtained.
- Continue mixing, and cool to 70°C to 75°C.

10. Add ferrous gluconate with mixing, and dissolve at 70°C to 75°C.
11. Check for the absence of undissolved material.
12. Check volume, if necessary. Replace lost purified water by heating with additional previously boiled purified water, QS to 750 mL.
13. Cool with mixing to room temperature (25–30°C) while bubbling CO₂ gas through.
14. Continue the CO₂ gas bubbling for balance of the process.
15. Add and dissolve each ingredient in this order: thiamine hydrochloride, pyridoxine hydrochloride, and ascorbic acid.
16. Dissolve oil orange in ethyl alcohol and add to mixture with stirring.
17. Heat polysorbate 80 to 50°C to 60°C, and hold for approximately 10 minutes with slow mixing.
18. Add and dissolve butylated hydroxyanisole.
19. Mix slowly and saturate with CO₂ while cooling to 25°C to 30°C.
20. Add and dissolve viosterol in corn oil and vitamin A palmitate, mixing well and continuing CO₂ gas bubbling.
21. Add polysorbate solution to main batch, and mix thoroughly.
22. Rinse container with a portion of the main batch, and add.
23. Heat 50 mL purified water to 35°C to 40°C while bubbling CO₂ gas through.
24. Add the caramel color.
25. Mix well until uniform consistency is obtained.
26. Add to main batch.
27. Rinse container with a small quantity of purified water that has been previously saturated with CO₂ gas.
28. Add to the main batch.
29. Add purified water that has been previously saturated with CO₂ gas, QS to 1 L.
30. Filter without using a filter aid. Cycle to achieve clarity.
31. Maintain carbon dioxide cover.

VITAMIN B COMPLEX, VITAMIN A, VITAMIN C, VITAMIN D, AND MINERAL TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
61.00	1	Ascorbic acid (coated), EC	61.00
5.50	2	Calcium pantothenate	5.50
8.00 µg	3	Cyanocobalamin	0.008
4.00	4	Copper sulfate, 5H ₂ O	4.00
1.70	5	Magnesium oxide (heavy)	1.70
10.00	6	Nicotinamide	10.00
0.575	7	Pyridoxine hydrochloride	0.575
0.16	8	Potassium iodide	0.16
2.30	9	Riboflavin	2.30
3.25	10	Thiamine mononitrate	3.25
24.00	11	Vitamin A palmitate (250,000 IU/g)	24.00
4.80	12	Vitamin D ₃ powder (100,000 IU/g)	4.80
2.20	13	Zinc sulfate, 7H ₂ O	2.20
19.265	14	Lactose monohydrate	19.265
25.00	15	Cellulose (microcrystalline) (Avicel™ PH102)	25.00
3.00	16	Povidone (PVP K-90)	3.00
6.50	17	Cellulose (microcrystalline) (Avicel™ PH102)	6.50
7.00	18	Crospovidone (Kollidon® CL)	7.00
1.00	19	Colloidal silicon dioxide (Aerosil® 200)	1.00
0.75	20	Magnesium stearate	0.75
3.00	21	Microcrystalline cellulose (powder)	3.00
–	22	Alcohol (absolute)	18.46

MANUFACTURING DIRECTIONS

1. Dissolve item 16 in item 22 using a stirrer.
2. Dissolve item 3 while stirring to obtain a clear solution.
3. Press items 2, 6, 7, 9, 10, 14, and 15 through a 500 µm stainless steel sieve in a sifter.
4. Load into mixer, and mix for 5 minutes at high speed.

5. Knead the dry powder with binding solution while mixing at high speed for 3 minutes.
6. After the addition is complete, scrape the sides and blades.
7. Mix for an additional 2 minutes using a mixer and chopper at high speed. Check the end point of granulation.
8. (The end point occurs when the granulation consists of few or no lumps.) If required, add an additional quantity of item 22, and record this extra quantity of item 22.
9. Unload the wet granules in stainless steel trays for drying.
10. Transfer the trays to an oven.
11. Keep the door partially open.
12. Switch on the oven, with air circulation, heater switched off, for 2 hours to evaporate alcohol.
13. Close the door of the oven.
14. Dry the granules at 55°C for 12 hours.
15. After 4 hours of drying, scrape the semidried granules to break up the lumps to promote uniform drying.
16. Check the LOD (limit: 0.8–1.2%).
17. If required, dry further at 55°C for 2 hours.
18. Check the LOD.
19. Grind the dried granules through a 1.25 mm sieve using a granulator set at medium speed.
20. Load granules into the blender.
21. Mix items 4 and 13 and 3.08 g of item 17 in a polyethylene bag.
22. Mill through a Fitz mill using sieve number 1530–0030 (knives forward, medium speed).
23. Collect in stainless steel drum.
24. Add to blender.
25. Sift items 1, 11, and 12 through a 630 μm sieve.
26. Add to blender.
27. Sift items 5, 8, 18, 19, and 21 and 3.42 g of item 17 through a 500 μm sieve.
28. Add to blender.
29. Mix for 5 minutes.
30. Sift item 20 through a 250 μm sieve.
31. Mix a portion of the powder mix (approximately 3.85 g) with sieved item 20.
32. Add to the blender.
33. Mix for 1 minute.
34. Compress 185 mg per tablet using 7 mm round, concave punches.
35. Coat using a subcoat, a color coat, and a finishing coat (see Appendix).

VITAMIN B COMPLEX, VITAMIN A, VITAMIN C, VITAMIN D, AND VITAMIN E PEDIATRIC DROPS

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
8333 IU	1	Vitamin A palmitate (1.7 M IU/g) (50% excess)	7.35
666 IU	2	Vitamin D (40 M IU/g) (Cholecalciferol)	0.021
75.00	3	Polysorbate 80 (Tween 80)	75.00
0.005	4	Lemon oil terpeneless	0.050
0.88	5	Vitamin E (oily) (alpha-tocopheryl acetate)	0.88
0.50	6	Edetate disodium (sodium EDTA)	0.50
83.33	7	Ascorbic acid (30% excess)	108.33
1.00	8	Saccharin sodium	1.00
2.50	9	Thiamine hydrochloride (50% excess)	3.75
16.66	10	Nicotinamide (5% excess)	17.50
0.833	11	Pyridoxine hydrochloride (5.6% excess)	0.88
2.00	12	Riboflavin sodium phosphate (7.9% excess as riboflavin)	2.16
700.00	13	Glycerin (glycerol)	700.00
250.00	14	Purified water	250.00

MANUFACTURING DIRECTIONS

1. This product is a microemulsion and is a thermolabile preparation.
2. The temperature of the solution must not exceed 25°C at the time of processing.
3. Add 200 g of purified water to the manufacturing vessel.
4. Bubble nitrogen gas during all stages of the process.
5. Charge items 6 to 12 one by one into the manufacturing vessel while mixing.
6. Check that all materials are dissolved completely.
7. Load item 13 into the manufacturing vessel while mixing at slow speed.
8. Mix for 5 minutes.
9. Add item 3 in a separate stainless steel container.
10. Mix items 1, 2, 4, and 5 one by one using stirrer.
11. Mix for 1 hour at slow speed.
12. Add oil-phase preparation to the aqueous phase at a rate of 4 mL/min while mixing at slow speed, and continue nitrogen gas bubbling throughout the process.

13. Rinse the oil-phase container with 50 g of nitrogen-bubbled and cooled purified water, and transfer the rinsings to the manufacturing vessel.
14. Adjust the volume to 1 L using nitrogen-bubbled purified water.
15. Mix for 15 minutes at slow speed.
16. Check and record the volume and pH (limit: pH 2.8–4.2).
17. Filter the solution through a Sartorius prefilter and 0.2 µm membrane filter into receiving tank.
18. Bubble with nitrogen gas for 15 minutes.

VITAMIN B COMPLEX, VITAMIN C, AND CALCIUM EFFERVESCENT TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
7.00	1	Thiamine mononitrate	7.00
5.00	2	Riboflavin	5.00
25.00	3	Nicotinamide	25.00
20.00	4	Pyridoxine hydrochloride	20.00
12.00	5	Calcium D-pantothenate	12.00
75.00	6	Calcium carbonate	75.00
164.00	7	Calcium glycerophosphate	164.00
400.00	8	Sodium bicarbonate	400.00
300.00	9	Tartaric acid (powder)	300.00
400.00	10	Sucrose (crystalline)	400.00
350.00	11	Sucrose (powder)	350.00
50.00	12	Kollidon® 30	50.00
10.00	13	Kollidon® 30	10.00
QS	14	Isopropanol	QS
550.00	15	Ascorbic acid (powder)	550.00
2.00	16	Riboflavin	2.00
5.00	17	Cyanocobalamin (gelatin-coated, 0.1%)	5.00
40.00	18	PEG-6000 (powder)	40.00
50.00	19	Kollidon® CL	50.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 12 with solution of item 19.
2. Granulate items 13 to 18 separately, dry at 60°C with vacuum, mix with item 1, and blend.
3. Compress 2.5 g using 20 mm planar punches at medium to high compression force.

VITAMIN B COMPLEX, VITAMIN C, AND FERROUS SULFATE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
300.00	1	Ferrous sulfate	300.00
15.00	2	Kollidon® 30	15.00
6.00	3	Kollidon® 30	6.00
QS	4	2-Propanol	QS
45.00	5	Thiamine mononitrate	45.00
10.00	6	Riboflavin	10.00
82.00	7	Pyridoxine hydrochloride	82.00
69.00	8	Nicotinamide	69.00
470.00	9	Ascorbic acid (powder)	470.00
690.00	10	Ludipress®	690.00
50.00	11	PEG-6000 (powder)	50.00
9.00	12	Aerosil® 200	9.00

MANUFACTURING DIRECTIONS

1. Granulate the mixture of items 1 to 2 with solution of items 5 to 12.
2. Pass through a 0.8 mm sieve.
3. Mix with items 3 and 4.
4. Compress with high compressive force 25 to 30 kN. Compress 1750 mg in 20 mm biplanar punches.

VITAMIN B COMPLEX, VITAMIN C, AND IRON SYRUP

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
QS	1	Glucose (liquid), NF	QS to 1 L
225.00	2	Purified water, USP	225.00
0.30	3	Methylparaben	0.30
1.00	4	Acid benzoic, USP	1.00
5.00	5	Alcohol (ethanol; 190 proof, nonbeverage), USP	5.00
10.00	6	Nicotinamide niacinamide (white powder), USP	10.00
10.00	7	Riboflavin; use riboflavin 5-phosphate sodium	10.00
2.00	8	Pyridoxine hydrochloride, USP	2.00
20.00	9	Ascorbic acid (white powder), USP	28.00
0.03	10	Dye	0.03
0.02	11	Dye	0.02
2.00	12	Thiamine hydrochloride (powder, regular), USP	2.40
2.00	13	D-Pantothenyl alcohol	2.50
2.00 µg	14	Vitamin B ₁₂ (cyanocobalamin, USP)	3.40 mg
200.00	15	Sucrose, NF	200.00
0.028 mL	16	Flavor	2.80 mL
QS	17	Hydrochloric acid	2.00 mL
QS	18	Carbon dioxide gas	QS

MANUFACTURING DIRECTIONS

1. This preparation is susceptible to oxidation and must be protected from air and sunlight at all times.
2. Carbon dioxide must be used extensively to prevent oxygen from reacting with the materials.
3. All purified water must be boiled prior to use for 10 minutes and cooled under CO₂ protection.
4. Charge 100 mL of purified water into a suitably sized stainless steel tank.
5. Add the riboflavin, nicotinamide, benzoic acid, and paraben.
6. Rinse the tank down with 10 mL purified water, seal, and heat with mixing to 95°C.
7. Continue mixing and heating for 15 minutes until solution is complete.
8. Commence cooling with continuous mixing.
9. When the solution has cooled to 50°C to 70°C, add and dissolve the sugar.
10. Commence CO₂ protection when the temperature reaches 40°C.
11. Slurry the ascorbic acid in 75 or 110 mL of CO₂-saturated purified water (use the smaller quantity only if using a total of 225 mL water), and add to bulk solution when temperature has reached 25°C to 35°C.

12. Rinse the ascorbic acid vessel with 10 mL purified water, and add rinsings to bulk.
13. Mix for at least 30 minutes.
14. Dissolve thiamine and pyridoxine in 20 mL CO₂-saturated purified water, and add to bulk solution at 25°C to 35°C.
15. Add 10 mL CO₂-saturated purified water to the D-pantothenyl alcohol, and warm on a water bath until solution is complete.
16. Add vitamin B₁₂, and mix until dissolved.
17. Add and dissolve dyes.
18. Add this solution to the bulk solution, and mix thoroughly.
19. Mix flavor with 95% of alcohol, and add to the bulk solution.
20. Rinse the container with the remaining alcohol, and add to the bulk with vigorous agitation.
21. Check pH (range: 3.0–3.3).
22. Use hydrochloric acid to adjust if necessary.
23. Adjust the final volume with liquid glucose.
24. Filter through suitable medium until clear and bright.

VITAMIN B COMPLEX, VITAMIN C, AND IRON SYRUP

Bill of Materials			
Scale (mg/ 5 mL)	Item	Material Name	Qty/L (g)
QS	1	Sorbitol solution, USP	QS to 1 L
QS	2	Purified water, USP	225.00
0.20	3	Methylparaben	0.20
0.020	4	Propylparaben, NF	0.02
2.00	5	Nicotinamide niacinamide (white powder), USP	10.00
10.00	6	Riboflavin; use riboflavin 5-phosphate sodium, with excess	10.64
10.00	7	Iron sulfate (ferrous sulfate; granular), USP	10.00
3.60	8	Saccharin sodium (powder), USP	3.60
2.00	9	Pyridoxine hydrochloride, USP	2.00
25.00	10	Ascorbic acid (white powder), USP, with excess	28.00
0.03	11	Dye	0.030
0.02	12	Dye	0.020
2.00	13	Thiamine hydrochloride (powder, regular), USP, with excess	2.40
2.00	14	D-Pantothenyl alcohol, with excess	2.50
2.0 µg	15	Vitamin B ₁₂ cyanocobalamin, USP, with excess	3.40 mg
1.00	16	Flavor	1.00
10.00	17	Propylene glycol, USP	10.00
QS	18	Hydrochloric acid	2.00 mL
–	19	HyFlo filter aid	1.00
QS	20	Carbon dioxide gas	QS

MANUFACTURING DIRECTIONS

1. This preparation is susceptible to oxidation and must be protected from air and sunlight at all times.
2. Carbon dioxide must be used extensively to prevent oxygen from reacting with the materials.
3. All purified water must be boiled prior to use for 10 minutes and cooled under CO₂ protection.
4. Charge 950 g of sorbitol solution into a jacketed stainless steel tank, and heat to 95°C to 100°C.
5. Heat 250 mL of purified water to boiling for 10 minutes, and bubble CO₂ into it while cooling to room temperature.
6. Add, with stirring, the parabens, niacinamide, and riboflavin 5-phosphate sodium.
7. Rinse the container with 5 mL of water.
8. Stir well.
9. Mix until solution is obtained, and check the clarity.
10. Remove the source of heat from the vessel.
11. Thoroughly deoxygenate the liquid by bubbling CO₂ through the liquid, and allow to cool to 50°C to 60°C.
12. Heat 15 mL of water to 70°C, saturate with CO₂, and dissolve saccharin sodium (item 8) and pyridoxine hydrochloride in 5 mL of water. Add to the main bulk.
13. Rinse the container with 2.5 mL of water.
14. Cool the solution to 30°C with CO₂ protection.
15. Dissolve ascorbic acid in 120 mL of water.
16. Rinse the container with 5 mL of water.
17. Dissolve dyes in 3 mL of water.
18. Rinse the container with 2 mL of water.
19. Mix dye solution with ascorbic acid solution.
20. Add this to the main bulk with stirring.
21. Dissolve thiamine in 30 mL of water, and add to the main bulk.
22. Rinse the container with 2.5 mL of water.
23. Add 10 mL of water to the D-pantothenyl alcohol, and warm up on a water bath until in solution.
24. Add this mixture to the main bulk.
25. Rinse the container with 2.5 mL of water.
26. Dissolve vitamin B₁₂ in 12.5 mL of water, and add to the main bulk.
27. Rinse the container with 2.5 mL of water.
28. Mix flavor with 7.5 g of propylene glycol until mixture is homogeneous, and add to the main bulk.
29. Rinse the container with 2.5 g of propylene glycol, and add to the main bulk with vigorous agitation.
30. Check pH (range: 3.0–3.3).
31. Use hydrochloric acid to adjust if necessary.
32. Adjust the volume of the product with sorbitol solution, and mix for 30 minutes to ensure homogeneity.
33. Add the HyFlo filter aid, and mix.
34. Filter the liquid through a filter press previously washed in purified water.
35. Transfer the clear filtrate into a clean, closed vessel.
36. Mix for 15 minutes while bubbling CO₂ gas.

VITAMIN B COMPLEX, VITAMIN C, AND VITAMIN E TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Niacinamide, (white powder), USP	100.00
750.00	2	Ascorbic acid; use sodium ascorbate (microcrystalline), USP	843.65
30.00	3	Calcium pantothenate, USP	30.00
10.00	4	Riboflavin, USP	10.00
5.00	5	Pyridoxine hydrochloride, USP	5.25
40.00	6	Povidone, USP	40.00
68.00	7	Anhydrous isopropyl alcohol	68.00
15.00	8	Thiamine mononitrate (powder), USP	15.75
24.79	9	Vitamin E, USP, D,L- α -tocopheryl acid succinate	33.71
150.00 μ g	10	Folic acid (powder), USP	0.18
5.00	11	Magnesium stearate	5.00
40.00	12	Cellulose (microcrystalline), NF	40.00
4.00 μ g	13	Vitamin B ₁₂ ; use cyanocobalamin powder in gelatin (1000 μ g/g)	4.20

MANUFACTURING DIRECTIONS

1. Avoid unnecessary exposure to light and moisture.
2. Mill the nicotinamide and the sodium ascorbate through a 600 μ m screen fitted to a Fitz mill or similar (impact forward, high speed).
3. Load into a suitable mass mixer.
4. Load calcium pantothenate, riboflavin, and pyridoxine hydrochloride into the mass mixer.
5. Dry blend for 5 minutes.
6. Dissolve povidone in alcohol (approximately 84 mL) in a separate container.
7. While mixing the blended powders, add the povidone solution.
8. Continue to mix until a satisfactory granule mass is obtained.
9. If required, use additional alcohol.
10. Granulate through a Fitz mill, or similar, using a 5/8 in. band (15.88 mm aperture or similar) or a 4.76 mm screen with knives forward at slow speed.
11. Dry the granulation at 49°C to less than 1.5% LOD.
12. Sift the dry granulation through a 1.19 mm screen.
13. Pass remaining coarse granules through a No. 2 band (1.59 mm aperture or similar) using a Fitz mill or similar (knives forward, medium speed).
14. Blend together the thiamine mononitrate, vitamin E, folic acid, magnesium stearate, and a portion of the microcrystalline cellulose.
15. Mill blended powders through a 600 μ m screen (impact forward, high speed).
16. Care must be taken to prevent losses.

17. Load half of the base granulation, the balance of the microcrystalline cellulose, and the powder blend into a suitable blender.
18. Blend for 5 minutes.
19. Add balance of base granulation, and blend for 15 minutes.
20. Do not mill cyanocobalamin.
21. Blend together by hand the cyanocobalamin with a portion of the blended powders.
22. Return to the blender, and blend for 15 minutes.
23. Compress using ovaloid-shaped punches.
24. Seal tablets with a subcoat, and then apply color coat and finishing coating.

VITAMIN C AND CALCIUM CARBONATE EFFERVESCENT TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
300.00	1	Calcium; use calcium carbonate	315.00
450.00	2	Sodium bicarbonate/tartaric acid (powder)	450.00
600.00	3	Kollidon® 30	600.00
35.00	4	Kollidon® 30	35.00
200.00	5	Isopropanol	200.00
400.00	6	Sucrose (crystalline)	400.00
500.00	7	Ascorbic acid (crystalline, with excess)	550.00
120.00	8	Kollidon® CL	120.00
60.00	9	PEG-6000 (powder)	60.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 3 with a solution of items 4 and 5, mix with item 6, and dry.
2. Add items 7 to 9, and press with high compressive force at a maximum atmospheric RH of 30%.
3. Compress 2500 mg in 20 mm biplanar punches.

VITAMIN C AND VITAMIN E LOZENGES

Bill of Materials			
Scale (mg/ lozenge)	Item	Material Name	Qty/1000 Lozenges (g)
100.00	1	Ascorbic acid (crystalline)	100.00
50.00	2	Vitamin E acetate (dry powder, SD 50)	100.00
400.00	3	Dextrose	400.00
4.00	4	Kollidon® 90 F	4.00
25.00	5	Isopropanol	25.00
6.00	6	PEG-6000 (powder)	6.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 to 4 with isopropanol, dry, pass through a 0.8 mm sieve, mix with item 6, and press with high compression force.
2. Compress 600 mg using 12 mm biplanar punches.

VITAMIN C CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Ascorbic acid: 222.20 mg ascorbic acid and 312.50 mg sodium ascorbate microcrystalline	500.00
850.00	2	Sorbitol (granular)	850.00
100.00	3	Lactose (120 mesh)	100.00
3.30	4	FD&C Yellow dye No. 5 lake	3.30
82.90	5	Cellulose (microcrystalline), NF (Avicel™ PH101)	82.90
11.60	6	Silica gel	11.60
8.29	7	Flavor	8.29
0.50	8	Flavor	0.50
8.29	9	Sodium cyclamate	8.29
33.20	10	Magnesium stearate	33.20

MANUFACTURING DIRECTIONS

1. Pass the ascorbic acid, sodium ascorbate, sorbitol, lactose, FD&C Yellow dye, microcrystalline cellulose, silica gel, flavors, and sodium cyclamate through a 420 µm screen.
2. Using a comminuting mill, pass the coarse granules through a 420 µm screen (knives forward, medium speed).
3. Transfer milled materials to a suitable blender, and blend for 5 minutes.
4. Screen the magnesium stearate by hand through an 840 µm screen, and transfer to blender.
5. Mix for 1 minute.
6. Compress using 18 mm standard concave punches.

VITAMIN C CHEWABLE TABLETS

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
422.00	1	Ascorbic acid (powder)	422.00
283.00	2	Microcrystalline cellulose	283.00
130.00	3	Sucrose (powder)	130.00
80.00	4	Sucrose (crystalline)	80.00
24.00	5	Kollidon® VA 64	24.00
24.00	6	Cyclamate sodium	24.00
20.00	7	PEG-6000 (powder)	20.00
12.00	8	Orange flavor and strawberry flavor	12.00
2.00	9	Aerosil® 200	2.00
1.00	10	Saccharin sodium	1.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm sieve, and press into tablets with medium to high compression force.
2. Compress 250 mg (for 100 mg strength), 1250 mg (for 500 mg strength), or 2500 mg (for 500 mg strength).

VITAMIN C CHEWABLE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Ascorbic acid (crystalline)	500.00
1100.00	2	Sorbitol (crystalline)	1100.00
200.00	3	Sucrose (crystalline)	200.00
200.00	4	Sucrose (powder)	200.00
300.00	5	Dextrose	30.00
100.00	6	PEG-6000 (powder)	100.00
10.00	7	Magnesium stearate	10.00
10.00	8	Aerosil® 200	10.00
1.00	9	Saccharin sodium	1.00
10.00	10	Cyclamate sodium	10.00
30.00	11	Orange flavor	30.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with medium to high compression force.
2. Compress 2080 mg using 20 mm biplanar punches.

VITAMIN C CHEWABLE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Ascorbic acid (crystalline)	100.00
450.00	2	Sodium ascorbate (crystalline)	450.00
264.00	3	Sorbitol (crystalline)	264.00
200.00	4	Sucrose (crystalline)	200.00
200.00	5	Sucrose (powder)	200.00
300.00	6	Dextrose	300.00
60.00	7	PEG-6000 (powder)	60.00
3.00	8	Magnesium stearate	3.00
4.00	9	Aerosil® 200	4.00
1.00	10	Saccharin sodium	1.00
10.00	11	Cyclamate sodium	10.00
20.00	12	Orange flavor	20.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with medium to high compression force.
2. Compress 1295 mg using 16 mm biplanar punches.

VITAMIN C CHEWABLE TABLETS

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
6.70	1	Anhydrous silica (colloidal) (Aerosil® 200)	6.70
40.00	2	Cellulose (microcrystalline) (Avicel™ PH101)	40.00
6.50	3	Aspartame	6.50
170.00	4	Ascorbic acid (coated), EC	170.00
10.50	5	Orange flavor (dry)	10.50
13.00	6	Carmellose sodium (sodium CMC 7 MFD)	13.00
2.80	7	Orange dye	2.80
470.00	8	Dextrates, NF	470.00
19.50	9	Magnesium stearate	19.50
13.00	10	Stearic acid (fine powder)	13.00
160.00	11	Sorbitol (powder)	160.00
388.00	12	Sodium ascorbate (granular)	388.00

MANUFACTURING DIRECTIONS

1. Processing should be done in a controlled temperature and humidity area (limit: RH, 40–50%; temperature, 20–25°C).
2. Mix items 2 and 7 in a polyethylene bag for 1 to 2 minutes.
3. Sift twice through a 250 µm sieve.

4. Collect in a polyethylene bag, and check the uniformity of dispersion.
5. If required, sift again.
6. Mix items 3, 5, and 6 in a polyethylene bag for 1 to 2 minutes.
7. Sift once through a 250 μm sieve.
8. Add to the first step, and mix for 1 to 2 minutes.
9. Sift items 4, 8, 11, and 12 once through a 1000 μm sieve, and collect in a stainless steel drum.
10. Add the sieved materials from the preceding steps to the stainless steel drum.
11. Mix in a drum blender for 2 to 3 minutes.
12. Mix items 1, 9, and 10 in a polyethylene bag for 1 to 2 minutes.
13. Sift twice through a 500 μm sieve.
14. Add 25 to 30 g of granules to the lubricant mixture.
15. Mix for 1 to 2 minutes.
16. Add this mixture to the granules.
17. Mix in a drum blender for 1 minute.
18. Check the moisture content (limit: moisture content NMT 3.5%).
19. Check temperature and humidity before beginning compression (limit: RH, 40–50%; temperature, 20–25°C).
20. Compress 1300 mg per tablet using 16 mm punches.
21. Fill appropriate amounts for lower strength (e.g., 100 mg tablets in 10 mm punches).

VITAMIN C CHEWABLE TABLETS WITH DEXTROSE

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Ascorbic acid (crystalline); use ascorbic acid (coated, 97.5%), EC	110.00
500.00	2	Dextrose	500.00
4.00	3	Kollidon® 90 F	4.00
30.00–50.00	4	Water and/or isopropanol	30.00–50.00
6.00	5	PEG-6000 (powder)	6.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 and 2 with solution of items 4 and 5 (in a fluidized bed), sieve, add item 3, and press with high compression force.
2. Compress 620 mg in 12 mm biplanar punches.
3. If no fluidized bed is available, the use of water as a granulation solvent should be avoided.
4. The use of coated ascorbic acid does not increase the stability.

VITAMIN C CHEWABLE TABLETS WITH FRUCTOSE

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
120.00	1	Ascorbic acid (powder)	120.00
500.00	2	Fructose	500.00
200.00	3	Ludipress®	200.00
100.00	4	Avicel™ PH101	100.00
15.00	5	Kollidon® VA 64	15.00
4.00	6	Aerosil® 200	4.00
35.00	7	PEG-6000 (powder)	35.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with high compression force.
2. Compress 970 mg in 12 mm biplanar punches.

VITAMIN C CHEWABLE TABLETS WITH SUCROSE

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Ascorbic acid	500.00
850.00	2	Sucrose, crystalline	850.00
575.00	3	Avicel™ PH101	575.00
60.00	4	Kollidon® VA 64	60.00
15.00	5	Magnesium stearate	15.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with medium compression force.
2. Compress 2000 mg in 20 mm biplanar punches.

VITAMIN C DROPS

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Quantity/L (g)
100.00	1	Ascorbic acid (white powder), USP	100.00
979.00	2	Propylene glycol, USP	979.00

MANUFACTURING DIRECTIONS

1. Keep under CO₂ protection at all times. Avoid contact with iron. Use stainless steel or glass-lined equipment only.
2. Load 868 g propylene glycol into a glass-lined or suitable stainless steel jacketed tank.
3. While mixing, heat to 70°C to 80°C.
4. Bubble CO₂ gas into the propylene glycol from the bottom of the tank.
5. Add and dissolve the ascorbic acid into the propylene glycol with a minimum of stirring under CO₂ protection.
6. When the ascorbic acid is in solution, immediately cool to approximately 25°C while continuing to mix.
7. Also, while cooling, change adding CO₂ from the bottom of the tank to adding it at the top of the tank.
8. QS to 1 L, using propylene glycol, and mix for at least 10 minutes.
9. Use a prefilter pad and a lint-free filter paper. Recirculate the product through the filter press until sparkling clear.

VITAMIN C EFFERVESCENT TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
1000.00	1	Vitamin C (as ascorbic acid)	1000.00
800.00	2	Tartaric acid (fine crystals)	800.00
1000.00	3	Sodium bicarbonate	1000.00
0.50	4	Riboflavin	0.50
20.00	5	Saccharin sodium	20.00
20.00	6	Sodium chloride (milled)	20.00
50.00	7	Lime flavor	50.00
1709.50	8	Sugar (fine crystals)	1709.50
QS	9	Alcohol	QS

MANUFACTURING DIRECTIONS

1. All operations must be carried out at a RH of less than 40% at 25°C.
2. Active substance granulates: If saccharin sodium is lumpy, sieve it by means of a centrifugal granulator (1 mm) or a 3 mm band sieve.
3. Suck into the mixer the entire amount of sugar, ascorbic acid, tartaric acid, and saccharin sodium (previously sieved, if required), together with first part sieved sodium bicarbonate (open filter, closed bypass; jacket temperature of 40°C); backflash filter twice, evacuate to approximately 800 mbar, and close filter.
4. Mix with mixer for approximately 10 minutes (jacket temperature 40°C) at a speed of 50 rpm.

5. Turn off the mixer, and evacuate to 10 mbar (open filter, closed bypass; jacket temperature of 40°C).
6. Separately dissolve or suspend riboflavin in alcohol.
7. Suck this granulating liquid into the evacuated vessel at a mixer speed of 30 rpm (closed filter, closed bypass; jacket temperature of 40°C).
8. With jacket heating turned off, granulate up to a product temperature of 60°C at a mixer speed of 110 rpm (time required is approximately 20–25 minutes).
9. At a jacket temperature of 56°C and a mixer rotation speed of approximately 15 rpm, dry for 2 to 5 minutes (closed filter, open bypass).
10. When dust develops in the course of further drying, close the bypass and open the filter.
11. At a mixer speed of 20 rpm and interval setting (2 min/15 s), continue the drying at a jacket temperature of approximately 58°C and vacuum of 10 mbar until a total drying time of 10 to 20 minutes is reached.
12. Sieve the active substance granulate by sucking it by means of vacuum at a jacket temperature of approximately 59°C and a mixer speed of 20 rpm through a Buehler universal mill (1.5 mm screen) directly into a suitable container.
13. Preferable RH of the active substance is less than 10%.
14. Sieve milled sodium chloride and lime flavor through a round hand sieve (1 mm) with a diameter of approximately 38 cm. Add to sieved sodium carbonate (second part) in a mixing drum, and mix (e.g., tumble mix, 19 rpm for 10 minutes).
15. Combine this dry mix (sucked by vacuum) with the active substance granulate.
16. Finally, add the remaining sieved and lump-free sodium bicarbonate (third part).
17. Mix the mixture that is ready for compression for 45 minutes.
18. The preferable RH of the mixture is less than 20%.
19. In a suitable rotary tablet press, compress effervescent tablets with a weight of 4600 mg and a hardness of 8 kpi.

VITAMIN C EFFERVESCENT TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Ascorbic acid (powder), with excess	112.00
200.00	2	Sorbitol (instant)	200.00
1000.00	3	Anhydrous citric acid	1000.00
587.00	4	Sodium bicarbonate	587.00
65.00	5	PEG-6000 (powder)	65.00
10.00	6	Lemon flavor	10.00
25.00	7	Cyclamate sodium	25.00
1.00	8	Saccharin sodium	1.00

MANUFACTURING DIRECTIONS

1. Dry the sodium bicarbonate for 1 hour at 100°C, mix with the other components, pass all through a 0.8 mm sieve, and press with high compression force at a maximum atmospheric RH of 30%.
2. Compress 2050 mg in 20 mm biplanar punches.

VITAMIN C EFFERVESCENT TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
1000.00	1	Ascorbic acid (crystalline)	1000.00
800.00	2	Sorbitol (crystalline)	800.00
150.00	3	Anhydrous citric acid	150.00
660.00	4	Sodium bicarbonate	660.00
80.00	5	PEG-6000 (powder)	80.00
QS	6	Lemon flavor	QS
QS	7	Cyclamate sodium	QS
QS	8	Saccharin sodium	QS

MANUFACTURING DIRECTIONS

1. Dry the sodium bicarbonate for 1 hour at 100°C, mix with the other components, pass all through a 0.8 mm sieve, and press with high compression force at a maximum atmospheric RH of 30%.
2. Compress 2690 mg in 20 mm biplanar punches.

VITAMIN C EFFERVESCENT TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
500.00	1	Sodium hydrogen carbonate	500.00
430.00	2	Tartaric acid	430.00
8.00	3	Kollidon® 25	8.00
0.20	4	2-Propanol	200.00 mg
550.00	5	Ascorbic acid (crystalline)	550.00
660.00	6	Sucrose	660.00
67.00	7	PEG-6000 (powder)	67.00
67.00	8	Dextrose (powder)	67.00
10.00	9	Orange flavor	10.00
1.00	10	Saccharin sodium	1.00

MANUFACTURING DIRECTIONS

1. Granulate mixture of items 1 and 2 with solution of items 2 and 3, pass through a 0.5 mm sieve, and dry at 60°C.
2. Dry mixture of items 5 and 6 at 60°C.
3. Mix together with the previous granules and with items 7 to 10.

4. At a maximum atmospheric RH of 30%, press to effervescent tablets.
5. Compress 2300 mg in 20 mm biplanar punches.

VITAMIN C TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Ascorbic acid (coated), with excess	104.00
2.40	2	Anhydrous colloidal silica (Aerosil® 200)	2.40
60.00	3	Cellulose (microcrystalline) (Avicel™ PH102)	60.00
0.13	4	FD&C Yellow dye No.10 lake	0.13
37.00	5	Lactose (spray dried)	37.00
3.20	6	Glyceryl behenate (glyceryl monostearate)	3.20
2.40	7	Stearic acid (fine powder)	2.40
1.00	8	Magnesium stearate	1.00

MANUFACTURING DIRECTIONS

1. Processing should be done under controlled temperature and humidity (limit: RH, 40–50%; temperature, 20–25°C).
2. Mix items 5 and 4 in a polyethylene bag for 1 to 2 minutes.
3. Sift twice through a 630 µm sieve.
4. Collect in a polyethylene bag.
5. Check the uniformity of dispersion.
6. If required, sift again.
7. Sift item 3.
8. Sift mixture from first step and item 2 through a 630 µm sieve.
9. Load into a drum blender.
10. Sift item 4 through a 630 µm sieve.
11. Load into the mix in the drum blender.
12. Mix items 6, 7, and 8 in a polyethylene bag for 1 to 2 minutes.
13. Sift through a 250 µm sieve.
14. Collect in a polyethylene bag.
15. Add 13.33 g to 20.00 g of granules to the lubricant mixture.
16. Mix for 1 to 2 minutes.
17. Add this to the mix in a stainless steel drum blender.
18. Mix in a drum blender for 2 minutes.
19. Check the temperature and humidity before beginning compression (limit: RH, 40–45%; temperature, 20–25°C).
20. Compress 210 mg in 8 mm round concave punches.

VITAMIN C TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Ascorbic acid (powder)	100.00
232.00	2	Ludipress®	232.00
1.00	3	Magnesium stearate	1.00

MANUFACTURING DIRECTIONS

1. Mix all components, sieve, and press into 335 mg tablets.
2. Compression force affects disintegration time.

VITAMIN C TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
200.00	1	Ascorbic acid (powder)	200.00
231.00– 256.00	2	Ludipress®	231.00– 256.00
25.00	3	Kollidon® VA 64	25.00
15.00	4	Kollidon® CL	15.00
1.20	5	Aerosil® 200	1.20
2.50	6	Magnesium stearate	2.50

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm screen, and press with medium compression force (18 kN).
2. Compress 499 mg in 12 mm biplanar punches.

VITAMIN E AND BENZOCAINE SOLUTION

Bill of Materials			
Scale (mg/ mL)	Item	Material Name	Qty/L (g)
50.00	1	Vitamin E acetate	50.00
20.00	2	Benzocaine	20.00
50.00	3	Lutrol F 127	50.00
250.00	4	Cremophor (RH, 40%)	250.00
2.00	5	Sorbic acid	2.00
628.00	6	Water	628.00

MANUFACTURING DIRECTIONS

1. Dissolve sorbic acid and benzocaine in water at 60°C, and slowly add the heated mixture of vitamin E acetate and Cremophor at an RH of 40% and temperature of 60°C to 65°C.

2. Cool the clear solution to approximately 5°C, and dissolve Lutrol F 127 to obtain a clear, colorless viscous liquid.

VITAMIN E CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
100.00	1	Vitamin E acetate (SD 50)	200.00
493.00	2	Ludipress®	493.00
390.00	3	Sorbitol (crystalline)	390.00
100.00	4	Mannitol	100.00
400.00	5	Dicalcium phosphate (granulated with 5% Kollidon® 30)	400.00
7.00	6	Aerosil® 200	7.00
3.00	7	Magnesium stearate	3.00

MANUFACTURING DIRECTIONS

1. Mix all components, pass through a 0.8 mm screen, and press with high compression force.
2. Compress 711 mg in 12 mm biplanar punches.

VITAMIN E CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
150.00	1	Vitamin E acetate (dry powder, 50%)	300.00
300.00	2	Sorbitol	300.00
6.00	3	Aerosil® 200	6.00
0.20	4	Saccharin sodium	0.20
6.00	5	Magnesium stearate	6.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with high compression force.
2. Compress 620 mg in 12 mm biplanar punches.

VITAMIN E CHEWABLE TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
400.00	1	Vitamin E acetate (dry powder, SD 50)	800.00
790.00	2	Ludipress®	790.00
20.00	3	Aerosil® 200	20.00
QS	4	Flavors	QS

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.5 mm sieve, mix, and press with high compression force.
2. Compress 1665 mg tablets in 20 mm biplanar punches.

VITAMIN E CONCENTRATE (WATER-MISCIBLE)

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
105.00	1	Vitamin E acetate	105.00
250.00	2	Cremophor (RH, 40%)	250.00
QS	3	Preservative	QS
QS	4	Water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Heat the mixture of items 1 and 2 and solution of item 3 in item 4 separately to approximately 65°C.
2. Slowly add to the well-stirred solution to obtain a clear, colorless liquid that is miscible with water.

VITAMIN E DROPS

Bill of Materials			
Scale (mg/mL)	Item	Material Name	Qty/L (g)
50.00	1	Vitamin E acetate	50.00
160.00	2	Cremophor (RH, 40%)	160.00
QS	3	Preservative	QS
QS	4	Water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Heat mixture of items 1 and 2 and solution of item 3 in 4 to approximately 65°C.
2. Add them slowly to obtain a clear or lightly opalescent, colorless liquid.

VITAMIN E GEL CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
100.00	1	Vitamin E acetate	100.00
150.00	2	Propylene glycol (pharma)	150.00
200.00	3	Lutrol F 127	200.00
550.00	4	Water	550.00

MANUFACTURING DIRECTIONS

1. Mix vitamin E acetate with propylene glycol, and add the water.
2. After cooling to approximately 6°C, slowly dissolve Lutrol F 127 in the well-stirred mixture.
3. Maintain cool until the air bubbles escape to obtain a turbid white gel at temperatures from 20°C to 50°C with viscosity at 25°C of approximately 120,000 mPa.

VITAMIN E SOFTGEL CAPSULES

Bill of Materials			
Scale (mg/Capsule)	Item	Material Name	Qty/1000 Capsules (g)
400.00	1	Vitamin E preparation, USP	400.00
25.00	2	Soybean oil, USP	25.00
QS	3	Gelatin mass (clear)	QS

MANUFACTURING DIRECTIONS

1. Weigh items 1 and 2, and transfer into a suitable stainless steel container; mix for a minimum of 1 hour, screen, and transfer into tanks through a No. 80 to No. 100 mesh of stainless steel.
2. Encapsulate 425 mg of mixture into size 7.5 oval capsules using clear gelatin mass.

VITAMIN E SOLUTION WITH ETHANOL

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Qty/L (g)
0.10	1	Vitamin E acetate	0.10
4.00–5.00	2	Cremophor, EL	4.00–5.00
570.00	3	Water	570.00
380.00	4	Ethanol (96%)	380.00

MANUFACTURING DIRECTIONS

1. Heat mixture of item 1 and 2 to approximately 60°C. Stir well.
2. Slowly add the warm solvent mixture of items 3 and 4 to obtain a clear, colorless liquid of low viscosity.

VITAMIN E TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
50.00	1	Vitamin E acetate (dry powder, SD 50)	100.00
140.00	2	Mannitol	140.00
140.00	3	Tabletose®	140.00
15.00	4	Kollidon® VA 64	15.00
2.00	5	Magnesium stearate	2.00
10.00	6	Aerosil® 200	10.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with high compression force.
2. Compress 410 mg in 12 mm biplanar punches.

VITAMIN E TABLETS

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Qty/1000 Tablets (g)
50.00	1	Vitamin E acetate (dry powder, SD 50)	100.00
300.00	2	Sorbitol (crystalline)	300.00
3.00	3	Magnesium stearate	3.00
3.00	4	Aerosil® 200	3.00

MANUFACTURING DIRECTIONS

1. Pass all components through a 0.8 mm sieve, mix, and press with high compression force.
2. Compress 413 mg in 12 mm biplanar punches.

ZINC OXIDE LOTION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
7.00	1	Magnesium aluminum silicate	7.00
641.00	2	Water	641.00
7.00	3	Unimulsc C	7.00
30.00	4	Propylene glycol	30.00
30.00	5	Eucalyptus oil	30.00
30.00	6	Lanolin oil	30.00
50.00	7	Dimethicone (350 cS)	50.00
50.00	8	Benzoate alcohol (C12–C15)	50.00
100.00	9	Polysorbate 80	100.00
50.00	10	Zinc oxide	50.00
10.00	11	Cornstarch	10.00
QS	12	Preservatives	QS

MANUFACTURING DIRECTIONS

1. Slowly add item 1 to the water, agitating with maximum shear until smooth.
2. Add items 3 and 4, mixing each time until uniform.
3. Mix items 5 to 10 until uniform, and mix with other portions until uniform.
4. Add items 11 and 12, and mix until smooth.

ZINC OXIDE OINTMENT

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
120.00	1	Cetearyl alcohol, PEG-40 castor oil, and sodium cetearyl sulfate	120.00
180.00	2	Petrolatum	180.00
60.00	3	Oleoyl oleate	60.00
60.00	4	Mineral oil (light)	60.00
100.00	5	Zinc oxide	100.00
QS	6	Water	QS
10.00	7	Propylene glycol, diazolidinyl urea, methylparaben, and propylparaben	10.00

MANUFACTURING DIRECTIONS

1. Mix and heat items 1 to 5 to 70°C to 75°C.
2. Mix and heat items 6 and 7 to 70°C to 75°C.
3. While stirring, add second mixture to first mixture.
4. Begin cooling, and continue stirring until batch reaches 30°C; then, homogenize.

ZINC PYRITHIONE SHAMPOO

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/1000 Tablets (g)
547.50	1	Deionized water	547.50
7.50	2	Hydroxyethylcellulose	7.50
347.00	3	TEA-lauryl sulfate	347.00
43.00	4	PEG-20 lanolin alcohol ether	43.00
20.00	5	Glycol stearate	20.00
15.00	6	Cocamide MEA	15.00
10.00	7	Zinc pyrithione (48%)	20.00
QS	8	Fragrance, preservative	QS

MANUFACTURING DIRECTIONS

1. Add item 2 to the water, and mix.
2. In a separate vessel, combine items 3 to 5, heat to 80°C, and mix.
3. Cool to 50°C.
4. Add items 6 and 7, and mix.
5. Add this mixture to mixture of item 2.
6. Cool to 40°C, and add item 8.

ZINC UNDECYLENATE CREAM

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
7.50	1	Magnesium aluminum silicate	7.50
487.50	2	Deionized water	487.50
100.00	3	Sorbitol 70%	100.00
10.00	4	Polysorbate 80	10.00
200.00	5	Zinc undecylenate	200.00
50.00	6	Caprylic acid	50.00
30.00	7	C12–C15 benzoate alcohol	30.00
15.00	8	Polysorbate 80	15.00
20.00	9	C18–C36 acid	20.00
80.00	10	Glyceryl stearate and PEG-100 stearate	80.00
QS	11	Preservatives	QS

MANUFACTURING DIRECTIONS

1. Slowly add item 1 in the water, mixing with maximum available shear until smooth.
2. Add items 2 to 5 in order, mixing each until uniform.
3. Avoid incorporating air. Heat with stirring to 70°C to 75°C.
4. Heat items 6 to 10 separately to 70°C to 75°C, and add to the mixture with mixing while cooling. Fill at 45°C to 50°C.

ZIRCONIUM OXIDE LOTION

Bill of Materials			
Scale (mg/g)	Item	Material Name	Qty/kg (g)
15.00	1	Magnesium aluminum silicate	15.00
3.00	2	Carboxymethylcellulose sodium (medium viscosity)	3.00
796.50	3	Water	796.50
40.00	4	Zirconium oxide	40.00
50.00	5	Propylene glycol	50.00
80.00	6	Isopropyl alcohol	80.00
15.00	7	Benzocaine	15.00
0.50	8	Menthol	0.50
QS	9	Preservative	QS

MANUFACTURING DIRECTIONS

1. Dry blend items 1 and 2, and slowly add them to the water while agitating with maximum shear until smooth.
2. Add items 4 and 5 and then items 6 to 9. Mix.

PART III

Cosmetic Formulations



Taylor & Francis

Taylor & Francis Group

<http://taylorandfrancis.com>

Cosmetic Formulations

LIGHT LIP GLOSS

Ingredient	Content (w/w%)
Pentaerythrityl tetraistearate	37.99
Triisostearin	4.00
Diisostearyl malate	4.00
Glyceryl behenate/eicosadioate	3.00
Polyethylene terephthalate polymethyl methacrylate	1.00
C.i. 15985	0.01
Hydrogenated polyisobutene ^a	50.00
Total	100.00

^a Kinetic viscosity (98.9°C): 300 mm²/s

MANUFACTURING DIRECTIONS

1. Heat all ingredients to 80°C, and dissolve them.
2. Mix uniformly.
3. Pour into a mold, and cool to 25°C.

HEAVY LIP GLOSS

Ingredient	Content (w/w%)
Pentaerythrityl tetraistearate	28.00
Triisostearin	10.00
Diisostearyl malate	8.00
Glyceryl behenate/eicosadioate	2.00
Polyethylene terephthalate Polymethyl methacrylate	2.00
Hydrogenated polyisobutene ^a	50.00
Total	100.00

^a Kinetic viscosity (98.9°C): 800 mm²/s

MANUFACTURING DIRECTIONS

1. Manufacturing Directions Heat all ingredients to 80°C, and dissolve them.
2. Mix uniformly.
3. Pour into a mold, and cool to 25°C.

LIP CARE PASTE

	Ingredient	Content (w/w%)
A	Polyglyceryl-10 behenate/eicosadioate	4.00
	Glycerin	24.00
	Diglycerin	7.00
	Water	5.00
B	Glyceryl behenate/eicosadioate	3.00
	Diisostearyl malate	54.50
C	Pigment base	2.50
Total	100.00	

PIGMENT BASE : PENTAERYTHRITYL TETRAISOSTEARATE (60.0 w/w%), C.I. 45440 (32.0 w/w%), C.I.19140 (8.0 w/w%)

MANUFACTURING DIRECTIONS

1. Manufacturing Directions Heat A ingredients to 80°C, and dissolve.
2. Mix uniformly.
3. Heat B ingredients to 80°C, and dissolve.
4. Mix uniformly.
5. Add product of step 4 to product of step 2 while mixing by a dispersion mixer.
6. Cool to 60°C.
7. Add C ingredients slowly while mixing.
8. Cool to 25°C.

LIPSTICK, BASIC

Ingredient	Content (w/w%)
Polyglyceryl-2 triisostearate	36.00
Neopentylglycol dicaprates	16.00
Hydrogenated polydecene	6.00
Dipentaerythrityl hexahydroxystearate/ hexastearate/ hexarosinate	16.00
Cholesteryl hydroxystearate	2.00
Ceresin	7.00
<i>Euphorbia cerifera</i> (candelilla) wax	7.00
Pigment base ^a	10.00
Total	100.00

^a PIGMENT BASE: (DIISOSTEARYL MALATE) (50.0 w/w%), TITANIUM DIOXIDE (30.0 w/w%), C.I. 15850 (D&C Red No.6) (10.0 w/w%), C.I. 15850 (D&C Red No.7) (5.0 w/w%), MICA (5.0 w/w%)

MANUFACTURING DIRECTIONS

1. Manufacturing Directions Heat all ingredients to 90°C and dissolve them.
2. Disperse uniformly by a dispersion mixer.
3. Pour into a mold, and cool to 20°C rapidly.

LIPSTICK, LIGHT GLOSSY

Ingredient	Content (w/w%)
Dipentaerythrityl tripolyhydroxystearate	12.00
Polyglyceryl-2 tetraistearate	24.00
Diisostearyl malate	18.00
Hydrogenated polydecene	23.00
Ceresin	12.00
Polyethylene	1.00
Pigment base ^a	10.00
Total	100.00

^a PIGMENT BASE: (DIISOSTEARYL MALATE) (50.0 w/w%), TITANIUM DIOXIDE (30.0 w/w%), C.I. 15850 (D&C Red No.6) (10.0 w/w%), C.I. 15850 (D&C Red No.7) (5.0 w/w%), MICA (5.0 w/w%)

MANUFACTURING DIRECTIONS

1. Manufacturing Directions Heat all ingredients to 100°C, and dissolve them.
2. Disperse uniformly by a dispersion mixer.
3. Pour into a mold, and cool to 20°C rapidly.

LIPSTICK, CLEAR

Ingredient	Content (w/w%)
Triethylhexanoin	10.00
Hydrogenated polydecene	11.00
Diisostearyl malate	36.50
Cetyl ethylhexanoate	5.00
Dipentaerythrityl hexahydroxystearate/hexastearate/hexarosinate	12.00
Trehalose isostearate esters	5.00
<i>Euphorbia cerifera</i> (candelilla) wax	4.00
Paraffin	3.00
Beeswax	1.50
<i>Copernicia cerifera</i> (carnauba) wax	1.00
Pigment base ^a	6.00
Pigment mixture ^b	5.00
Total	100.00

^a PIGMENT BASE: (DIISOSTEARYL MALATE) (50.0 w/w%), TITANIUM DIOXIDE (30.0 w/w%), C.I. 15850 (D&C Red No. 6) (10.0 w/w%), C.I. 15850 (D&C Red No. 7) (5.0 w/w%), MICA (5.0 w/w%)

^b PIGMENT MIXTURE: MICA (46.5 wt/wt%), TITANIUM DIOXIDE (43.0 wt/wt%), IRON OXIDES (5.5 w/w%), ALUMINA (5.0 w/w%)

MANUFACTURING DIRECTIONS

1. Manufacturing Directions Heat all ingredients to 90°C, and dissolve them.
2. Disperse uniformly by a dispersion mixer.
3. Pour into a mold, and cool to 20°C rapidly.

LIPSTICK, SMOOTH

Ingredient	Content (w/w%)
Glyceryl tribehenate/isostearate/eicosandioate	6.00
Polyglyceryl-2 tetraistearate	12.00
Hydrogenated polydecene	33.00
Diisostearyl malate	26.00
Ceresin	11.00
Pigment base ^a	12.00
Total	100.00

^a PIGMENT BASE: (DIISOSTEARYL MALATE) (50.0 w/w%), TITANIUM DIOXIDE (30.0 w/w%), C.I. 15850 (D&C Red No. 6) (10.0 w/w%), C.I. 15850 (D&C Red No. 7) (5.0 w/w%), MICA (5.0 w/w%)

MANUFACTURING DIRECTIONS

1. Manufacturing Directions Heat all ingredients to 90°C, and dissolve them.
2. Disperse uniformly by a dispersion mixer.
3. Pour into a mold, and cool to 20°C rapidly.

LIPSTICK (MOISTURE-RICH LIPSTICK)

Ingredient	Content (w/w%)
Dipentaerythrityl tripolyhydroxystearate	5.00
Glycerin	1.00
Triethylhexanoin	15.00
Polyglyceryl-2 triisostearate	24.00
Diisostearyl malate	19.00
Dipentaerythrityl hexahydroxystearate/hexastearate/hexarosinate	10.00
Ceresin	4.80
<i>Euphorbia cerifera</i> (candelilla) wax	8.00
Microcrystalline wax	3.20
Pigment base ^a	10.00
Total	100.00

MANUFACTURING DIRECTIONS

1. Heat all ingredients to 90°C, and dissolve.
2. Disperse uniformly by a dispersion mixer.
3. Pour into a mold, and cool to 20°C rapidly.

BASE CREAM

	Ingredient	Content (w/w%)
A	Isotridecyl isononanoate	2.00
	Trehalose isostearate esters	1.00
	Cyclopentasiloxane	29.52
	Dimethicone/peg-10/15 cross polymer, Dimethicone	1.00
	Peg-10 dimethicone	4.00
	Titanium dioxide	3.00
	Iron oxides	0.23
	Vinyl dimethicone/methicone Silsesquioxane crosspolymer	10.00
	Polymethyl methacrylate	5.00
	Tocopherol	0.05
B	Ethanol	5.00
	Butylene glycol	3.00
	Sodium chloride	0.50
	Methylparaben	0.20
	Phenoxyethanol	0.50
	Water	35.00
	Total	100.00

MANUFACTURING DIRECTIONS

1. Dissolve A ingredients at 25°C, and disperse uniformly.
2. Dissolve B ingredients at 25°C, and mix uniformly.
3. Add product of step 2 slowly to product of step 1 while mixing by a dispersion mixer.

OIL-BASED FOUNDATION

Ingredient	Content (w/w%)
Hydrogenated polydecene	17.00
Ethylhexyl palmitate	9.50
Trehalose isostearate esters	1.00
Phenyl trimethicone	4.50
Dimethicone	14.75
Microcrystalline wax	2.00
Paraffin	6.00
Titanium dioxide	9.52
Iron oxides	4.08
Mica	21.50
Polymethyl methacrylate	10.00
Tocopherol	0.05
Butylparaben	0.05
Methylparaben	0.05
Total	100.00

MANUFACTURING DIRECTIONS

1. Heat all ingredients to 80°C, and dissolve.
2. Disperse uniformly.
3. Grind by a three-roll mill.
4. Heat to 80°C.
5. Pour into a mold.
6. Cool to 0°C.

SUNSCREEN (MOISTURE TYPE)

	Ingredient	Content (w/w%)
A	Diisostearyl malate	5.50
	Glyceryl tribehenate/isostearate/eicosandioate	3.00
	Cyclopentasiloxane	13.50
	Dimethicone ^a	9.00
	Peg-10 dimethicone	3.00
B	Titanium dioxide	9.00
	Butylene glycol	5.00
	Sodium chloride	1.00
	Methylparaben	0.20
	Water	50.80
	Total	100.00

^a Kinetic viscosity (25.0°C): 10 mm²/s

MANUFACTURING DIRECTIONS

1. Manufacturing Directions Heat A ingredients to 70°C, and dissolve.
2. Disperse uniformly.
3. Heat B ingredients to 70°C, and dissolve.
4. Mix uniformly.
5. Add product of step 4 slowly to product of step 2 while mixing by a dispersion mixer.
6. Cool to 30°C.

SUNSCREEN (FRESH TYPE)

	Ingredient	Content (w/w%)
A	Erythrityl triethylhexanoate	4.50
	Glyceryl tribehenate/isostearate/eicosandioate	3.00
	Cyclopentasiloxane	13.50
	Dimethicone ^a	9.00
	Peg-10 dimethicone	3.00
B	Titanium dioxide	10.00
	Butylene glycol	5.00
	Sodium chloride	1.00
	Methylparaben	0.20
	Water	50.80
	Total	100.00

^a Kinetic viscosity (25.0°C): 10 mm²/s

MANUFACTURING DIRECTIONS

1. Manufacturing Directions Heat A ingredients to 70°C, and dissolve.
2. Disperse uniformly.
3. Heat B ingredients to 70°C, and dissolve.
4. Mix uniformly.
5. Add product of step 4 slowly to product of step 2 while mixing by a dispersion mixer.
6. Cool to 30°C.

WATERPROOF EYE LINER

Ingredient	Content (w/w%)
Glyceryl tribehenate/isostearate/eicosandioate	8.00
Erythrityl triethylhexanoate	1.00
Microcrystalline wax	6.00
Silica	1.00
Hydrogenated polyisobutene ^a	58.00
Iron oxides	15.00
Mica	11.00
Total	100.00

^a Kinetic viscosity (37.8°C): 1.28 mm²/s

MANUFACTURING DIRECTIONS

1. Manufacturing Directions Heat all ingredients to 90°C, and dissolve.
2. Disperse uniformly by a dispersion mixer.
3. Pour into a mold, and cool to 25°C.

**OIL-BASED FACIAL CLEANSER
(AVAILABLE IN WET CONDITION)**

	Ingredient	Content (w/w%)
A	Polyglyceryl-10 dioleate	14.00
	Polyglyceryl-2 sesquicaprylate	6.00
	Cetyl ethylhexanoate	79.90
B	Perfume	0.10
	Total	100.00

MANUFACTURING DIRECTIONS

1. Heat A ingredients to 80°C, and dissolve.
2. Mix uniformly.
3. Cool to 25°C.
4. Add B ingredients to product of step 3, and mix uniformly.

**OIL-BASED FACIAL CLEANSER
(FOR HEAVY MAKE-UP)**

	Ingredient	Content (w/w%)
A	Polyglyceryl-10 dioleate	14.00
	Polyglyceryl-2 sesquicaprylate	6.00
	Cetyl ethylhexanoate	71.90
	Isononyl isononanoate	8.00
B	Perfume	0.10
	Total	100.00

MANUFACTURING DIRECTIONS

1. Heat A ingredients to 80°C, and dissolve.
2. Mix uniformly.
3. Cool to 25°C.
4. Add B ingredients to product of step 3, and mix it uniformly.

OIL-FREE FACIAL CLEANSER (LIQUID)

Ingredient	Content (w/w%)
Peg-20 glyceryl triisostearate	10.00
Peg-20 glyceryl isostearate	10.00
Dipropylene glycol	30.00
Sodium citrate	0.07
Citric acid	0.03
Water	49.80
Perfume	0.10
Total	100.00

MANUFACTURING DIRECTIONS

1. Dissolve all ingredients at 25°C.
2. Mix uniformly.

OIL-FREE FACIAL CLEANSER (GEL)

	Ingredient	Content (w/w%)
A	Polyglyceryl-10 behenate/eicosadioate	5.00
	PEG-20 glyceryl triisostearate	12.50
	PEG-20 glyceryl isostearate	12.50
	Dipropylene glycol	30.00
	Glycerin	10.00
	Water	17.20
B	1% carbomer solution (aq.)	10.00
C	1% sodium hydroxide solution (aq.)	2.60
D	Perfume	0.20
	Total	100.00

MANUFACTURING DIRECTIONS

1. Heat A ingredients to 80°C, and dissolve.
2. Disperse uniformly by a dispersion mixer, and cool to 50°C.
3. Add B ingredients to product of step 2 while mixing.
4. Add C ingredients to product of step 3 while mixing.
5. Add D ingredients to product of step 4 while mixing.
6. Cool to 25°C.

MAKE-UP REMOVER (SEPARATE TYPE)

	Ingredient	Content (w/w%)
A	Erythrityl triethylhexanoate	15.00
	Cyclopentasiloxane	25.00
B	Butylene glycol	20.00
	Sodium chloride	1.00
	Water	38.90
	0.1% C.I. 42090 solution (aq.)	0.10
	Total	100.00

MANUFACTURING DIRECTIONS

1. Dissolve A ingredients at 25°C, and mix uniformly.
2. Dissolve B ingredients at 25°C, and mix uniformly.
3. Pour both mixes into a mold.

CLEANSING PASTE

	Ingredient	Content (w/w%)
A	Polyglyceryl-10 behenate/eicosadioate	7.00
	Polyglyceryl-10 oleate	1.00
	Glycerin	24.00
	Butylene glycol	10.00
	Water	8.00
B	Glyceryl behenate/eicosadioate	3.00
	Hydrogenated lecithin	1.00
	Ethylhexyl palmitate	31.90
	<i>Olea europaea</i> (olive) fruit oil	14.00
C	Perfume	0.10
	Total	100.00

MANUFACTURING DIRECTIONS

1. Heat A ingredients to 75°C, and dissolve.
2. Mix uniformly.
3. Heat B ingredients to 75°C, and dissolve.
4. Mix uniformly.
5. Add product of step 4 to product of step 2 while mixing by a dispersion mixer.
6. Cool to 60°C.
7. Add C ingredients to product of step 6, and cool to 25°C.

MASSAGE GEL

		Content
		(w/w %)
		Ingredient
A	3-hydrogenated lecithin	1.00
	Isopentyldiol	10.00
	Glycerin	30.00
	Water	3.00
B	Triethylhexanoin	18.00
	Mineral oil	38.00
	Total	100.00

MANUFACTURING DIRECTIONS

1. Heat A ingredients to 80°C, and dissolve.
2. Mix uniformly.
3. Heat B ingredients to 80°C, and dissolve.
4. Mix uniformly.
5. Add product of step 4 very slowly to product of step 2 while mixing by a dispersion mixer.
6. Continue to mix after adding for over 10 minutes.
7. Cool product of step 6 to 50°C while mixing by a dispersion mixer.
8. Cool to 25°C without mixing.

Part IV

Tablet Coating Formulations



Taylor & Francis

Taylor & Francis Group

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INTRODUCTION

Solid dosage forms are frequently coated for varied purposes, including the following:

- Mask taste and smell.
- Offer protection from the environment.
- Provide protection from gastric acid (enteric coating).
- Make dose easy to swallow.
- Provide identification.
- Add esthetic appeal.
- Hide surface defects.

Many types of coatings are available.

I. Sugar coating: Compressed tablets are coated with a colored or uncolored sugar layer that is water soluble and quickly dissolves after swallowing. The sugar coat protects the enclosed drug from the environment and provides a barrier to objectionable taste or odor. The sugar coat also enhances the appearance of the compressed tablet and permits manufacturing information to be imprinted. Sugar coating provides a combination of insulation, taste masking, smoothing the tablet core, coloring, and modified release. The disadvantages of sugar coating are the time and expertise required in the coating process and increased size, weight, and shipping costs. The sugar-coating process involves five separate operations:

a. Sealing/waterproofing: Prior to applying any sugar/water syrup, the tablet cores must be sealed, thoroughly dried, and free of all residual solvents. The seal coat provides a moisture barrier and hardness to the surface of the tablet in order to minimize attritional effects. Core tablets having very rapid disintegration rates conceivably could start the disintegration process during the initial phase of sugar coating. The sealants are generally water-insoluble polymers/film formers applied from an organic solvent solution. The quantities of material applied as a sealing coat will depend primarily on the tablet porosity, since highly porous tablets will tend to soak up the first application of solution, thus preventing it from spreading uniformly across the surface of every tablet in the batch. Hence, one or more further applications of resin solution may be required to ensure that the tablet cores are sealed effectively. Common materials used as a sealant include shellac, zinc sulfate, cellulose acetate phthalate (CAP), polyvinylacetate phthalate, hydroxypropyl cellulose, hydroxypropyl methylcellulose, etc.

b. Subcoating: Subcoating is the actual start of the sugar-coating process and provides the rapid buildup necessary to round up the tablet edge. It also acts as the foundation for the smoothing and color coats. Generally, two methods are used for subcoating. Dusting with powder and then drying is required when applying gum based solution and the routine is repeated until the desired shape is achieved. The other method is where a suspension of dry powder in gum/sucrose solution is applied, followed by drying the tablets. Thus, subcoating is a sandwich of alternate layers of gum and powder. It is necessary to remove the bulk of the water after each application of coating syrup.

c. Grossing/smoothing: The grossing/smoothing process is specifically for smoothing and filing the irregularity on the surface generated during subcoating. It also increases the tablet size to a predetermined dimension. If the subcoating is rough with a large amount of irregularities, then the use of grossing syrup containing suspended solids will provide more rapid buildup and better filling qualities. Smoothing usually can be accomplished by the application of a simple syrup solution (approximately 60%–70% sugar solid). This syrup generally contains pigments, starch, gelatin, acacia, or opacifier if required. Small quantities of color suspension can be applied to impart a tint of the desired color when there are irregularities in coating.

d. Color coating: This stage is often critical in the successful completion of a sugar coating process and involves the multiple application of syrup solution (60%–70% sugar solid) containing the requisite coloring matter. Mainly soluble dyes were used in the sugar coating to achieve the desired color, since a soluble dye will migrate to the surface during drying. But nowadays, insoluble certified lakes have virtually replaced the soluble dyes in pharmaceutical tablet coating. The most efficient process for color coating involves the use of a predispersed opacified lake suspension.

e. Polishing: Sugar-coated tablets need to be polished to achieve a final elegance. Polishing is achieved by applying a mixture of waxes such as beeswax, carnauba wax, candelilla wax, or hard paraffin wax to tablets in a polishing pan.

II. **Film Coating:** Film coating is the deposition of a thin film of polymer surrounding the tablet core. Conventional pan equipment may be used, but nowadays, more sophisticated equipment is employed to provide a high degree of automation and coating time. The polymer is solubilized into solvent. Other additives such as plasticizers and pigments are added. The resulting solution is sprayed onto a rotated tablet bed. The drying conditions cause removal of the solvent, giving a thin deposition of coating material around each tablet core. Usually, a spray process is employed in the preparation of film-coated tablets. The Accela Cota is the prototype of a perforated cylindrical drum providing high drying air capacity. Fluidized-bed equipment has made a considerable impact; here, tablets are moving in a stream of air passing through the perforated bottom of a cylindrical column. With a smaller cylindrical insert, the stream of cores is rising in the center of the device together with a spray mist applied in the middle of the bottom. For fluidized-bed coating, very hard tablets (hardness >20 N) have to be used. The fundamental requirements are independent of the actual type of equipment being used and include adequate means of atomizing the spray liquid for application to the tablet core, adequate mixing and agitation of the tablet bed, and sufficient heat input in the form of drying air to provide the latent heat of evaporation of the solvent. This is particularly important with aqueous-based spraying and good exhaust facilities to remove dust and solvent-laden air. The materials used in film coating include the following:

a. Film formers

i. **Hydroxypropyl methylcellulose (HPMC):** This is available in different viscosity grades. It is a polymer of choice for air suspension and pan spray coating systems because of its solubility characteristics in gastric fluid and organic and aqueous solvent systems. The advantages are that it does not affect tablet disintegration and drug availability; it is cheap, flexible, and highly resistant to heat, light, and moisture; it has no taste and odor; and color and other additives can be easily incorporated. The disadvantage is that when it is used alone, the polymer has a tendency to bridge or fill the debossed tablet surfaces. So, a mixture of HPMC and other polymers/plasticizers is used.

ii. **Methylhydroxy ethylcellulose (MHEC):** This is available in a wide variety of viscosity grades. It is not as frequently used as HPMC, because it is soluble in fewer organic solvents.

iii. **Ethylcellulose (EC):** Depending on the degree of ethoxy substitution, different viscosity grades are available. It is completely

insoluble in water and gastric fluids. Hence, it is used in combination with water-soluble additives such as HPMC and not alone. Unplasticized ethylcellulose films are brittle and require film modifiers to obtain an acceptable film formulation. Aquacoat is an aqueous polymeric dispersion utilizing ethylcellulose. These pseudolatex systems contain high-solids, low-viscosity compositions that have coating properties quite different from those of regular ethylcellulose solution.

iv. **Hydroxypropyl cellulose (HPC):** This is soluble in water below 40°C (insoluble above 45°C), gastric fluid, and many polar organic solvents. HPC is extremely tacky as it dries from the solution system. It is used for sub-coating and not for color or glass coating. It gives a very flexible film.

v. **Povidone:** The degree of polymerization decides the molecular weight of the material. It is available in four viscosity grades: K-15, K-30, K-60, and K-90. The average molecular weight of these grades is 10,000, 40,000, 160,000, and 360,000, respectively. K-30 is widely used as a tablet binder and in tablet coating. It has excellent solubility in a wide variety of organic solvents, water, and gastric and intestinal fluids. Povidone can be cross-linked with other materials to produce films with enteric properties. It is used to improve the dispersion of colorants in coating solution.

vi. **Sodium carboxymethyl cellulose:** This is available in medium-, high-, and extra high-viscosity grades. It is easily dispersed in water to form colloidal solutions but is insoluble in most organic solvents and hence, not a material of choice for coating solutions based on organic solvents. Films prepared using it are brittle but adhere well to tablets. Partially dried films are tacky. So, coating compositions must be modified with additives.

vii. **Polyethylene glycols (PEG):** PEG with low molecular weights (200–600) are liquid at room temperature and are used as plasticizers. High-molecular weight PEG (900–8000 series) are white, waxy solids at room temperature. A combination of PEG waxes with CAP gives films that are soluble in gastric fluids.

viii. **Acrylate polymers:** These are marketed under the name of Eudragit®. Eudragit® E is a cationic copolymer. Only Eudragit® E is freely soluble in gastric fluid up to pH 5 and expandable and permeable above pH 5. This material is available as an organic

- solution (12.5% in isopropanol/acetone), a solid material, or a 30% aqueous dispersion. Eudragit® RL and RS are copolymers with a low content of quaternary ammonium groups. These are available only as organic solutions and solid materials. They produce films for delayed action (pH dependent).
- b. Solvents: Mostly, solvents are used either alone or in combination with water, ethanol, methanol, isopropanol, chloroform, acetone, methylene chloride, etc. Water is more often used, because there are no environmental and economic considerations. For drugs that readily hydrolyze in the presence of water, nonaqueous solvents are used.
 - c. Plasticizers: As solvent is removed, most polymeric materials tend to pack together in a three-dimensional honeycomb arrangement. Both internal and external plasticizing techniques are used to modify the quality of the film. A combination of plasticizers may be used to get the desired effect. The concentration of plasticizer is expressed in relation to the polymer being plasticized. Recommended levels of plasticizers range from 1% to 50% by weight of the film former. Commonly used plasticizers are castor oil, propylene glycol (PG), glycerin, lower-molecular weight (200–400 series) PEG, surfactants, etc. For aqueous coating, PEG and PG are more used, while castor oil and spans are primarily used for organic solvent-based coating solutions. An external plasticizer should be soluble in the solvent system used for dissolving the film former and the plasticizer. The plasticizer and the film former must be at least partially soluble or miscible in each other.
 - d. Colorants: Colorants can be used in solution form or in suspension form. To achieve proper distribution of suspended colorants in the coating solution requires the use of powdered colorants (<10 microns). Most common colorants in use are certified FD&C or D&C colorants. These are synthetic dyes or lakes. Lakes are the choice for sugar or film coating, as they give reproducible results. The concentration of colorants in the coating solutions depends on the color shade desired, the type of dye, and the concentration of opaquant-extenders. If a very light shade is desired, a concentration of less than 0.01% may be adequate; on the other hand, if a dark color is desired, a concentration of more than 2.0% may be required. Inorganic materials (e.g., iron oxide) and natural coloring materials (e.g., anthocyanins, carotenoids, etc.) are also used to prepare coating solutions. Magenta red dye is nonabsorbable in biologic systems and resistant to degradation in the gastrointestinal tract. Opaspray® (opaque color concentrate for film coating) and Opadry® (complete film coating concentrate) are promoted as achieving less lot-to-lot color variation.
 - e. Opaquant-extenders: These are very fine inorganic powders used to provide more pastel colors and increase film coverage. These inorganic materials provide a white coat or mask the color of the tablet core. Colorants are very expensive, and high concentrations are required. These inorganic materials are cheap. In the presence of these inorganic materials, the amount of colorants required decreases. The most commonly used materials are titanium dioxide, silicate (talc and aluminum silicates), carbonates (magnesium carbonates), oxides (magnesium oxide), and hydroxides (aluminum hydroxides).
 - f. Other components: Flavors, sweeteners, surfactants, antioxidants, antimicrobials, etc. may be incorporated into the coating solution.
- III. Enteric Coating: This can be applied as one homogeneous layer, which can be white–opaque or colored. The advantage is that only one application is needed. In a two-layer system, the enteric formulation is applied first, followed by colored film. Both layers can be of enteric polymer, or only the basic layer can contain enteric polymer while the top layer is a fast-disintegrating and water-soluble polymer. Polymers used for enteric coating include the following:
- a. Cellulose acetate phthalate (CAP): This is widely used in industry. Aquateric is a reconstituted colloidal dispersion of latex particles. It is composed of solid or semisolid polymer spheres of CAP ranging in size from 0.05 to 3 microns. Cellulose acetate trimellitate (CAT), developed as an ammoniated aqueous formulation, showed faster dissolution than a similar formulation of CAP. Disadvantages include: It dissolves above pH 6 only, delays the absorption of drugs, is hygroscopic and permeable to moisture in comparison with other enteric polymer, and is susceptible to hydrolytic removal of phthalic and acetic acid, changing the film properties. CAP films are brittle and usually used with other hydrophobic film-forming materials.
 - b. Acrylate polymers: Eudragit® L & Eudragit® S are two forms of commercially available enteric acrylic resins. Both of them produce films resistant to gastric fluid. Eudragit® L and S are soluble in intestinal fluid at pH 6 and 7, respectively. Eudragit® L is available as an organic solution (in isopropanol), solid, or aqueous dispersion. Eudragit® S is available only as an organic solution (in isopropanol) and a solid.
 - c. Hydroxypropyl methylcellulose phthalate: HPMCP 50, 55, and 55-s (also called HP-50, HP-55, and HP-55-s) is widely used. HP-55 is

recommended for general enteric preparation, HP-50 and HP-55-s for special cases. These polymers dissolve at pH 5 to 5.5.

- d. Polyvinyl acetate phthalate: This is similar to HP-55 in stability and pH-dependent solubility.
- e. Enteric coating can be combined with polysaccharides that are degraded by enzymes in the colon; e.g., cyclodextrin and galactomannan.

IV. Controlled-Release Coating: Polymers such as modified acrylates, water-insoluble cellulose (ethylcellulose), etc., used for controlled-release coating.

V. Compressed Coating: This type of coating requires a specialized tablet machine. Compression coating is not widely used, but it has advantages in some cases in which the tablet core cannot tolerate organic solvent or water and yet needs to be coated for taste masking or to provide delayed or enteric properties to the finished product, and also to avoid incompatibility by separating incompatible ingredients.

VI. Electrostatic Coating: Electrostatic coating is an efficient method of applying coating to conductive substrates. A strong electrostatic charge is applied to the substrate. The coating material containing conductive ionic species of opposite charge is sprayed onto the charged substrate. Complete and uniform coating of corners and adaptability of this method to such relatively nonconductive substrates as pharmaceuticals are limited.

VII. Dip Coating: Coating is applied to the tablet cores by dipping them into the coating liquid. The wet tablets are dried in a conventional manner in a coating pan. Alternative dipping and drying steps may be repeated several times to obtain the desired coating. This process lacks the speed, versatility, and reliability of spray-coating techniques. Specialized equipment has been developed to dip coat tablets, but no commercial pharmaceutical application has been obtained.

VIII. Vacuum Film Coating: Vacuum film coating is a new coating procedure that employs a specially designed

baffled pan. The pan is hot water jacketed, and it can be sealed to achieve a vacuum system. The tablets are placed in the sealed pan, and the air in the pan is displaced by nitrogen before the desired vacuum level is obtained. The coating solution is then applied with an airless spray system. The heated pan causes evaporation, and the vapor is removed by the vacuum system. Because there is no high-velocity heated air, the energy requirement is low, and coating efficiency is high. Organic solvent can be effectively used with this coating system with minimum environmental or safety concerns.

Formulations for tablet coating are often proprietary to various manufacturers, as these address several formulation needs, as described previously. The suppliers of coating ingredients are often very open to sharing the coating technology, and companies are highly encouraged to make use of them, more particularly where the coating materials have an open Drug Master File (DMF) available for regulatory filings. The following companies are a very good source of information:

Eudragit® (www.pharma-polymers.com/pharma-polymers/en/eudragit/)

Colorcon® (www.colorcon.com/products/coatings)

Methocel/Ethocel (www.dow.com/dowexcipients/applications/tablet_coating.htm)

The advantage of using these prepackaged formulations is consistency in color matching, as well as other considerations regarding ease of use. The most significant aspect remains the choice of colors, which often determines the method of manufacturing the coating solutions. With a limited choice of dyes and lakes available for selection, manufacturers often use a combination of several colors and dyes along with agents such as talc for opaqueness to obtain the desired color and protection.

Given in the following is a current listing of approved colors in various regulatory regions.

APPROVED DRUG COLORANTS FOR INTERNAL USE IN JAPAN-1^A

Name	CAS Number	Color Index Number	Precedent Limit	Compendia
Black Iron Oxide	12227-89-3	77499	1.539 mg	JPE
Caramel			1500 mg	JPE
Carbon Black	1333-86-4	77268:1	0.096 mg	JPE
Carmine	1390-65-4	75470	1.8 mg	JPE
β-Carotene	7235-40-7	40800	0.1%	JPE
Copper Chlorophyll			1.8 mg	Japan Pharmaceutical Codex
Glycyrrhiza Extract			300 mg	JP
Gold Leaf	7440-57-5		14 mg	JPE
Light Anhydrous Silicic Acid	7631-86-9		2.6 g	JP
Medicinal Carbon	16291-96-6		150 mg	JP
2-Octyldodecyl Myristate	22766-83-2		100 mg	JPE
Orange Essence			15 mg	JPE
Powdered Green Tea			100 mg	JPE
Red Ferric Oxide	1309-37-1	77491	95.4 mg	JPE
Riboflavin	83-88-5		0.8 mg	JP
Riboflavin Butyrate			0.4 mg	JP
Riboflavin Sodium Phosphate			2 mg	JP
Rose Oil	8007-01-0		0.1 mg	NF
Rye Green Leaf Extract			2 mg	JPE
Sodium Copper Chlorophyllin			75 mg	JPC
Sodium Hydroxide	1310-73-2		224 mg	JP
Talc	14807-96-6		3384 mg	JP
Titanium Oxide	13463-67-7	77891	384 mg	JP
Yellow Ferric Oxide	1310-14-1	77492	5.67 mg	JPE

Note: JP: Japanese Pharmacopoeia; JPE: Japanese Pharmaceutical Excipient Directory; JPC: Japanese Pharmaceutical Codex; NF: National Formulary

^a These colorants appear in the application column in the Japanese Pharmaceutical Excipients Directory 2007 (Japanese Version) as coloring agents. Precedent limits are quoted from the Japanese Pharmaceutical Excipients Directory 2007 (Japanese version). Each limit represents the maximum daily intake that a patient should consume from the use of a particular dosage form.

APPROVED DRUG COLORANTS FOR INTERNAL USE IN JAPAN-2^A

Name	Alternate Name	Color Index Number	CAS Number	Precedent Limit
Amaranth ^c	Red No. 2, Acid Red 27	16185	915-67-3	b
Erythrosine ^c	Red No. 3, Acid Red 51	45430	16423-68-0	b
New Coccine (Ponceau 4R) ^c	Red No. 102, Acid Red 18	16255	2611-82-7	b
Phloxine B	Red No. 104(1), Acid Red 92	45410	18472-87-2	b
Rose Bengal	Red No. 105(1), Acid Red 94	45440	632-69-9	b
Acid Red	Red No. 106, Acid Red 52	45100		b
Tartrazine ^c	Yellow No. 4, Acid Yellow 23	19140	1934-21-0	b
Sunset Yellow FCF ^c	Yellow No. 5	15985	2783-94-0	b
Fast Green FCF	Green No. 3	42053	2353-45-9	b
Brilliant Blue FCF ^c	Blue No. 1	42090	3844-45-9	b
Indigo Carmine ^c	Blue No. 2, Acid Blue 74	73015	860-22-0	*c

^a Based on colors approved by the Ministry of Health and Welfare (MHW) "Ministerial Ordinance to establish Tar colors which can be used in Pharmaceuticals"; No. 30; August 31, 1966. Aluminum lakes of these colors are also authorized.

^b Not more than 0.1% by weight of color (lake or dye) can be used in a dosage form. If one colorant was combined with other colorants, total weight of these colorants must be less than 0.1% of the final product.

^c These colorants make the list of the application column in the Japanese Pharmaceutical Excipients Directory 2007 (Japanese Version) as coloring agents.

APPROVED DRUG COLORANTS FOR USE IN CANADA

I. COLORANTS APPROVED FOR INTERNAL AND EXTERNAL DRUG USE

Color	Alternate Name	Color Index Number	CAS Number
Acid Fuchsin D	D&C Red No. 33	17200	3567-66-6
Alizarin Cyanine Green F	D&C Green No. 5	61570	4403-90-1
Allura Red AC	FD&C Red No. 40	16035	25956-17-6
Amaranth	Delisted FD&C Red No. 2	16185	915-67-3
Anthocyanin (derived from juice expressed from fresh edible fruits or vegetables)			
β-apo-8' Carotenal	—	40820	1107-26-2
Brilliant Blue FCF Sodium Salt	FD&C Blue No. 0	42090	3844-45-8
Brilliant Blue FCF Ammonium Salt	D&C Blue No. 4	42090	6371-85-2
Canthaxanthin	—	40850	514-78-3
Caramel	—	—	—
Carbon Black	—	77266	1333-86-4
Carmine	—	75470	1260-17-9
Carmoisine	Azorubine	14720	3567-69-9
β-Carotene	—	40800	7235-40-7
Chlorophyll	—	75810	479-61-8
Eosin YS Acid Form	D&C Red No. 21	45380:2	15086-94-9
Eosin YS Sodium Salt	D&C Red No. 22	45380	17372-87-1
Erythrosine	FD&C Red No. 3	45430	16423-68-0
Fast Green FCF	FD&C Green No. 3	42053	2353-45-9
Flaming Red	D&C Red No. 36	12085	2814-77-9
Helindone Pink CN	D&C Red No. 30	73360	2379-74-0
Indigo	D&C Blue No. 6	73000	482-89-3
Indigotine	FD&C Blue No. 2	73015	860-22-0
Iron Oxides	Iron Oxide Red	77491	1309-37-1
	Iron Oxide Yellow	77492	51274-00-1
	Iron Oxide Black	77499	12227-89-3
Lithol Rubin B Sodium Salt	D&C Red No. 6	15850	5858-81-1
Lithol Rubin B Calcium Salt	D&C Red No. 7	15850:1	5281-04-9
Phloxine B Sodium Salt	D&C Red No. 28	45410	18472-87-2
Phloxine B Acid Form	D&C Red No. 27	45410:1	13473-26-2
Ponceau 4R	—	16255	2611-82-7
Ponceau SX	FD&C Red No. 4	14700	4548-53-2
Quinoline Yellow WS	D&C Yellow No. 10	47005	8004-92-0
Riboflavin	—	—	83-88-5
Sunset Yellow FCF	FD&C Yellow No. 6	15985	2783-94-0
Tartrazine	FD&C Yellow No. 5	19140	1934-21-0
Titanium Dioxide	—	77891	13463-67-7

II. COLORANTS APPROVED FOR EXTERNAL DRUG USE

Color	Alternate Name	Color Index Number	CAS Number
Acid Violet	Ext. D&C Violet No. 2	60730	—
Alizuroil Purple SS	D&C Violet No. 2	60725	81-48-1
Annatto	—	75120	—
Bismuth Oxychloride	—	77163	—
Chromium Hydroxide Green	Pigment Green 18	77289	—
Dibromofluorescein (Solvent Red 72)	D&C Orange No. 5	45370:1	—
Deep Maroon	D&C Red No. 34	15880:1	6417-83-0
Ferric Ferrocyanide	—	77510	—
Guanine	—	75170	—
Orange II	D&C Orange No. 4	15510	633-96-5
Manganese Violet	—	77742	—
Mica	—	77019	—
Pyranine Concentrated	D&C Green No. 8	59040	6358-69-6
Quinizarin Green SS	D&C Green No. 6	61565	128-80-3
Toney Red	D&C Red No. 17	26100	85-86-9
Uranine Acid Form	D&C Yellow No. 7	45350:1	7/5/2321
Uranine Sodium Salt	D&C Yellow No. 8	45350	518-47-8
Zinc Oxide	—	77947	—

APPROVED DRUG COLORANTS LISTED BY THE EUROPEAN UNION

Color	E Number	Color Index Number	Alternate Names
Allura Red AC	E129	16035	FD&C Red No. 40
Aluminum	E173	77000	—
Amaranth	E123	16185	Delisted FD&C Red No. 2
Anthocyanins	E163	—	—
Beetroot Red	E162	—	Betainin
Beta apo-8'-Carotenal	E160e	40820	—
Beta apo-8'-Carotenoic Acidethyl Ester	E160f	40825	—
Brilliant Black BN	E151	28440	Black PN
Brilliant Blue FCF	E133	42090	FD&C Blue No. 1
Brown HT	E155	20285	—
Calcium Carbonate	E170	77220	—
Canthaxanthin	E161g	40850	—
Caramel	E150a	—	—
Caramel, Caustic Sulphite	E150b	—	—
Caramel,-Ammonia	E150c	—	—
Caramel, Sulphite Ammonia	E150d	—	—
Carbon Vegetable Black	E153	77268:1	Carbo Medicinalis Vegetalis
Carmine	E120	75470	Carmine 40, Carminic Acid
Carmoisine	E122	14720	Azorubine
Carotene		75130	Alpha, Beta, and Gamma Carotene
i. Mixed Carotenes	E160a(i)	75130	—
ii. Beta-Carotene	E160a(ii)	40800	—
Chlorophylls/Chlorophyllins		—	—
i. Chlorophylls	E140(i)	75810	—
ii. Chlorophyllins	E140(ii)	75815	—
Chlorophylls/Chlorophyllins Copper Complexes		75815	—
i. Copper Complexes of Chlorophylls	E141(i)	—	—
ii. Copper Complexes of Chlorophyllins	E141(ii)	—	—

(Continued)

Color	E Number	Color Index Number	Alternate Names
Cochineal	E120	75470	Carminic Acid
Erythrosine	E127	45430	FD&C Red No. 3
Gold	E175	77480	—
Green S	E142	44090	Acid Brilliant Green BS
Indigotine	E132	73015	FD&C Blue No. 2, Indigo Carmine
Iron Oxides and Hydroxides	E172	77491	Iron Oxide Red
		77492	Iron Oxide Yellow
		77499	Iron Oxide Black
Lutein	E161b	—	—
Lycopene	E160d	—	—
Paprika Extract	E160c	—	Capsanthin, Capsorubin
Patent Blue V	E131	42051	Acid Blue 3
Ponceau 4R	E124	16255	Cochineal Red A
Quinoline Yellow ^a	E104	47005	China Yellow
Riboflavin		—	—
i. Riboflavin	E101(i)	—	—
ii. Riboflavin-5'-Phosphate	E101(ii)	—	—
Sunset Yellow FCF	E110	15985	FD&C Yellow No. 6, Orange Yellow S
Tartrazine	E102	19140	FD&C Yellow No. 5
Titanium Dioxide	E171	77891	—
Turmeric	E100	75300	Curcumin

This list is derived from Annex 1 of Directive 94/36/EC, colors permitted for use in foodstuffs. European Medicines Agency (EMA) Guideline EMA/CHMP/QWP/396951/2006 states that colorants mentioned in this annex are permitted for use in medicinal products.

^a This is not D&C Yellow No. 10. Although the C.I. numbers are the same, the dyes differ in composition. Quinoline yellow is primarily the disulfonated quinoline dye, whereas D&C Yellow No. 10 is the monosulfonated color. Quinoline yellow is not accepted for use in the United States; conversely, D&C Yellow No. 10 cannot be used in the EU.

COLOR ADDITIVES EXEMPT FROM CERTIFICATION PERMITTED FOR USE IN THE UNITED STATES^A

Color	Color Index Number	CAS Number	21 CFR References			
			Food	Drug	Cosmetic	Medical Devices
Algae Meal (Dried)	—	—	73.275	—	—	—
Algae Meal (Haematococcus)	—	—	73.185	—	—	—
Alumina	77002	1332-73-6	—	73.1010	—	—
Aluminum Powder	77000	7429-90-5	—	73.1645	73.2645	—
Annatto Extract	75120	8015-67-6	73.30	73.1030	73.2030	—
Astaxanthin	—	—	73.35	—	—	—
Beta-apo-8'-Carotenal	40820	1107-26-2	73.90	—	—	—
Beta Carotene	40800	7235-40-7	73.95	73.1095	73.2095	—
Beet Powder	—	57917-55-2	73.40	—	—	—
Bismuth Citrate	—	—	—	—	73.2110	—
Bismuth Oxychloride	77163	7787-59-9	—	73.1162	73.2162	—
Bronze Powder	77440	7440-50-8	—	73.1646	73.2646	—
		7740-66-6				
Calcium Carbonate	77220	471-34-1	—	73.1070	—	—
Canthaxanthin	40850	514-78-3	73.75	73.1075	—	—
Caramel	—	—	73.85	73.1085	73.2085	—
Carbazole Violet	51319	6358-30-1	—	—	—	73.3107
Carmine	75470	1390-65-4	73.100	73.1100	73.2087	—
Carrot Oil	—	—	73.300	—	—	—
Chlorophyllin Copper Complex	75810	—	—	73.1125	73.2125	73.3110
Chromium-Cobalt-Aluminum Oxide	77343	68187-11-1	—	73.1015	—	73.3110a

(Continued)

Color	Color Index Number	CAS Number	21 CFR References			
			Food	Drug	Cosmetic	Medical Devices
Chromium Hydroxide Green	77289	12182-82-0	—	73.1326	73.2326	—
Chromium Oxide Greens	77288	1308-38-9	—	73.1327	73.2327	73.3111
C.I. Vat Orange 1	59105	—	—	—	—	73.3112
Cochineal Extract	75470	1260-17-9	73.100	73.1100	—	—
Corn Endosperm Oil	—	—	73.315	—	—	—
Copper Powder	77400	7440-50-6	—	73.1647	73.2647	—
1,4-Bis [(2-hydroxyethyl) amino]-9,10-anthracenedione bis(2-propenoic) ester copolymers		10956-07-1				73.3100
1,4-Bis [(2-methylphenyl)amino]-9,10-anthracenedione		6737-68-4				73.3105
1,4-Bis[4-(2-methacryloxyethyl) phenylamino]-9,10-anthraquinone copolymers		121888-69-5				73.3106
2-[[2,5-Diethoxy-4-[(4-methylphenyl) thiol]phenyl] azo]-1,3,5-benzenetriol	—	—	—	—	—	73.3115
16,23-Dihydrodinaphtho[2,3-a:2',3'-i] naph[2',3':6,7]indolo[2,3-c] carbazole-5,10,15,17,22,24-hexone	70800	2475-33-4				73.3117
N,N'-(9,10-Dihydro-9,10-dioxo-1,5-anthracenediyl) bis-benzamide	61725	82-18-8				73.3118
7,16-Dichloro-6,15-dihydro-5,9,14,18-anthrazinetetrone	69825	130-20-1				73.3119
16,17-Dimethoxydinaphtho[1,2,3-cd:3',2',1'-lm] perylene-5,10 dione	59825	128-58-5				73.3120
4-[2,4-(Dimethylphenyl) azo]-2,4-dihydro-5-methyl-2-phenyl-3H-pyrazol-3-one		6407-78-9				73.3122
Dihydroxy Acetone	—	62147-49-3	—	73.1150	73.2150	—
Disodium EDTA Copper	—	—	—	—	73.2120	—
6-Ethoxy-2-(6-ethoxy-3-oxobenzo[<i>b</i>]thien-2-(3H)-ylidene)benzo[<i>b</i>] thiophen-3-(2H)-one	73335	3263-31-8				73.3123
Ferric Ammonium Citrate	—	1185-57-5	—	73.1025	—	—
Ferric Ammonium Ferrocyanide	77510	25869-00-5	—	73.1298	73.2298	—
Ferric Ferrocyanide	77510	14038-43-8	—	73.1299	73.2299	—
Ferrous Gluconate	—	299-29-6	73.160	—	—	—
Ferrous Lactate	—	5905-52-2	73.165	—	—	—
Fruit Juice	—	—	73.250	—	—	—
Grape Color Extract	—	—	73.169			—
Grape Skin Extract	—	—	73.170	—	—	—
Guaiazulene	—	489-84-9	—	—	73.2180	—
Guanine	75170	68-94-0	—	73.1329	73.2329	—
		73-40-5				
Henna	75480	83-72-7	—	—	73.2190	—
Iron Oxides, Synthetic	77491 (Red)	1309-37-1	73.200	73.1200	73.2250	73.3125
	77492 (Yellow)	51274-00-1				
	77499 (Black)	12227-89-3				
Lead Acetate	—	6080-56-4	—	—	73.2396	—
Logwood Extract	75290	8005-33-2	—	73.1410	—	—
Manganese Violet	77742	10101-66-3	—	—	73.2775	—
Mica	77019	12001-26-2	—	73.1496	73.2496	—
Mica-Based Pearlescent Pigment	—	—	73.350	73.1350	—	73.3128
Paprika	—	—	73.340	—	—	—
Paprika Oleoresin	—	8023-77-6	73.345	—	—	—
Phaffia Yeast	—	—	73.355	—	—	—
Potassium Sodium Copper Chlorophyllin	75180			73.1125	73.2125	
Phthalocyanine Green	74260	1328-53-6	—	—	—	73.3124
Poly(Hydroxyethyl Methacrylate)-Dye Copolymers						73.3121
Pyrogallol	76515	87-66-1	—	73.1375	—	—
Pyrophyllite	44004	8047-76-5	—	73.1400	73.2400	—
Riboflavin	—	83-88-5	73.450	—	—	—

(Continued)

Color	Color Index Number	CAS Number	21 CFR References			
			Food	Drug	Cosmetic	Medical Devices
Saffron		42553-65-1				
	75100	27876-94-4	73.500	—	—	—
Silver	77820	7440-22-4	—	—	73.2500	—
Sodium Copper Chlorophyllin	75815	28302-36-5	73.125	—	—	—
Tagetes Meal and Extract	75125	—	73.295	—	—	—
Talc	77019	14807-96-6	—	73.1550	—	—
Toasted Cotton Seed Meal	—	—	73.140	—	—	—
Titanium Dioxide	77891	13463-67-7	73.575	73.1575	73.2575	73.3126
Tomato Lycopene Extract and Concentrate			73.585	—	—	—
Turmeric	75300	458-37-7	73.600	—	—	—
Turmeric Oleoresin	75300	458-37-7	73.615	—	—	—
Ultramarine Blue	77007	57455-37-5	73.50	—	73.2725	—
Ultramarine Green	77013	—	—	—	73.2725	—
Ultramarine Pink	77007	127-96-9	—	—	73.2725	—
Ultramarine Red	77007	127-96-9	—	—	73.2725	—
Ultramarine Violet	77007	127-96-9	—	—	73.2725	—
Vegetable Juice	—	—	73.260	—	—	—
Vinyl Alcohol/Methyl Methacrylate Dye Reaction Products						73.3127
Zinc Oxide	77947	1314-13-2	—	73.1991	73.2991	—
Luminescent Zinc Sulfide	—	—	—	—	73.2995	—

^a Based on 21 CFR 2007. Restrictions may exist limiting the use of some of these colors to specific applications (i.e., external drug use only, etc.). Additionally, there may be quantitative limits for the use of some colors. The specific 21 CFR reference for each color should be reviewed to determine potential restriction status.

PROVISIONALLY LISTED COLOR ADDITIVES SUBJECT TO U.S. CERTIFICATION^A

Color	Common Name	Color Index Number	CAS Number	21 CFR References		
				Food	Drug	Cosmetic
FD&C Lakes	Lakes	See Individual Color	See Individual Color	82.51	82.51	82.51
D&C Lakes	Lakes	See Individual Color	See Individual Color		82.1051	82.1051
Ext. D&C Lakes	Lakes	See Individual Color	See Individual Color		82.2051	82.2051
FD&C Blue No. 1 Lake	Brilliant Blue FCF	42090:2	68921-42-6	82.101	82.101	82.101
FD&C Blue No. 2 Lake	Indigotine	73015:1	16521-38-3	82.102	82.102	82.102
D&C Blue No. 4 Lake	Alphazurine FG	42090	6371-85-3	—	82.1104	82.1104
FD&C Green No. 3 Lake	Fast Green FCF	42053	2353-45-9	82.203	82.203	82.203
D&C Green No. 5 Lake	Alizarin Cyanine Green F	61575	4403-90-1	—	82.1205	82.1205
D&C Green No. 6 Lake	Quinizarine Green SS	61565	128-80-3	—	82.1206	82.1206
D&C Orange No. 4 Lake	Orange II	15510:2	633-96-5	—	82.1254	82.1254
D&C Orange No. 5 Lake	Dibromofluorescein	45370:2	596-03-2	—	82.1255	82.1255
D&C Orange No. 10 Lake	Diiodofluorescein	45425:2	38577-97-8	—	82.1260	82.1260
D&C Orange No. 11 Lake	Erythrosine Yellowish Na	45425:2	38577-97-8	—	82.1261	81.1261
FD&C Red No. 4 Lake	Ponceau SX	14700	4548-53-2	82.304	82.304	82.304
D&C Red No. 6 Lake	Lithol Rubin B	15850:2	17852-98-1	—	82.1306	82.1306
D&C Red No. 7 Lake	Lithol Rubin B Ca	15850:1	5281-04-9	—	82.1307	82.1307
D&C Red No. 17 Lake	Toney Lake	26100	85-86-9	—	82.1317	82.1317
D&C Red No. 21 Lake	Tetrabromofluorescein	45380:3	15086-94-9	—	82.1321	82.1321
D&C Red No. 22 Lake	Eosine	45380:3	17372-87-1	—	82.1322	82.1322
D&C Red No. 27 Lake	Tetrachloro Tetrabromofluorescein	45410:2	13473-26-2		82.1327	82.1327

(Continued)

Color	Common Name	Color Index Number	CAS Number	21 CFR References		
				Food	Drug	Cosmetic
D&C Red No. 28 Lake	Phloxine B	45410:2	18472-87-02	—	82.1328	82.1328
D&C Red No. 30 Lake	Helindone Pink CN	73360	2379-74-0	—	82.1330	82.1330
D&C Red No. 31 Lake	Brilliant Lake Red R	15800:1	6371-76-2	—	82.1331	82.1331
D&C Red No. 33 Lake	Acid Fuchsin	17200	3567-66-6	—	82.1333	82.1333
D&C Red No. 34 Lake	Lake Bordeaux B	15880:1	6417-83-0	—	82.1334	82.1334
D&C Red No. 36 Lake	Flaming Red	12085	2814-77-9	—	82.1336	82.1336
D&C Violet No. 2 Lake	Alizuro Purple SS	60725	81-48-1	—	82.1602	82.1602
FD&C Yellow No. 5 Lake	Tartrazine	19140:1	12225-21-7	82.705	82.705	82.705
FD&C Yellow No. 6 Lake	Sunset Yellow FCF	15985:1	15790-07-5	82.706	82.706	82.706
D&C Yellow No. 7 Lake	Fluorescein	45350:1	2321-07-5	—	82.1707	82.1707
Ext. D&C Yellow No. 7 Lake	Naphthol Yellow S	10316	846-70-8	—	82.2707a	82.2707a
D&C Yellow No. 8 Lake	Uranine	45350	518-47-8	—	82.1708	82.1708
D&C Yellow No. 10 Lake	Quinoline Yellow WS	47005:1	68814-04-0	—	82.1710	82.1710

^a Based on 21 CFR 2007. Restrictions may exist limiting the use of some of these colors to specific applications (i.e., external drug use only, etc.).

Additionally, there may be quantitative limits for the use of some colors. The specific 21 CFR reference for each color should be reviewed to determine potential restriction status.

LIST OF PERMANENTLY LISTED COLOR ADDITIVES SUBJECT TO U.S. CERTIFICATION^A

Color	Common Name	Color Index Number	CAS Number	Food	21 CFR References		
					Drug	Cosmetic	Medical Devices
D&C Black No. 2	Carbon Black	77266	1333-86-4	—	—	74.2052	—
D&C Black No. 3	Bone Black	77267	8021-99-6	—	—	74.2053	—
FD&C Blue No. 1	Brilliant Blue FCF	42090	2650-18-2	74.101	74.1101	74.2101	—
FD&C Blue No. 2	Indigotine	73015	860-22-0	74.102	74.1102	—	74.3102
D&C Blue No. 4	Alphazurine FG	42090	6371-85-3	—	74.1104	74.2104	—
D&C Blue No. 6	Indigo	73000	482-89-3	—	—	—	74.3106
D&C Blue No. 9	Indanthrene Blue	69825	130-20-1	—	74.1109	—	—
D&C Brown No. 1	Resorcin Brown	20170	1320-07-6	—	—	74.2151	—
FD&C Green No. 3	Fast Green FCF	42053	2353-45-9	74.203	74.1203	74.2203	—
D&C Green No. 5	Alizarin Cyanine Green F	61570	4403-90-1	—	74.1205	74.2205	—
D&C Green No. 6	Quinizarine Green SS	61565	128-80-3	—	74.1206	74.2206	74.3206
D&C Green No. 8	Pyranine Concentrated	59040	63-58-69-6	—	74.1208	74.2208	—
Orange B	—	19235	—	74.250	—	—	—
D&C Orange No. 4	Orange II	15510	633-96-5	—	74.1254	74.2254	—
D&C Orange No. 5	Dibromofluorescein	45370:1	596-03-2	—	74.1255	74.2255	—
D&C Orange No. 10	Diiodofluorescein	45425:1	38577-97-8	—	74.1260	74.2260	—
D&C Orange No. 11	Erythrosine Yellowish Na	45425	38577-97-8	—	74.1261	74.2261	—
[Phthalocyaninato (2-)] Copper	Copper Phthalocyanine	74160	147-14-8	—	—	—	74.3045
FD&C Red No. 3	Erythrosine	45430	16423-68-0	74.303	74.1303	—	—
FD&C Red No. 4	Ponceau SX	14700	4548-53-2	—	74.1304	74.2304	—
D&C Red No. 6	Lithol Rubin B	15850	5858-81-1	—	74.1306	74.2306	—
D&C Red No. 7	Lithol Rubin B Ca	15850:1	4/9/5281	—	74.1307	74.2307	—
D&C Red No. 17	Toney Red	26100	85-86-9	—	74.1317	74.2317	74.3230
D&C Red No. 21	Tetrabromofluorescein	45380:2	15086-94-9	—	74.1321	74.2321	—
D&C Red No. 22	Eosine	45380	17372-87-1	—	74.1322	74.2322	—
D&C Red No. 27	Tetrachloro Tetrabromofluorescein	45410:1	13473-26-2	—	74.1327	74.2327	—
D&C Red No. 28	Phloxine B	45410	18472-87-2	—	74.1328	74.2328	—
D&C Red No. 30	Helindone Pink CN	73360	2379-74-0	—	74.1330	74.2330	—

(Continued)

Color	Common Name	Color Index		Food	21 CFR References		
		Number	CAS Number		Drug	Cosmetic	Medical Devices
D&C Red No. 31	Brilliant Lake Red R	15800:1	6371-76-2	—	74.1331	74.2331	—
D&C Red No. 33	Acid Fuchsin	17200	3567-66-6	—	74.1333	74.2333	—
D&C Red No. 34	Lake Bordeaux B	15880:1	6417-83-0	—	74.1334	74.2334	—
D&C Red No. 36	Flaming Red	12085	2814-77-9	—	74.1336	74.2336	—
D&C Red No. 39	Alba Red	13058	6371-55-7	—	74.1339	—	—
FD&C Red No. 40	Allura Red AC	16035	25956-17-6	74.340	74.1340	74.2340	—
FD&C Red No. 40 Lake	Allura Red AC	16035:1	68583-95-9	74.340	74.1340	74.2340	—
Citrus Red No. 2	—	12156	6358-53-8	74.302	—	—	—
D&C Violet No. 2	Alizuro Purple SS	60725	81-48-1	—	74.1602	74.2602	74.3602
Ext. D&C Violet No. 2	Alizarin Violet	60730	4430-18-6	—	—	74.2602a	—
FD&C Yellow No. 5	Tartrazine	19140	1934-21-0	74.705	74.1705	74.2705	—
FD&C Yellow No. 6	Sunset Yellow FCF	15985	2783-94-0	74.706	74.1706	74.2706	—
D&C Yellow No. 7	Fluorescein	45350:1	7/5/2321	—	74.1707	74.2707	—
Ext. D&C Yellow No. 7	Naphthol Yellow S	10316	846-70-8	—	74.1707a	74.2707a	—
D&C Yellow No. 8	Uranine	45350	518-47-8	—	74.1708	74.2708	—
D&C Yellow No. 10	Quinoline Yellow WS	47005	8004-92-0	—	74.1710	74.2710	74.3710
D&C Yellow No. 11	Quinoline Yellow SS	47000	8003-22-3	—	74.1711	74.2711	—

^a Based on 21 CFR 2007. Restrictions may exist limiting the use of some of these colors to specific applications (i.e., external drug use only, etc.).

Additionally, there may be quantitative limits for the use of some colors. The specific 21 CFR reference for each color should be reviewed to determine potential restriction status.

Another choice confronting manufacturers is whether to use an aqueous coating or an organic coating system; both have their advantages and disadvantages. While organic coatings provide greater protection against moisture uptake during the coating process (important for moisture-sensitive ingredients) and are easier to apply because of the fast evaporation of solvents, problems encountered with these coatings include environmental control of organic solvents going into the atmosphere, the need to perform solvent residue tests, and the need to have explosion-proof facilities; thus, aqueous coating systems are often preferred.

CELLULOSE BASED

Cellulose acetate phthalate (CAP)

Caution: Check with regulatory authorities about approved states of all dyes before using them.

HYDROXYPROPYL METHYLCELLULOSE (METHOCEL, HPMC) AQUEOUS COATINGS

Methocel-based coatings in an aqueous base are the most popular coating options; two methods of making solutions are possible.

If a lake is used, then alcohol is also included (see, for example, Holberry Red).

A. BRITE ROSE

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methylcellulose 2910 (15 cps)	60.00 g
2.00	2	PEG-400 (low color)	20.00 g
2.00	3	PEG-8000	20.00 g
0.25	4	FD&C Red No. 30 Lake	2.50 g
2.00	5	Titanium dioxide (special coating grade)	20.00 g
QS	6	Deionized purified water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Place 250 mL of water into a suitable container, and heat to 60°C to 70°C.
2. With gentle stirring, disperse the hydroxypropyl methylcellulose onto the hot water; when the cellulose has wetted, quickly add 250 mL of cold water.

3. Stir until the dispersion is homogeneous, although the solution of cellulose may not be complete.
4. Dissolve PEG-8000 in 50 mL of water, and then add to the preceding step.
5. Add PEG-400 to the basic solution.
6. Load a suitable-size ball jar with the FD&C Red Dye No. 30 and titanium dioxide.
7. Add sufficient water to cover the pigment and balls.
8. Mill overnight or for 12 hours.
9. Other pigment reduction methods may be used to yield a particle size not greater than 1.0 μm .
10. Add milled pigments to the base solution from the previous step, and bring the volume up with cold water.
11. Use within 7 days.

B. CHERRY RED

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methylcellulose 2910 (15 cps)	60.00 g
2.00	2	PEG-400 (low color)	20.00 g
2.00	3	PEG-8000	20.00 g
1.80	4	FD&C Red No. 3 Lake	18.00 g
0.10	5	FD&C Red No. 2 (Amaranth)	1.00 g
2.10	6	Titanium dioxide (special coating grade)	21.00 g
QS	7	Deionized purified water, USP	QS to 1 L

C. GERANIUM ROSE

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methylcellulose 2910 (15 cps)	60.00 g
2.00	2	PEG-400 (low color), NF	20.00 g
2.00	3	PEG-8000	20.00 g
0.24	4	FD&C Red No. 3 Lake	2.00 g
QS	5	Deionized purified water, USP	QS to 1 L

D. GLOSS

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
3.33	1	Hydroxypropyl methylcellulose 2910 (15 cps)	33.33 g
1.66	2	PEG-400 (low color), NF	16.66 g
QS	3	Deionized purified water, USP	QS to 1 L

E. RED

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methylcellulose 2910 (15 cps)	60.00 g
2.00	2	PEG-400 (low color), NF	20.00 g
2.00	3	PEG-8000	20.00 g
.50	4	FD&C Red No. 3 Lake	25.00 g
0.50	5	Titanium dioxide	5.00 g
QS	6	Deionized purified water, USP	QS to 1 L

F. MODERATE RED

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methylcellulose 2910 (15 cps)	60.00 g
2.00	2	PEG-400 (low color), NF	20.00 g
2.00	3	PEG-8000	20.00 g
0.50	4	FD&C Yellow No. 3 Aluminum Lake	5.00 g
2.50	5	Ponceau Red Dye 4R lake	25.00 g
1.00	6	Titanium dioxide (special coating grade), USP	10.00 g
QS	7	Deionized purified water, USP	QS to 1 L

G. CLEAR

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methylcellulose 2910 (15 cps)	60.00 g
0.10	2	Sorbic acid	1.00 g
2.00	3	Alcohol (200 proof), SD 3A	20.00 mL
2.00	4	PEG-400 (low color) ^a	20.00 g
2.00	5	PEG-8000 (optional)	20.00 g
QS	6	Deionized purified water	QS to 1 L

^a Increase amount to 6.00 if item 5 is not used.

MANUFACTURING DIRECTIONS

1. Place approximately 500 mL of water into a suitable vessel.
2. Heat water to 65°C to 70°C.
3. Add the PEG-8000 to the hot water, and dissolve (if used).

4. While maintaining gentle agitation, sprinkle the hydroxypropyl methylcellulose onto the surface of the hot water solution.
5. Position stirring head to avoid excessive entrainment of air.
6. When the cellulose has been dispersed, add the PEG-400.
7. Continue to stir until dispersion is homogeneous, although solution of cellulose may not be complete.
8. Stop stirring, and allow solution to stand until entrained air is removed.
9. Dissolve sorbic acid in alcohol, and ensure that the solution is complete.
10. When the solution from the preceding step is clear, add 250 mL of cold water, mix well, and add sorbic acid solution.
11. Mix, then bring up to volume with cold water.
12. Store coating solution in well-filled, well-sealed containers.
13. Use within 3 months.

H. GREEN

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methylcellulose 2910 (15 cps)	60.00 g
0.10	2	Sorbic acid	1.00 g
2.00 v/v	3	Alcohol (200 proof), SD 3A	20.00 mL
2.00	4	PEG-400 (low color)	20.00 g
2.00	5	PEG-8000	20.00 g
1.00	6	Titanium dioxide (coating grade)	10.00 g
0.01	7	Yellow E104 Aluminum Lake	0.10 g
0.0032	8	FD&C Blue No. 1 Lake (11%–13%)	0.032 g
QS	9	Deionized purified water	QS to 1 L

I. HOLBERRY RED

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methylcellulose 2910 (15 cps)	60.00 g
0.10	2	Sorbic acid	1.00 g
2.00 v/v	3	Alcohol (200 proof), SD 3A	20.00 mL
2.00	4	PEG-400 (low color)	20.00 g
2.00	5	PEG-8000	20.00 g
1.00	6	Titanium dioxide (coating grade)	10.00 g
1.50	7	FD&C Red No. 40 Lake (29%)	15.00 g
0.50	8	FD&C Blue No. 3 Lake	5.00 g
QS	9	Deionized purified water	QS to 1 L

J. SUN ORANGE

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
6.00	1	Hydroxypropyl methylcellulose 2910 (15 cps)	60.00 g
0.17	2	Sorbic acid, NF	1.70 g
2.00 v/v	3	Alcohol (200 proof), SD 3A	20.00 mL
2.00	4	PEG-400 (low color), NF	20.00 g
2.00	5	PEG-8000	20.00 g
2.38	6	Titanium dioxide (coating grade), USP	23.80 g
2.47	7	FD&C Yellow No. 5	24.70 g
0.16	8	FD&C Yellow No. 6	1.60 g
QS	9	Deionized purified water, USP	QS to 1 L

K. OPADRY YELLOW

Bill of Materials			
Scale (mg/ caplet)	Item	Material Name	Quantity/1000 Caplets (g)
10.00	1	Hydroxypropyl methylcellulose (hypromellose)	10.00
4.00	2	Talc (fine powder)	4.00
1.60	3	PEG-4000	1.60
1.20	4	Titanium dioxide	1.20
0.30	5	FD&C Blue No. 1 Lake	0.30
0.50	6	FD&C Blue No. 2 (dispersed)	0.50
0.75	7	Opadry-OY-S 29019 (clear)	0.75
QS	8	Purified water	225.00

MANUFACTURING DIRECTIONS

1. The formula for this coating solution is prepared to obtain a weight gain of 10 mg per caplet (around 600 mg in weight).
2. Disperse item 1 in 175 g of purified water (70°C–80°C) while stirring.
3. Hold overnight for complete dispersion.
4. Disperse items 2 and 3 in 25 g of purified water (25°C–30°C).
5. Hold overnight for complete hydration.
6. Add mixture from previous step.
7. Homogenize using a homogenizer (gap setting = 1.5 mm).
8. Homogenize items 4, 5, and 6 in 50 g of hypromellose dispersion from the previous step twice, using a homogenizer (gap setting = 1.5 mm).
9. Pass the dispersion twice through a 90 µm sieve.
10. (*Note:* This is a critical step; follow instructions closely to prevent foreign particles and spots.) Preparation of polishing solution: Disperse item 7 in 25 g of purified water with slow stirring.
11. Make a vortex by slow stirring, and add the powder in such a way as to avoid foam formation.

L. OPADRY YELLOW

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
10.00	1	Hydroxypropyl methylcellulose (hypromellose)	10.00
4.00	2	Talc (fine powder)	4.00
1.60	3	PEG-4000	1.60
1.34	4	Titanium dioxide	1.34
0.046	5	Sunset Yellow E110, FCF	0.046
1.34	6	FD&C Yellow No. 10 Lake	1.34
0.75	7	Opadry-OY-S 29019 (clear)	0.75
QS	8	Purified water	225.00

M. OPADRY RED

Bill of Materials			
Scale (mg/caplet)	Item	Material Name	Quantity/1000 Caplets (g)
10.00	1	Hydroxypropyl methylcellulose (hypromellose)	10.00
4.00	2	Talc (fine powder)	4.00
1.60	3	PEG-4000	1.60
1.34	4	Titanium dioxide	1.34
0.15	5	Iron oxide red	0.15
0.75	6	Opadry-OY-S (clear)	0.75
QS	7	Purified water	225.00

N. OPADRY GREEN

Bill of Materials			
Scale (mg/caplet)	Item	Material Name	Quantity/1000 Caplets (g)
10.00	1	Hydroxypropyl methylcellulose (hypromellose)	10.00
4.00	2	Talc (fine powder)	4.00
1.60	3	PEG-4000	1.60
2.125	4	Titanium dioxide	2.125
0.053	5	FD&C Blue No. 1 Lake	0.053
0.15	6	FD&C Yellow No. 10 Lake	0.15
0.75	7	Opadry-OY-S (clear)	0.75
QS	8	Purified water	225.00

MANUFACTURING DIRECTIONS

1. Disperse item 1 in 175 g of purified water (70°C–80°C) while stirring.
2. Keep overnight for complete dispersion.
3. Disperse items 2 and 3 in 25 g of purified water (25°C–30°C).
4. Keep overnight for complete hydration.
5. Add together, and homogenize using homogenizer (gap setting = 1.5 mm).
6. Homogenize items 4, 5, and 6 in 50 g of hypromellose dispersion twice using homogenizer (gap setting = 1.5 mm).
7. Pass the dispersion twice through a 90 µm sieve.
8. (*Note:* This is a critical step; follow instructions closely to prevent foreign particles and spots.) Disperse item 7 in 25 g of purified water while stirring slowly.
9. Make a vortex by slow stirring, and add the powder in such a way as to avoid foam formation.

10. Follow the parameters for coating in Accela Cota:

Caplet load	620 g
Pan speed	4 rpm
Drying air temperature	70°C–75°C
Exhaust temperature	50°C–55°C
Fluid pressure	15–20 psi
Valve on spray gun	One revolution open
Atomizing pressure	55 psi
Nozzle orifice	1 mm
Nozzle distance to bed	250–280 mm
Difference of air pressure	–1.0 to –1.5 cm
Spray rate	200–225 g/min
Coating time	3.0–3.5 hours

11. Stir the dispersion at slow speed (6–10 rpm) continuously.
12. Spray the polishing solution under the same conditions as previously, adjusting the spray rate to 180 g/min.
13. Check the caplet surface every 5 minutes for sticking.
14. If sticking tends to appear, stop the coating immediately.
15. When the spraying is over, roll the tablets in a pan for 10 minutes with cold air blowing onto the caplets.
16. Unload the film-coated caplets into stainless steel containers lined with polyethylene bags.
17. Appearance is a light green, film-coated caplet that is smooth, with no sticking or chipping on the caplet surface.
18. Weight gain per caplet is NLT 10 mg/tablet.

O. WHITE COATING

Bill of Materials			
Scale (mg/tablet)	Item	Material Name	Quantity/1000 Tablets (g)
22.75	1	Hypromellose	22.75
4.54	2	Polyethylene glycol	4.54
12.50	3	Talc (fine powder)	12.50
10.00	4	Titanium dioxide	10.00
1.30	5	FD&C Yellow No. 10 Lake	1.30
—	6	Purified water	~24.00
—	7	Ethanol (95%)	~21.00

HYDROXYPROPYL METHYLCELLULOSE OPAQUE ORGANIC COATING**A. BRITE GREEN**

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L (g)
1.00	1	Titanium dioxide	10.00
50.00 v/v	2	Alcohol (200 proof), SD 3A	~397.00
1.69	3	PEG-400 (low color), NF	16.90
0.02	4	FD&C Yellow No. 5	0.20
0.0068	5	FD&C Blue No. 1	0.068
4.00	6	Hydroxypropyl methylcellulose 2910 (15 cps)	40.00
QS	7	Methylene chloride	~625.00

MANUFACTURING DIRECTIONS

1. Charge titanium dioxide and QS with alcohol into a Ball mill.
2. Mill the material for 16 hours.
3. Place 465 mL alcohol into a suitable mixing tank.
4. Start agitation.
5. Slowly add PEG-400 to mixing tank.
6. Mix for 5 minutes.
7. Add FD&C Yellow to the mixing tank with continued agitation.
8. Rinse bottle with alcohol tapped from mixing tank.
9. Return rinse to mixing tank.
10. Add FD&C Blue to the mixing tank, and rinse.
11. Mix for 2 hours.
12. Tap approximately 10 mL of solution from mixing tank after 0.5, 1, and 1.5 hours of mixing.
13. Put solution back into mixing tank. (*Note:* Tapping solution ensures that dye is not tapped into lower valve and/or pipeline.) Rinse the Ball mill with two rinses of 11.6 mL alcohol.
14. Reseal the Ball mill, and allow it to run for 2 to 5 minutes between rinses.
15. Empty content of the Ball mill and rinses into mixing tank.
16. Slowly sprinkle hydroxypropyl methylcellulose into mixing tank with constant agitation.
17. Agitate for an additional 15 minutes. (*Note:* Prevent the development of lumps by slowly sprinkling hydroxypropyl methylcellulose into the alcohol.) After mixing for 10 minutes, tap approximately 10 mL from the mixing tank, and put back into tank to recirculate.

18. Add sufficient methylene chloride (~474 mL) to bring up to volume.
19. Continue agitation for 2 hours.
20. After 0.5, 1, and 1.5 hours, tap approximately 10 mL of solution from mixing tank, and put back into mixing tank to recirculate.
21. (*Note:* No residue should be present in the solution when tapped at 1.5 hours; if some is present, then continue agitation, and tap every 15 minutes until no residue is observed.) (*Caution:* Avoid contact with methylene chloride and vapors; they may have toxic effects when swallowed or inhaled.) (*Note:* Nitrogen pressure may be used to assist bottle filling.) Strain mixing tank contents through two-ply cheesecloth, or similar, into suitable approved containers (one-half the total number of bottles). (*Note:* Lumps may obstruct spray nozzle.)

B. RED MAHOGANY

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L (g)
0.40	1	Titanium dioxide	4.00
45.00 v/v	2	Alcohol (200 proof), SD 3A	~375.30
0.40	3	Vanillin (crystals)	4.00
1.00	4	Propylene glycol	10.00
1.50	5	FD&C Red No. 40 Lake (29%)	15.00
1.00	6	Brown lake blend	10.00
4.00	7	Hydroxypropyl methylcellulose 2910 (15 cps)	40.00
QS	8	Methylene chloride	~530.40

C. SUN ORANGE

Bill of Materials			
Scale (%)	Item	Material Name	Quantity/L (g)
3.00 (w/v)	1	Titanium dioxide	30.00
50.00 (v/v)	2	Alcohol (200 proof), SD 3A	~397.00
2.11 (w/v)	3	Propylene glycol	21.10
3.11 (w/v)	4	FD&C Yellow No. 5	31.10
0.20 (w/v)	5	FD&C Yellow No. 6	2.00
4.00 (w/v)	6	Hydroxypropyl methylcellulose 2910 (15 cps)	40.00
QS	7	Methylene chloride	~625.00

D. DARK RED

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L (g)
1.00	1	Titanium dioxide	10.00
20.00 v/v	2	Alcohol (200 proof), SD 3A	~200.00 mL
2.00	3	PEG-400 (low color)	20.00
0.02	4	Ponceau 4R dye (red)	20.00
0.0068	5	FD&C Blue No. 1	0.068
2.95	6	Hydroxypropyl methylcellulose 2910 (15 cps)	29.50
QS	7	Methylene chloride	QS to 1 L

E. DEEP YELLOW

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
2.00	1	Titanium dioxide	20.00 g
50.00	2	Alcohol (200 proof), SD 3A	~397.00 g
2.00	3	PEG-400 (low color)	20.00 g
2.00	4	FD&C Yellow No. 5 Lake	20.00 g
2.95	5	Hydroxypropyl methylcellulose 2910 (15 cps)	29.50 g
QS	6	Methylene chloride	QS to 1 L

F. PALE YELLOW

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
1.50	1	Titanium dioxide	15.00 g
50.00	2	Alcohol (200 proof), SD 3A	~397.00 g
2.00	3	PEG-400 (low color), NF	20.00 g
0.50	4	FD&C Yellow No. 10 Aluminum Lake (14–17%)	5.00 g
2.95	5	Hydroxypropyl methylcellulose 2910 (15 cps)	29.50 g
QS	6	Methylene chloride	QS to 1 L

G. SCARLET RED

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
2.00	1	Titanium dioxide	20.00 g
20.00	2	Alcohol (200 proof), SD 3A	~200.00 g
2.00	3	PEG-400 (low color), NF	20.00 g
2.00	4	FD&C Yellow No. 7 Lake	20.00 g
1.00	5	FD&C Yellow No. 5 Lake	10.00 g
2.95	6	Hydroxypropyl methylcellulose 2910 (15 cps)	29.50 g
QS	7	Methylene chloride	QS to 1 L

HYDROXYPROPYL METHYLCELLULOSE/ HYDROXYPROPYL CELLULOSE (KLUCEL®) COATING

A. WHITE

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
2.00	1	Titanium dioxide	20.00 g
0.50	2	Hydroxypropyl cellulose, NC	5.00 g
45.00	3	Alcohol (200 proof), SD 3A	~450.00 g
2.00	4	Propylene glycol	20.00 g
4.50	5	Hydroxypropyl methylcellulose 2910 (15 cps)	45.00 g
QS	6	Methylene chloride	QS to 1 L

MANUFACTURING DIRECTIONS

1. Place titanium dioxide and sufficient methylene chloride into suitable sized ball jars to cover the balls.
2. Mill for not less than 16 hours.

3. While mixing alcohol, add and disperse hydroxypropyl methylcellulose, hydroxypropyl cellulose, and propylene glycol, followed by 250 mL of methylene chloride.
4. Continue mixing until the dissolution is complete.
5. While mixing the solution from the second step, empty into it the contents of the ball jar, rinse the balls and jar with methylene chloride, add the rinsings to the batch, and mix.
6. Bring the batch up to volume with methylene chloride, and mix well until homogeneous.
7. Strain the batch through muslin into suitable, approved bottles.
8. Seal and store.

HYDROXYPROPYL METHYLCELLULOSE/ ETHYLCELLULOSE COATING

A. REDDISH ORANGE OPAQUE

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
1.16	1	Titanium dioxide	11.60 g
45.00	2	Alcohol (dehydrated; 200 proof)	~450.00 g
0.20	3	Vanillin (crystals), NF	2.00 g
0.50	4	Albumen powder (white hen egg)	5.00 g
2.00	3	PEG-400 (low color), NF	20.00 g
1.30	4	FD&C Red No. 3	13.00 g
0.05	5	FD&C Red No. 2 (Amaranth), USP	0.50 g
0.20	6	FD&C Yellow No. 6	2.00 g
2.95	5	Hydroxypropyl methylcellulose 2910, USP (15 cps)	29.50 g
QS	6	Methylene chloride	QS to 1 L

MANUFACTURING DIRECTIONS

1. Load vanillin, albumen, titanium dioxide, FD&C Red No. 3, FD&C Red No. 2, and FD&C Yellow No. 6 into a suitable-size ball jar.
2. Add sufficient methylene chloride to cover the pigments and balls.
3. Mill for 24 hours.
4. Measure 400 mL of alcohol into a suitable stainless steel container.
5. Sprinkle the hydroxypropyl methylcellulose/ethylcellulose onto the surface of the alcohol while stirring vigorously.
6. When the hydroxypropyl methylcellulose/ethylcellulose has been wetted, quickly add 300 mL methylene chloride while stirring vigorously.

7. Add the PEG-400 to the solution, and rinse the container with the remaining alcohol; add the rinsings to the bulk.
8. Empty the contents of the ball jar from the first step into the coating solution from the previous step while stirring vigorously.
9. Rinse the ball jar with methylene chloride; add the rinsings to the bulk.
10. Bring up to volume with methylene chloride.

B. SUBCOATING SOLUTION

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
45.00	1	Alcohol (190 proof), USP	450.00 mL
0.50	2	Hydroxypropyl cellulose, NF	5.00 g
4.50	3	Hydroxypropyl methylcellulose 2910, USP (15 cps)	45.00 g
QS	4	Methylene chloride	QS to 1 L

HYDROXY METHYLCELLULOSE/HYDROXY ETHYL-CELLULOSE COATING

A. BLUE

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
1.00	1	Hydroxy methylcellulose	10.00 g
1.00	2	Hydroxy ethylcellulose (15 cps)	10.00 g
0.312	3	Titanium dioxide	3.12 g
1.00	4	FD&C Blue No. 1 Lake (12%)	10.00 g
0.375	5	Castor oil (odorless)	3.75 g
0.375	6	Sorbitan monooleate	3.75 g
50.00	7	Alcohol (200 proof), SD 3A	500.00 mL
QS	8	Methylene chloride	QS to 1 L

MANUFACTURING DIRECTIONS

1. Premix hydroxy methylcellulose and hydroxy ethylcellulose, and add to 440 mL alcohol with rapid agitation.
2. Mix for not less than 1 hour.
3. Place FD&C Blue and titanium dioxide into a ball mill.
4. Cover the balls and materials with 60 mL of alcohol, and mill for 16 hours.
5. Add contents to mixing tank, and add the castor oil and sorbitan monooleate.

6. Rinse the ball mill with methylene chloride, and add the rinsings to the mixing tank.
7. Bring up to a volume of 1 L with methylene chloride, and mix for at least 1 hour.

B. CLEAR (50:50)

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
1.00	1	Hydroxy methylcellulose	10.00 g
1.00	2	Hydroxy ethylcellulose, USP (15 cps)	10.00 g
0.375	3	Castor oil (odorless)	3.75 g
50.00	4	Alcohol (200 proof), SD 3A	500.00 mL
QS	5	Methylene chloride	QS to 1 L

HYDROXY METHYLCELLULOSE/HYDROXY ETHYLCELLULOSE COATING

A. CLEAR

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
1.00	1	Hydroxy methylcellulose	10.00 g
1.00	2	Hydroxy ethylcellulose, USP (15 cps)	10.00 g
0.375	3	Castor oil (odorless), USP	3.75 mL
50.00	4	Alcohol (200 proof), SD 3A	500.00 mL
QS	5	Methylene chloride	QS to 1 L

MANUFACTURING DIRECTIONS

1. Place alcohol into mixing tank.
2. Turn on mixer to mixing speed; maintain mixing speed throughout preparation of coating solution.
3. Add hydroxy methylcellulose and hydroxy ethylcellulose into the mixing tank.
4. Let mix for 1 hour.
5. Add methylene chloride (~500 mL) to bring the final volume up to 1 L.
6. Mix for 1 hour.
7. Solution need not be agitated at all times.
8. Keep tank tightly closed at all times.
9. Rubber stoppers on bottles must be protected from methylene chloride with a polyethylene layer.

POLYVINYLPIRROLIDONE (PVP) COATINGS

A. SUBCOATING

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
20.00	1	Povidone USP K-29–32 ^a	200.00 g
80.00	2	Alcohol (200 proof), SD 3A	800 mL

^a May be substituted with Kollidon® VA 64 (polyvinylpyrrolidone/vinylacetate copolymer; 10%), and item 2 can be replaced with isopropyl alcohol.

MANUFACTURING DIRECTIONS

1. Spray the solution onto the warm tablet cores (30°C–40°C) for a few minutes before continuing with the main aqueous coating procedure.
2. An amount of 0.4 mg/cm² tablet surface is sufficient for good subcoating protection.
3. No plasticizer is needed in this formulation due to the plasticity of Kollidon® VA 64.

B. KOLLIDON® VA 64 (POLYVINYLPIRROLIDONE/ VINYLACETATE COPOLYMER, BASF)

Bill of Materials			
Scale (% w/w)	Item	Material Name	Quantity/kg
5.00	1	Kollidon® VA 64	50.00 g
4.00	2	Lutrol E 6000	40.00 g
0.50	3	Glycerin, USP	5.00 g
1.50	4	Iron oxide or lake	15.00 g
3.00	5	Titanium dioxide	30.00 g
5.00	6	Talc	50.00 g
QS	7	Purified water	QS to 1 L

MANUFACTURING DIRECTIONS

1. Pass the suspension through a disk mill prior to use, and spray under the following conditions.

SUGAR-COATING PAN

Spray gun	Walther WAXV with 1 mm nozzle
Spraying time	3 seconds
Pause	0.5 seconds
Dry air	6 seconds
Pause	3 seconds

ACCELA COTA (CONTINUOUS SPRAYING)

Spray gun	Walther WAXV with 0.8 mm nozzle
Temperature at inlet	45°C
Temperature at outlet	38°C
Spraying pressure	2 bar
Spraying time	~50 minutes

If the film is too sticky, a certain part of the Kollidon® should be substituted by HPMC or sucrose.

KOLLIDON® VA 64 AND POLYVINYL ALCOHOL

Bill of Materials			
Scale (% w/w)	Item	Material Name	Quantity/kg
5.0	1	Kollidon® VA 64	50.00 g
4.00	2	Lutrol E 6000	40.00 g
6.00	3	Polyvinyl alcohol	60.00 g
68.00	4	Purified water	680.00 g
0.50	5	Glycerin, USP	5.00 g
1.50	6	Iron oxide or lake	15.00 g
3.00	7	Titanium dioxide	30.00 g
5.00	8	Talc	50.00 g
QS	9	Purified water	168.00 g

MANUFACTURING DIRECTIONS

1. Dissolve items 1 to 3 in item 4, add polyvinyl alcohol, and stir for 45 minutes, avoiding the formation of too many air bubbles.
2. Suspend the pigments and talc in 168 mL of water, and pass this mixture through a colloid mill.
3. To obtain the final coating suspension, mix this solution with the first solution.

4. Suggested conditions for coating using Accela Cota are as follows.

Tablet core loading	5.0 kg
Amount of coating suspension	1.26 kg
Inlet air temperature	59°C
Outlet air temperature	46°C
Nozzle	1.0 mm
Rotation speed of the pan	15 rpm
Spraying pressure	2.0 bar
Spraying rate	15 g/min
Spraying time (continuously)	83 minutes
Final drying	5 minutes
Quantity of film former applied	~3 mg/cm ²

A. KOLLIDON® 30 AND SHELLAC

Bill of Materials			
Scale (% w/w)	Item	Material Name	Quantity/kg (g)
2.00	1	Kollidon® 25 or 30	20.00
17.70	2	Shellac	177.00
18.50	3	Titanium dioxide	185.00
6.50	4	Talc	65.00
1.50	5	Cetyl alcohol	15.00
3.00	6	Sorbitan trioleate	30.00
5.00	7	Color lake	50.00
QS	8	Isopropanol or alcohol	458.00

MANUFACTURING DIRECTIONS

1. Dissolve shellac and sorbitan trioleate in the warm solvent and then Kollidon® and cetyl alcohol.
2. Add titanium dioxide, talc, and lake, and then mix in the colloid mill.
3. Application of the coating suspension: About 50 g of suspension is applied to 1 kg of tablet cores in a conventional coating pan or in an Accela Cota pan (1–2 mg film formers/cm²).

B. KOLLIDON® VA 64 AND HYDROXYPROPYL METHYLCELLULOSE

Bill of Materials			
Scale (% w/w)	Item	Material Name	Quantity/kg
4.00	1	Kollidon® VA 64	53.00 g
1.00	2	Lutrol E 6000	12.00 g
6.00	3	Hydroxypropyl methylcellulose	79.00 g
1.50	4	Iron oxide or lake	18.00 g
3.00	5	Titanium dioxide	37.00 g
4.00	6	Talc	40.00 g
QS	7	Purified water	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Dissolve Lutrol and Kollidon® in a portion of the water, add hydroxypropyl methylcellulose, and stir for 45 minutes, avoiding the formation of too many air bubbles.
2. Suspend the pigments and talc in a portion of the water, and pass this mixture through a colloid mill.
3. Mix the two portions.
4. Conditions for coating using Accela Cota are as follows.

Tablet core loading	5.0 kg
Core size	9 mm biconvex
Amount of coating suspension applied	1.2 kg
Inlet air temperature	60°C
Outlet air temperature	40°C
Nozzle	1.0 mm
Rotation speed of the pan	12 rpm
Spraying pressure	2.0 bar
Spraying rate	50 g/min
Spraying time (continuously)	34 minutes
Final drying	2 minutes
Drying after spraying	5 minutes at 60°C
Quantity of film-former applied	3.14 mg/cm ²

C. POVIDONE, ETHYLCELLULOSE, AND TALC

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
7.50	1	Povidone (PVP K-29-32), USP	75.00 g
4.25	2	Ethylcellulose, NF	42.50 g
0.50	3	PEG-400, NF	5.00 g
5.00	4	Talc	50.00 g
45.00	5	Alcohol (200 proof), SD 3A	450.00 mL
QS	6	Methylene chloride, NF	QS to 1 L

MANUFACTURING DIRECTIONS

1. Dissolve Povidone in alcohol and then add PEG-400.
2. Add ethylcellulose to this solution.
3. Mix until evenly dispersed; then, bring up to volume with methylene chloride with constant stirring.
4. Add talc to this solution, and stir to ensure distribution.
5. Solution should be freshly prepared and used within 10 days of manufacture.
6. Thoroughly disperse talc before use.
7. If batch is more than 200 L, do not add talc.
8. If coating solution is manufactured without talc, then solution should be used within 4 weeks.

CELLULOSE ACETATE PHTHALATE AND CARBOWAX COATINGS**A. BRITE GREEN**

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/L
6.00	1	Cellulose acetate phthalate (carbowax)	60.00 g
1.86	2	Propylene glycol	18.65 g
0.66	3	Sorbitan monooleate (Span 80)	6.00 g
0.12	4	Castor oil (odorless)	1.25 g
0.85	5	FD&C Blue Dye No.1	0.85 g
3.11	6	FD&C Yellow Dye No. 5 lake	31.10 g
5.33	7	Titanium dioxide	53.30 g
21.58	8	Methylene chloride	215.00 g
QS	9	Acetone	QS to 1 L

MANUFACTURING DIRECTIONS

1. Place methylene chloride in a suitably sized mixing tank.
2. While stirring, add propylene glycol, Span 80, and castor oil.

3. To this mixture add cellulose acetate phthalate, and allow to soak overnight.
4. Load dyes and titanium dioxide into a suitable ball jar.
5. Add sufficient acetone to cover the raw materials and balls.
6. Ball mill overnight.
7. Melt carbowax with a portion of the acetone using gentle heat.
8. Add the melted carbowax to the mixture from the second step.
9. Empty contents of ball jar mill to this mixture.
10. Rinse the ball jar with acetone, and add rinsings.
11. Add acetone to volume, and mix well.
12. If necessary, strain solution through gauge before storage or use.

B. CHERRY RED

In the preceding formulation, use FD&C Red Dye No.3 (6.800 g), FD&C Red Dye No. 2 (Amaranth, USP; 1.00 g), and FD&C Yellow Dye (5.40 g).

C. CLEAR

Delete dyes.

D. ORANGE

Use FD&C Yellow Dye No. 6 (4.00 g) and FD&C Yellow Dye No. 5 (12.00 g).

SUGAR COATINGS**A. BASIC**

Bill of Materials			
Scale (% w/w)	Item	Material Name	Quantity/kg
4.00	1	Kollidon® VA 64	40.00 g
16.00	2	Sucrose	160.00 g
2.40	3	Titanium dioxide	24.00 g
1.20	4	Color lake	12.00 g
3.20	5	Lutrol E 4000	32.00 g
4.00	6	Talc	40.00 g
QS	7	Purified water	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Dissolve sucrose, Kollidon®, and Lutrol in the water, and suspend the other components.
2. Pass through a colloid mill.

3. Use the following conditions for use in Accela Cota.

Tablet core loading	5.00 kg
Amount of coating suspension	1.20 kg
Inlet air temperature	45°C
Outlet air temperature	35°C
Nozzle	0.80 mm
Rotation speed of the pan	15 rpm
Spraying pressure	2.0 bar
Spraying time (continuously)	50 minutes
Quantity of film former applied	4.00 mg/cm ²

B. AUTOMATIC

Bill of Materials

Scale (% w/w)	Item	Material Name	Quantity, g/kg
4.00	1	Kollidon® 30	40.00
38.00	2	Sucrose	380.00
4.50	3	Titanium dioxide	45.00
QS	4	Color lake	QS
4.50	5	Calcium carbonate	45.00
14.50	6	Talc	145.00
QS	7	Purified water	QS to 1 kg

MANUFACTURING DIRECTIONS

1. Dissolve sucrose in hot water; then, mix with glycerol.
2. Dissolve Kollidon®, and suspend the other components.
3. Coating procedure: Coat 4 kg of tablet cores with a weight of 420 mg each by spraying with 2.5 kg of the suspension in a conventional coating pan under the following conditions:

Spray phase	5 seconds
Interval	10 minutes
Drying phase (warm air)	10 minutes
Total coating time	16 hours

C. MANUAL, WHITE

Bill of Materials

Scale (% w/w)	Item	Material Name	Quantity/kg (g)
0.33	1	Kollidon® 30	3.36
0.29	2	Carmellose sodium	2.92
0.21	3	Aerosil® 200	2.14
QS	4	Color lake (white)	QS
1.62	5	Talc	16.20
0.10	6	Polysorbate or Cremophor RH40	1.00
1.40	7	Titanium dioxide	14.00
62.70	8	Sucrose	627.00
33.40	9	Purified water	334.00

MANUFACTURING DIRECTIONS

1. Dissolve Kollidon®, polysorbate or Cremophor, and sucrose in water, and suspend the other components in this solution.
2. Mix in a colloid mill.
3. Start with formulation without the color, and then apply the color coat.
4. The polishing can be done by means of a solution of beeswax or PEG-6000.

ENTERIC COATINGS

A. KOLLIcoat® AND KOLLIDON® ENTERIC FILM COATING

Bill of Materials

Scale (% w/w)	Item	Material Name	Quantity/kg
0.50	1	Titanium dioxide	5.00 g
2.00	2	Talc	20.00 g
0.50	3	Iron oxide	5.00 g
0.50	4	Kollidon® 25 or Kollidon® 30	5.00 g
50.00	5	Kollicoat® MAE 30 DP (methacrylic acid/ethyl acrylate copolymer, 1:1)	500.00 g
1.50	6	Triethyl citrate	15.00 g
QS	7	Purified water	QS to 1 kg

MANUFACTURING DIRECTIONS/CONDITIONS

Tablet core loading	5 kg
Core size	9 mm biconvex
Quantity of suspension applied	1890 g
Quantity of solids/cm ²	9 mg
Quantity of film-forming agent/cm ²	6 mg
Speed of the coating pan	12 rpm
Spray nozzle	0.8 mm
Spraying pressure	2.0 bar
Type of spraying	Continuous
Inlet air temperature	50°C
Outlet air temperature	~30°C
Spraying time	~60 minutes
Spraying rate	~30 g/min

EUDRAGIT® ENTERIC AQUEOUS

A. BRICK RED

Bill of Materials			
Scale (% w/w)	Item	Material Name	Quantity/kg (g)
46.667	1	Distilled purified water	466.667
1.519	2	Talc (powder)	15.198
0.798	3	Titanium dioxide (special coating grade)	7.983
1.55	4	Iron oxide, red	15.50
0.426	5	Polysorbate 80	4.262
0.015	6	Dimethyl polysiloxane emulsion (30%)	0.155
47.60	7	Eudragit®; use Eudragit® L 30D-55	476.00
1.426	8	Triethyl citrate (Eudraflex®)	14.259

MANUFACTURING DIRECTIONS

1. Weigh the quantity of water needed.
2. Put approximately 21.5% of the total quantity of water in a suitable mixing container.
3. Add talc powder, and stir vigorously until well suspended (approximately 20 minutes).
4. Add the following to this suspension, and mix thoroughly: titanium dioxide, iron oxide, Tween 80, and dimethyl polysiloxane emulsion (30%).

5. (*Note:* The pigments may require homogenizing with colloid, corundum disc mill, or ball mill.) Put the Eudragit® in a suitable mixing vessel, and add the following with continuous mixing: homogenized pigment mixture, Eudraflex® (i.e., triethyl citrate), and remaining quantity of water. *Note:* When PEG-8000 is used as a plasticizer, it should be incorporated as a 10% aqueous solution.

B. YELLOW

Bill of Materials			
Scale (% w/w)	Item	Material Name	Quantity/kg (g)
46.66	1	Distilled purified water	466.66
1.25	2	Talc (powder)	12.57
0.77	3	Titanium dioxide (special coating grade)	7.79
1.83	4	FD&C Yellow No. 10 Aluminum Lake (14% to 17%)	18.36
0.42	5	Polysorbate 80	4.27
0.01	6	Dimethyl polysiloxane emulsion (30%)	0.12
47.6	7	Eudragit®; use methacrylic acid copolymer, NF (Eudragit® L 30D-55)	476.00
1.42	8	Triethyl citrate (Eudraflex®)	14.21

C. BROWN

Bill of Materials			
Scale (% w/w)	Item	Material Name	Quantity/kg (g)
46.66	1	Distilled purified water	466.66
0.47	2	Titanium dioxide (special grade coating), USP	4.76
0.85	3	Iron oxide, black	8.53
2.26	4	Iron oxide, red	22.61
0.25	5	Iron oxide, yellow	2.57
0.42	6	Polysorbate 80	4.26
0.01	7	Dimethyl polysiloxane emulsion	0.09
47.63	8	Eudragit®; use Eudragit® L 30D-55	476.33
1.42	9	Triethyl citrate (Eudraflex®)	14.28

D. DARK ORANGE

Bill of Materials			
Scale (% w/w)	Item	Material Name	Quantity/kg (g)
46.66	1	Distilled purified water	466.66
2.51	2	Talc (powder)	25.18
0.39	3	Titanium dioxide (special coating grade)	3.92
0.93	4	FD&C Yellow No. 6 Aluminum Lake	9.32
0.42	5	Polysorbate 80	4.29
0.01	6	Dimethyl polysiloxane emulsion (30%)	0.13
47.63	7	Eudragit®; use Eudragit® L 30D-55	476.33
1.42	8	Triethyl citrate (Eudraflex®)	14.28

E. ORANGE

Bill of Materials			
Scale (% w/w)	Item	Material Name	Quantity/kg (g)
46.66	1	Distilled purified water	466.66
2.60	2	Talc (powder)	26.00
0.78	3	Titanium dioxide (special coating grade)	7.84
0.46	4	FD&C Yellow No. 6 Aluminum Lake	4.66
0.42	5	Polysorbate 80	4.27
0.01	6	Dimethyl polysiloxane emulsion (30%)	0.11
47.61	7	Eudragit®; use Eudragit® L 30D-55	476.16
1.42	8	Triethyl citrate (Eudraflex®)	14.29

F. DISPERSED ORANGE

Bill of Materials			
Scale (mg/ tablet)	Item	Material Name	Quantity/1000 Tablets (g)
0.92	1	Opagloss NA 7150	0.92
7.07	2	Methacrylic acid copolymer (Eudragit® L 100–55)	7.07
0.09	3	Sodium hydroxide pellets (caustic soda)	0.09
0.73	4	PEG-6000	0.73
2.50	5	Talc (fine powder)	2.50
0.10	6	Simethicone emulsion 30% (simethicone antifoam M30)	0.10
0.27	7	Povidone (PVP K-25)	0.27
50.00	8	Sucrose	50.00
0.54	9	Povidone (PVP K-25)	0.54
0.36	10	Titanium dioxide	0.36
0.36	11	FD&C Yellow No. 10 Lake	0.36
0.04	12	Dispersed orange ^a	0.04
1.07	13	Sucrose	1.07
0.38	14	Polishing emulsion	0.38
—	15	Purified water	65.41

^a Dispersed orange: This material is the aluminum lake of Sunset Yellow FCF (E110).

HYDROXYPROPYL METHYLCELLULOSE PHTHALATE ENTERIC COATING**A. CLEAR ENTERIC**

Bill of Materials			
Scale (%)	Item	Material Name	Quantity/kg
20.00 (v/v)	1	Acetone	200.00 mL
10.00 (v/v)	2	Purified water	100.00 mL
4.00 (w/v)	3	Hydroxypropyl methylcellulose	40.00 g
0.30 (w/v)	4	Vanillin (crystals)	3.00 g
0.40 (w/v)	5	Acetylated monoglycerides	4.00 g
QS	6	Alcohol (200 proof), SD 3A	QS to 1 L

MANUFACTURING DIRECTIONS

1. Charge acetone, purified water, and 470 mL of alcohol into a suitable mixing tank.
2. Add hydroxypropyl methylcellulose phthalate, vanillin crystals (if used), and the distilled acetylated monoglycerides.
3. Mix until a clear solution is obtained.
4. Bring up to 1 L with alcohol, and record volume used.
5. Mix for 1 hour.

B. ORCHID PINK OPAQUE

Bill of Materials			
Scale (%)	Item	Material Name	Quantity/kg
20.00 (v/v)	1	Acetone	200.00 mL
10.00 (v/v)	2	Purified water	100.00 mL
8.00 (w/v)	3	Hydroxypropyl methylcellulose phthalate	80.00 g
0.80 (w/v)	4	Diacetylated monoglycerides	8.00 g
0.06 (w/v)	5	Red D&C No. 30 Lake	0.60 g
0.006 (w/v)	6	FD&C Blue No. 2 Aluminum Lake (14%)	0.06 g
0.70 (w/v)	7	Titanium dioxide	7.00 g
QS	8	Alcohol (200 proof), SD 3A	1

C. LIGHT APRICOT ORANGE

Bill of Materials			
Scale (% w/v)	Item	Material Name	Quantity/kg
20.00 (v/v)	1	Acetone	200.00 mL
10.00 (v/v)	2	Purified water	100.00 mL
8.00 (w/v)	3	Hydroxypropyl methylcellulose phthalate	80.00 g
0.80 (w/v)	4	Diacetylated monoglycerides	8.00 g
0.10 (w/v)	5	FD&C Yellow No. 10 Aluminum Lake (14%–17%)	1.00 g
0.06 (w/v)	6	FD&C Red No. 3 Aluminum Lake (14%)	0.60 g
0.70 (w/v)	7	Titanium dioxide	7.00 g
QS	8	Alcohol (200 proof), SD 3A	To 1 kg

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