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January 17, 2003

Dockets Management Branch
Food & Drug Administration
Department of Health & Human Services
Room 1-23
12420 Parklawn Drive
Rockville, Maryland 20857

CITIZEN PETITION: DOCKET 75N-183H

The undersigned submit this petition under 21 CFR § 10.30 of the Federal Food, Drug & Cosmetic Act to request the Commissioner of Food & Drugs to take the following action on proposed 21 CFR Part 333, Topical Antimicrobial Drug Products for Over-the-Counter Human Use; Tentative Final Monograph for Health-Care Antiseptic Drug Products, 59 Fed. Reg. 31401 (June 17, 1994) ("Monograph"):

- Include indications for additional organisms, specifically viruses on the hands, in the Monograph.

The Soap and Detergent Association (SDA) and The Cosmetic, Toiletry, and Fragrance Association (CTFA) Industry Coalition ("Petitioner") requests that additional flexibility be incorporated in the Monograph by allowing topical antibacterial products (health-care personnel hand products, food handler products, and consumer hand products) which meet the performance criteria and labeling for antibacterial products in the Monograph to optionally make anti-viral indications, provided that such products meet test requirements and performance criteria that are indicative of anti-viral efficacy.

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ACTION REQUESTED

Petitioner requests that the Commissioner consider this petition to amend proposed 21 CFR 333, the June 17, 1994 Tentative Final Monograph for Health-Care Antiseptic Drug Products Proposed Rule [59 FR 31401] as follows:

- amend relevant sections of 21 CFR 333 including, § 333.450, § 333.455 and § 333.470 to include additional organisms, specifically viruses, and appropriate test methods, performance criteria and anti-viral labeling for health-care personnel hand products, food handler products, and consumer hand products in the Monograph; and

- amend § 333.470 to establish and maintain efficacy methods indicative of anti-viral activity in the Monograph by incorporating the most current voluntary consensus standards set by the American Society for Testing and Materials (ASTM), specifically the finger pad method (ASTM E 1838) and the hand method (ASTM E 2011).

STATEMENT OF GROUNDS

Consideration of this petition

In 1972 the Food and Drug Administration (FDA) began a comprehensive review of over-the-counter ("OTC") drug products sold in the United States. As part of the review process, FDA divided OTC drugs into categories. An advisory review panel comprised of non-government scientific experts, as well as industry and consumer representatives, evaluated and recommended for each category the conditions under which active ingredients were considered safe and effective for their intended use. Subsequently, FDA used these recommendations to promulgate proposed rules that would be finalized as final OTC monographs to regulate active ingredients used in products for self-care.

FDA's intent was to establish a flexible, adaptable process that would allow the sale of OTC products without requiring a new drug application for each condition; it was not the Agency's intent to limit OTC monograph conditions to those that existed in the 1970s when the FDA expert panels started their deliberations. The proposal to establish a monograph for reducing levels of bacteria on the skin was first made in the advanced notice of proposed rulemaking in 1974[(1)], with subsequent rulemakings in the tentative final monograph in 1978[(2)], tentative final monograph in 1991[(3)], and the tentative final monograph in 1994[(4)].

On August 25, 2000 Petitioner filed comments in response to the April 27, 2000 Federal Register notice [65 Fed. Reg. 24704] which requested comment on the development

and regulation of OTC drugs. In its response Petitioner advocated a transparent, collaborative and flexible approach for the OTC monograph process. This petition addresses a specific issue of monograph flexibility, namely that topical antimicrobial products should be allowed to make anti-viral indications as well, provided they meet the monograph test methods and performance criteria that are indicative of both antimicrobial and anti-viral efficacy.

FDA may evaluate the information submitted in this petition as part of its deliberations on the Final Monograph for Health-Care Antiseptic Drug Products. In fact, the Division of Antiviral Drug Products, Office of Drug Evaluation II and The Staff College of the Center for Drug Evaluation and Research at FDA evaluated anti-viral claims for topical antiseptics at a public workshop on May 31-June 1, 1994.

Petitioner's request that the Agency include viruses in the Health-Care Antiseptic Monograph is not subject to the requirements of a time and extent application (TEA) under 21 CFR 330.14. Credible published scientific directories referenced the use of these ingredients for anti-viral as well as antimicrobial conditions in the United States before the OTC drug review began in 1972[(5)].

Inclusion of viruses in the Monograph

From a public health perspective, it is important that FDA recognize that each monograph has the potential to provide consumers with the broadest possible health benefits from that category of product without the necessity of medical intervention. This opportunity is particularly important for a category that helps to prevent the spread of infection.

Viral diseases are widespread in the United States (see Appendix A and Appendix B). Because several active ingredients in antimicrobial products have also demonstrated anti-viral properties, FDA should use this opportunity to allow consumers to understand and evaluate the additional anti-viral benefits of these products in appropriate circumstances as part of this rulemaking. The Tentative Final Monograph for Health-Care Antiseptic Drug Products recognizes broad-spectrum antimicrobial activity as a desirable attribute for antimicrobial handwash products and, in § 333.470, lists test microorganisms for establishing broad-spectrum activity. The majority of the test organisms are bacteria, consistent with the current emphasis on bacteria in the Monograph. Petitioner agrees with the Agency's recognition that broad-spectrum antibacterial activity is a desirable attribute for topical antimicrobial products.

Hand transmission of viruses is recognized as an important factor in the occurrence of respiratory and enteric diseases, yet no viruses are listed in § 333.470. Exclusion of viruses from the Tentative Final Monograph is inconsistent with the precepts of both good hygiene and good health care. Consumers do not necessarily distinguish between bacteria and viruses when selecting a product that will prevent the spread of

infection. Because topical antimicrobial products are used to "reduce the number of micro-organisms on intact skin," § 333.403(c), exclusion of anti-viral benefits from the Monograph prevents consumers from fully evaluating the benefits of these products, resulting in an artificial distinction between removal of bacteria and removal of viruses from the skin.

Limiting the indications of the Monograph to bacteria is also contrary to data that show the efficacy of topical antimicrobial products against viruses. Several active ingredients, such as alcohol, povidone iodine, triclosan and chloroxylenol (PCMX), are known to have both antibacterial and anti-viral activity. It is therefore appropriate to permit antibacterial products that can meet the performance criteria indicative of anti-viral efficacy the option to make both antibacterial and anti-viral claims.

FDA has recognized the role that topical antimicrobial products may have in decreasing the number of viruses on the hands. For instance, although the Monograph for Health-Care Antiseptic Drug Products states that it is "...continuing to propose that viruses also not be included," the Agency also "...invites the submission of comments and specifically data on the role of other organisms, particularly viruses in nosocomial infections..." (See N. Comments on Testing, 59 FR 31401, 31431). Furthermore, in an FDA feedback meeting with Industry on July 21, 1998 and a Non-Prescription Drugs Advisory Committee meeting on July 29, 1998, Dr. Guzewich from the Center for Food Safety and Applied Nutrition discussed the role that viruses play in enteric illnesses and pointed out that viruses have been excluded from the Monograph. This represents a serious omission, given that poor hygiene among food workers is a significant cause of foodborne viral illnesses.

Not all categories of topical antimicrobial products in the Health-Care Continuum Model (submitted to FDA by Petitioner on June 13, 1995) should be labeled with anti-viral indication(s). Normal resident skin microflora does not include viruses, and the occurrence of viral infections as a result of surgery and other invasive procedures is not significant. Consequently, an anti-viral indication is not appropriate for pre-operative skin preparations, surgical scrubs, or consumer body products.

Many viruses, acquired as transient microflora, can survive several hours on hands. Transfer of virus can occur to and from hands, as well as between hands and fomites. The remaining product categories in the Health-Care Continuum Model, i.e., health-care personnel hand products, food handler products, and consumer hand products can be used to interrupt the hand transmission of transient respiratory and enteric viruses and mitigate the occurrence of disease. Health-care personnel hand products, food handler products, and consumer hand products are suitable candidates for anti-viral labeling.

Petitioner is providing the following data to support anti-viral indications for topical antibacterial products:

Section 1:	Review of anti-viral activity of topical antimicrobial active ingredients & finished products
Section 2:	Methods and performance criteria for anti-viral antiseptics
Section 3:	Proposed labeling for antimicrobial products making antibacterial and anti-viral claims
Appendix A:	Review of prevalence of enteric viral diseases in the United States
Appendix B:	Review of prevalence of respiratory viral diseases in the United States
Appendix C:	Virucidal review of skincare active ingredients and formulations
Appendix D:	Tables – Review of Published Data

Petitioner proposes a two-step labeling approach that is consistent with the language proposed in the Health-Care Continuum Model for topical antimicrobial health-care personnel hand products, food handler products, and consumer handwash products. Firstly, all OTC topical antibacterial products would have to meet the performance criteria for labeling antibacterial products according to the final Monograph. Secondly, provided antibacterial criteria have been met, it would then be optional to supplement antibacterial labeling with general anti-viral labeling for health-care personnel hand, food handler, and consumer hand products that comply with methods and performance criteria that are indicative of anti-viral efficacy. Indications for individual viruses are not proposed.

Anti-viral testing

As discussed in Petitioner's briefing document on finished product test methodology submitted to FDA September 29, 1999 and its citizen petition submitted June 1, 2001, the test methods of the final Monograph for Health Care Antiseptic Drug Products should be standardized, current, and have the flexibility of being appropriately updated to reflect new developments in science and technology. An external standard setting organization, the American Society for Testing and Materials (ASTM), has published methods which can be used to assess anti-viral activity of topical antimicrobials on the finger pads and hands (see Section 2). Petitioner recommends that FDA personnel actively participate in the ASTM process, and write the final Monograph to cross-reference ASTM methods for both anti-viral and antibacterial activity. Furthermore, Petitioner urges the Agency to establish and maintain efficacy methods that are indicative of anti-viral activity in the final Monograph by incorporating the voluntary consensus standards set by ASTM.

In order to establish anti-viral efficacy for topical antimicrobial products intended for use on the hands, we recommend that non-enveloped viruses, which are important in hand-to-hand and hand-to-fomite transmission, be tested according to the ASTM anti-viral

test methods. Product efficacy should be demonstrated against both a respiratory and an enteric pathogen. Either Human Rhinovirus Type 14 (ATCC VR-284) or Human Rhinovirus Type 37 (ATCC VR-1147), and Human Rotavirus Wa (ATCC VR-2018) are proposed as the test organisms.

Proposed anti-viral methods are provided in Section 2, Attachments 1 and 2. Products should be tested using either the finger pad method (ASTM E 1838 Standard Test Method for Determining the Virus-Eliminating Effectiveness of Liquid Hygienic Handwash Agents Using the Fingerpads of Adult Volunteers) or the hand method (ASTM E 2011Standard Test Method for Evaluation of Handwashing Formulations for Virus-Eliminating Activity Using the Entire Hand); these methods are essentially equivalent and product manufacturers should have the discretion to choose which ASTM method to use.

Topical products which are able to reduce the viral titer of both Rhinovirus and Rotavirus by 2 $\log_{10}$ greater than that achieved by a standard hard-water wash control (as defined in the ASTM method) can be labeled with anti-viral indications, in addition to antibacterial indications.

ENVIRONMENTAL IMPACT

According to 21 CFR 25.31(c), this petition qualifies for a categorical exclusion from the requirement for submission of an environmental assessment.

ECONOMIC IMPACT

According to 21 CFR 10.30(b), information on economic impact is to be submitted only when requested by the Commissioner following review of the petition.

CERTIFICATION

The undersigned certify that, to the best of their knowledge and belief, this petition includes all information and views on which the petition relies, and that it includes representative data known to the Petitioner, which are unfavorable to the petition.

Respectfully submitted,

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Vice President, Technical & International Affairs
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Thomas J. Donegan, Jr.
Vice President – Legal & General Counsel
The Cosmetic, Toiletry, and Fragrance Association

Attachments

cc: Charles J. Ganley, M.D. (HFD-560)
Ms. Debbie L. Lumpkins (HFD-560)

(1) September 13, 1974. OTC Topical Antimicrobial Products and Drug and Cosmetic products. Fed. Reg. 39, 179, 33102-33141.
(2) January 6, 1978. Over-the-Counter-Drugs Generally Recognized as Safe, Effective and not Misbranded. Fed. Reg. 43, 4, 1210-1249.
(3) July 22, 1991. Topical Antimicrobial Drug Products for Over-the-Counter Human Use; Tentative Final Monograph for First Aid Antiseptic Drug Products. Fed. Reg. 56, 140, 33644-33680.
(4) June 17, 1994. Topical Antimicrobial Drug Products for Over-the-Counter Human Use; Tentative Final Monograph for Health-Care Antiseptic Drug Products. Fed. Reg. 59, 116, 31401-31452.
(5) Medical Economics, Inc. Physicians' Desk Reference to Pharmaceutical Specialties and Biologicals (22 Ed. 1968) pp. 698, 954-55.