DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 310

[Docket No. 82N-0054]

Boil Ointment Drug Products for Over-the-Counter Human Use

AGENCY: Food and Drug Administration.

ACTION: Advance notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing an advance notice of proposed rulemaking that would classify boil ointment drug products for over-the-counter (OTC) human use as not generally recognized as safe and effective and as being misbranded. This notice is based on the recommendations of the Advisory Review Panel on OTC Miscellaneous External Drug Products and is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments by September 27, 1982 and reply comments by October 27, 1982.

ADDRESS: Written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Bureau of Drugs (HFD-510), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4960.

SUPPLEMENTARY INFORMATION: In accordance with Part 330 (21 CFR Part 330), FDA received on December 14, 1980 a report on OTC boil ointment drug products from the Advisory Review Panel on OTC Miscellaneous External Drug Products. FDA regulations (21 CFR 330.10(a)(6)) provide that the agency issue in the **Federal Register** a proposed order containing: (1) The monograph recommended by the Panel, which establishes conditions under which OTC boil ointment drug products are generally recognized as safe and effective and not misbranded; (2) a statement of the conditions excluded from the monograph because the Panel determined that they would result in the drugs' not being generally recognized as safe and effective or would result in misbranding; (3) a statement of the conditions excluded from the monograph because the Panel determined that the available data are insufficient to classify such conditions under either (1) or (2) above; and (4) the conclusions and recommendations of the Panel.

The Panel's recommendations on OTC boil ointment drug products contain no Category I or Category III conditions, and FDA is issuing the Panel's recommendations proposing Category II classification of OTC boil ointment drug products.

The unaltered conclusions and recommendations of the Panel are issued to stimulate discussion, evaluation, and comment on the full sweep of the Panel's deliberations. The report has been prepared independently of FDA, and the agency has not yet fully evaluated the report. This document represents the best scientific judgment of the Panel members, but does not necessarily reflect the agency's position on any particular matter contained in it. The Panel's findings appear in this document to obtain public comment before the agency reaches any decision on the Panel's recommendations that the ingredients in OTC boil ointment drug products be classified as Category II. If the agency proposes to adopt the Panel's recommendations, a regulation declaring these products to be new drugs within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(p)) will be proposed for inclusion in Part 310, Subpart E (21 CFR Part 310, Subpart E). The agency is including, in this advance notice of proposed rulemaking, a regulation based upon the Panel's recommendations in order to obtain full public comment at this time.

After reviewing all comments submitted in response to this document, FDA will issue in the **Federal Register** a notice of proposed rulemaking on OTC boil ointment drug products. The agency's position on OTC boil ointment drug products will be stated initially when that notice of proposed rulemaking is published in the **Federal Register**. In the notice of proposed rulemaking, the agency also will announce its initial determination whether the proposed rule is a major rule under Executive Order 12291 and will consider the requirements of the Regulatory Flexibility Act (5 U.S.C. 601-612). The present notice is referred to as an advance notice of proposed rulemaking to reflect its actual status and to clarify that the requirements of the Executive Order and the Regulatory Flexibility Act will be considered when the notice of proposed rulemaking is published. At that time FDA also will consider whether the proposed rule has a significant impact on the human environment under 21 CFR Part 25 (proposed in the **Federal Register** of December 11, 1979; 44 FR 71742).

The agency invites public comment regarding any impact that this rulemaking would have on OTC boil ointment drug products. Types of impact may include, but are not limited to, the following: increased costs due to relabeling, repackaging, or reformulating; removal of unsafe or ineffective products from the OTC market; and testing, if any. Comments regarding the impact of this rulemaking on OTC boil ointment drug products should be accompanied by appropriate documentation.

If FDA proposes to adopt the Panel's recommendations, the agency will propose that boil ointment drug products be eliminated from the OTC market, effective 6 months after the date of publication of a final rule in the **Federal Register**, regardless of whether further testing is undertaken to justify their future use.

In accordance with § 330.10(a)(2), the Panel and FDA have held as confidential all information concerning OTC boil ointment drug products submitted for consideration by the Panel. All this information will be put on public display in the Dockets Management Branch, Food and Drug Administration, after July 29, 1982, except to the extent that the person submitting it demonstrates that it falls within the confidentiality provisions of 18 U.S.C. 1905 or section 301(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331(j)). Requests for confidentiality should be submitted to William E. Gilbertson, Bureau of Drugs (HFD-510) (address above).

A proposed review of the safety, effectiveness, and labeling of all OTC drugs by independent advisory review panels was announced in the **Federal Register** of January 5, 1972 (37 FR 85). The final regulations providing for this OTC drug review under § 330.10 were published and made effective in the **Federal Register** of May 11, 1982 (37 FR 9464). In accordance with these regulations, a request for data and information on all active ingredients used in OTC miscellaneous external drug products was issued in the **Federal Register** of November 16, 1973 (38 FR 31697). (In making their categorizations with respect to "active" and "inactive" ingredients, the advisory review panels relied on their expertise and understanding of these terms. FDA has defined "active ingredient" in its current good manufacturing practice regulations (§ 210.3(b)(7), (21 CFR 210.3(b)(7))), as "any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of

disease, or to affect the structure or any function of the body of man or other animals. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in drug product in a modified form intended to furnish the specified activity or effect." An "inactive ingredient" is defined in § 210.3(b)(8) as "any component other than an 'active ingredient.' ") In the **Federal Register** of August 27, 1975 (40 FR 38179) a notice supplemented the initial notice with a detailed, but not necessarily all-inclusive, list of ingredients in miscellaneous external drug products to be considered in the OTC drug review. The list, which included boil ointment active ingredients, was provided to give guidance on the kinds of active ingredients for which data should be submitted. The notices of November 16, 1973, and August 27, 1975, informed OTC drug product manufacturers of the opportunity to submit data to the review at that time and of the applicability of the monographs from the OTC drug review to all OTC drug products.

Under § 330.10(a) (1) and (5), the Commissioner of Food and Drugs appointed the following Panel to review the information submitted and to prepare a report on the safety, effectiveness, and labeling of the active ingredients in these miscellaneous extenal drug products:

William E. Lotterhos, M.D., Chairman
Rose Dagirmanjian, Ph. D.
Vincent J. Derbes, M.D. (resigned July 1976)
George C. Cypress, M.D. (resigned November 1978)
Yelva L. Lynfield, M.D. (appointed October 1977)
Harry E. Morton, Sc. D.
Marianne N. O'Donoghue, M.D.
Chester J. Rossi, D.P.M.
J. Robert Hewson, M.D. (appointed September 1978)

Representatives of consumer and industry interests served as nonvoting members of the Panel. Marvin M. Lipman, M.D., of Consumers Union, served as the consumer liaison. Gavin Hildick-Smith, M.D., served as industry liaison from January until August 1975, followed by Bruce Semple, M.D., until February 1978. Both were nominated by the Proprietary Association. Saul A. Bell, Pharm. D., nominated by the Cosmetic, Toiletry, and Fragrance Association, also served as an industry liaison since June 1975.

Two nonvoting consultants, Albert A. Belmonte, Ph. D., and Jon J. Tanja, R.Ph., M.S., have provided assistance to the Panel since February 1977.

The following FDA employees assisted the Panel: John M. Davitt served as Executive Secretary until August 1977, followed by Authur Auer until September 1978, followed by John T. McElroy, J.D. Thomas D. DeCillis, R.Ph., served as Panel Administrator until April 1976, followed by Michael D. Kennedy until January 1978, followed by John T. McElroy, J.D. Joseph Hussion, R.Ph., served as Drug Information Analyst until April 1976, followed by Victor H. Lindmark, Pharm. D., until March 1978, followed by Thomas J. McGinnis, R.Ph.

The Advisory Review Panel on OTC Miscellaneous External Drug Products was charged with the review of many categories of drugs. Due to the large number of ingredients and varied labeling claims, the Panel decided to review and publish its findings separately for several drug categories and individual drug products. The Panel presents its conclusions and recommendations for OTC boil ointment drug products in this document. The Panel's findings on other categories of miscellaneous external drug products are being published periodically in the **Federal Register.**

The Panel was first convened on January 13, 1975 in an organizational meeting. Working meetings which dealt with the topic in this document were held on February 27 and 28, April 3 and 4, December 11 and 12, 1977; April 16 and 17, 1978; October 5 and 6, November 7 and 8, and December 14, 1980.

The minutes of the Panel meetings are on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration (address above).

No individuals requested to appear before the Panel to discuss OTC boil ointment drug products, nor was any individual requested to appear by the Panel.

The Panel has thoroughly reviewed the literature and data submissions, and has considered all pertinent information submitted through December 14, 1980 in arriving at its conclusions and recommendations.

In accordance with the OTC drug review regulations in § 330.10, the Panel classified OTC boil ointment drug products with respect to the following three categories:

Category I. Conditions under which OTC boil ointment drug products are generally recognized as safe and effective and are not misbranded.

Category II. Conditions under which OTC boil ointment drug products are not generally recognized as safe and effective or are misbranded.

Category III. Conditions for which the available data are insufficient to permit final classification at this time.

The Panel considered 24 active ingredients in boil ointment drug products and classified all ingredients in Category II.

In an attempt to make this review as extensive as possible and to aid manufacturers and other interested persons, the agency compiled a list of ingredients recognized, either through historical use or use in marketed products, as active ingredients contained in boil ointment products. Notices were published in the **Federal Register** of November 16, 1973 (38 FR 31697) and August 27, 1975 (40 FR 38179) requesting the submission of data and information on these ingredients or any other ingredients used in OTC boil ointment drug products.

A. Submissions of Data and Information

Pursuant to the above notices, the following submissions were received:

Firms and Marketed Products

Bowman Pharmaceuticals, Inc., Canton, OH 44702—Bowman Drawing Paste
Commerce Drug Co., Inc., Farmingdale, NY 11735—Boil-Ease
Press Chemical and Pharmaceutical Laboratories, Inc., Columbus, OH 43206—Epsal Ointment

B. Ingredients

1. *Labeled ingredients contained in marketed products submitted to the Panel.*

Benzocaine
Camphor
Ichthammol
Juniper tar (oil of cade)
Magnesium sulfate
Phenol
Rosin
Thymol

2. *Other ingredients.* The following list contains ingredients which appeared in the call-for-data notice published in the **Federal Register** of August 27, 1975 (40 FR 38179) and were not contained in marketed products submitted to the Panel.

Aminoacridine hydrochloride
Bismuth subnitrate
Cholesterol
Extract of ergot
Hexachlorophene
Isobutyl para-aminobenzoate
Lanolin
Menthol
Mercurous chloride
Methyl salicylate
Oil of sassafras
Oxyguinoline sulfate
Petrolatum
Pine tar
Rosin cerate
Zinc oxide

C. Classification of Ingredients

The Panel did not specifically review any of the ingredients in paragraph B. above. The Panel, however, recommends that all of these ingredients or any other ingredients contained in products labeled as boil ointments be placed in Category II. This recommendation is based on the Panel's conclusion that self-treatment of boils is not desirable because improper treatment or a delay in receiving proper professional treatment may cause the infection to spread. (See paragraph E. below—General Discussion.)

D. Referenced OTC Volumes

The "OTC Volumes" cited in this document include submissions made by interested persons in response to the call-for-data notices published in the **Federal Register** of November 16, 1973 (38 FR 31697) and August 27, 1975 (40 FR 38179). All of the information included in these volumes, except for those deletions which are made in accordance with the confidentiality provisions set forth in § 330.10(a)(2), will be put on public display after July 29, 1982. In the Dockets Management Branch (HFA–305), Food and Drug Administration, Room 4–62, 5600 Fishers Lane, Rockville, MD 20857.

E. General Discussion

A boil or furuncle can be defined as an abscess or pyogenic infection of a sweat gland or hair follicle, usually caused by *Staphylococcus aureus* (Refs. 1 and 2).

Most adults are continously exposed to staphylococci, but overt infection is infrequent. Approximately 5 percent of the population has one symptomatic staphylococcal infection per year, but these infections are usually minor (Ref. 3). The nasal reservoir appears to be the major source for dissemination of *S. aureus* and infection. Occasionally lesions of sporotrichosis or skin infiltration with neoplastic cells will resemble boils caused by staphylococcal infection. These lesions can be differentiated from boils by the failure to demonstrate staphylococci by culture or by a gram stain, by culturing *Sporothrix schenckii,* or by demonstrating leukemic or other neoplastic cells on biopsy (Ref. 3). Certain anaerobic bacteria may play a more important role in chronic skin ulcers, decubiti (bed sores), or soft tissue abscesses around the neck or perineal area (Ref. 3).

Some small boils recede without specific therapy. Sometimes moist heat allows a boil to point and drain spontaneously (Refs. 2 and 4). When boils become localized and show fluctuance (central softening indicating pus formation), incision and drainage by a doctor will hasten healing (Refs. 3 and 5). The use of systemic antimicrobial therapy is indicated for boils associated with a surrounding redness or those associated with fever, or located on the upper lip, nose, cheeks, or forehead (Refs. 2 and 5). Because there is a marked variability in the susceptibility of staphylococci to the commonly utilized antimicrobial agents, the responsible organism should be isolated and tested for susceptibility to antibiotics (Ref. 3).

Three submissions were received by the Panel (Refs. 6, 7, and 8). One of these submissions contained a brief statement on the effectiveness of a saturated solution of magnesium sulfate in a hydrophilic ointment base and described the product as "a drawing ointment for pimples, blackheads, boils, and carbuncles" (Ref. 8). The Panel concludes that drawing salves to treat boils do not have any merit. Self-treatment of boils is not in the best interest of the consumer because improper treatment or a delay in receiving proper professional treatment for boils may cause the infection to spread. Therefore, the Panel concludes that any product containing an ingredient listed in paragraph B. above, or any other product labeled for use as an OTC boil treatment, is Category II.

References

(1) "Dorland's Illustrated Medical Dictionary," W. B. Saunders Co., Philadelphia, p. 624, 1979.

(2) Arndt, K. A., "Manual of Dermatologic Therapeutics", 2d Ed., Little, Brown, and Co., Boston, pp. 25–31, 1978.

(3) Hoeprich, P. D., editor, "Infectious Diseases," 2d Ed., Harper and Row, Hagerstown, MD, pp. 785–793, 1977.

(4) "Determatologic Disorders," *in* "The Merck Manual," 13th Ed., edited by R. Berkow, Merck, Sharp, and Dohme Research Laboratories, Rahway, NJ, p. 1577, 1977.

(5) Domonkos, A. N,, "Andrews' Diseases of the Skin," 6th Ed., W. B. Saunders Co., Philadelphia, pp. 273–274, 1971.

(6) OTC Volume 160005.

(7) OTC Volume 160182.

(8) OTC Volume 160214.

List of Subjects in 21 CFR Part 310

New drugs.

PART 310—NEW DRUGS

Therefore, under the Federal Food, Drug, and Cosmetic Act (Secs. 201(p), 502, 505, 701, 52 Stat. 1041–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 352, 355, 371)), and the Administrative Procedure Act (secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704)), and under 21 CFR 5.11 as revised (see 47 FR 16010; April 14, 1982), the agency advises in this advance notice of proposed rulemaking that Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations would be amended in Part 310 by adding to Subpart E new § 310.531, to read as follows:

§ 310.531 Drug products containing active ingredients offered over-the-counter (OTC) for external use as boil ointments.

Aminoacridine hydrochloride, benzocaine, bismuth subnitrate, camphor, cholesterol, extract of ergot, hexachlorophene, ichthammol, isobutyl *para*-aminobenzoate, juniper tar (oil of cade), lanolin, magnesium sulfate, menthol, mercurous chloride, methyl salicylate, oil of sassafras, oxyquinoline sulfate, petrolatum, phenol, pine tar, rosin, rosin cerate, thymol, and zinc oxide have been present as ingredients in drug products for external use as boil ointments. There is a lack of adequate data to establish the safety and effectiveness of these, or any other, ingredients for OTC external use as boil ointments. therefore, any OTC drug product containing ingredients offered for external use as a boil ointment cannot be considered generally recognized as safe and effective.

(b) Any OTC drug product that is labled, represented, or promoted for external use as a boil ointment is misbranded under section 502 of the Federal Food, Drug, and Cosmetic Act and is regarded as a new drug within the meaning of section 201(p) of the act for which an approved new drug application under section 505 of the act and Part 314 of this chapter is required for marketing.

(c) A completed and signed "Notice of Claimed Investigational Exemption for a New Drug" (Form FD–1571), as set forth in § 312.1 of this chapter, is required to cover clinical investigations designed to obtain evidence that any drug product labeled, represented, or promoted OTC as a boil ointment for external use is safe and effective for the purpose intended.

(d) After the effective date of the final regulation, any such drug product initially introduced or initially delivered for introduction into interstate commerce that is not in compliance with this section is subject to regulatory action.

Interested persons may, on or before July 29, 1982, submit to the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62,, 5600 Fishers Lane, Rockville, MD 20857, written comments on this advance

notice of proposed rulemaking. Three copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Comments replying to comments may also be submitted on or before October 27, 1982. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: May 14, 1982.

Mark Novitch,

Acting Commissioner of Food and Drugs.

Dated: June 21, 1982.

Richard S. Schweiker,

Secretary of Health and Human Services.

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