DEPARTMENT OF HEALTH AND HUMAN SERVICES

21 CFR PARTS 347 and 348

[Docket No. 78N-021A]

Skin Protectant Drug Products for Over-the-Counter Human Use; Astringent Drug Products

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking amending the notice of proposed rulemaking for over-the-counter (OTC) skin protectant drug products and establishing conditions under which OTC astringent drug products are generally recognized as safe and effective, and not misbranded. FDA is issuing this notice of proposed rulemaking after considering the reports and recommendations of the Advisory Review Panel on OTC Miscellaneous External Drug Products and public comments on advance notices of proposed rulemaking that were based on those recommendations. This proposal is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments, objections, or requests for oral hearing on the proposed rulemaking before the Commissioner of Food and Drugs by June 2, 1989. New data by April 3, 1990. Comments on the new data by June 4, 1990. Written comments on the agency's economic impact determination by August 1, 1989.

ADDRESS: Written comments, objections, new data, or requests for oral hearing 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, Center for Drug Evaluation and Research (HFD-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-295-8000.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of September 7, 1982 (47 FR 39412 and 39436), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), advance notices of proposed rulemaking and reopened the administrative records for OTC external analgesic drug products and OTC skin protectant drug products to allow for consideration of the reports and recommendations on OTC astringent drug products prepared by the Advisory Review Panel on OTC Miscellaneous External Drug Products (Miscellaneous External Panel), which was the advisory review panel responsible for evaluating data on the active ingredients used as astringents. Interested persons were invited to submit comments by December 6, 1982. Reply comments in response to comments filed in the initial comment period could be submitted by January 5, 1983.

In accordance with § 330.10(a)(10), the data and information considered by the Panel were put on public display in the Dockets Management Branch, after deletion of a small amount of trade secret information.

In response to the advance notice of proposed rulemaking relating to the external analgesic use of OTC astringent drug products, four drug manufacturers, two trade associations, and one health professional submitted comments. In response to the advance notice of proposed rulemaking relating to the skin protectant use of OTC astringent drug products, one of the same manufacturers and the two same trade associations submitted comments. Copies of the comments received are on public display in the Dockets Management Branch.

In the **Federal Register** of February 15, 1983 (48 FR 6820), the agency published a notice of proposed rulemaking for OTC skin protectant drug products. The agency issued this notice after considering the report and recommendations of the Advisory Review Panel on OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Prevention and Treatment Drug Products (Topical Analgesic Panel) and public comments on an advance notice of proposed rulemaking that was based on those recommendations. Interested persons were invited to submit comments by April 18, 1983, new data by February 15, 1984, and comments on the new data by April 16, 1984.

The agency has determined that the external analgesic and skin protectant uses of OTC astringent drug products are so closely related that it would not serve the public interest to proceed with two separate rulemakings for the same ingredients. Accordingly, the agency is proposing in this document to combine the rulemakings for the external analgesic and skin protectant uses of OTC astringent drug products and to place the monograph for these products in the OTC skin protectant monograph. In this notice of proposed rulemaking, FDA states for the first time its position on the OTC uses of astringent drug products. Final agency action on this matter will occur with the publication at a future date of a final rule for OTC skin protectant drug products.

This proposal constitutes FDA's tentative adoption of the Panel's reports and recommendations on OTC astringent drug products as modified on the basis of the comments received and the agency's independent evaluation of the Panel's reports.

The OTC drug procedural regulations (21 CFR 330.10) now provide that any testing necessary to resolve the safety or effectiveness issues that formerly resulted in a Category III classification, and submission to FDA of the results of that testing or any other data, must be done during the OTC drug rulemaking process before the establishment of a final monograph. Accordingly, FDA will no longer use the terms "Category I" (generally recognized as safe and effective and not misbranded), "Category II" (not generally recognized as safe and effective or misbranded), and "Category III" (available data are insufficient to classify as safe and effective, and further testing is required) at the final monograph stage, but will use instead the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Categories II and III). This document retains the concepts of Categories I, II, and III at the tentative final monograph stage.

The agency advises that the conditions under which the drug products that are subject to this monograph would be generally recognized as safe and effective and not misbranded (monograph conditions) will be effective 12 months after the date of publication of the final monograph in the **Federal Register**. On or after that date, no OTC drug product that is subject to the monograph and that contains a nonmonograph condition, i.e., a condition that would cause the drug to be not generally recognized as safe and effective or to be misbranded, may be initially introduced or initially delivered for introduction into interstate commerce unless it is the subject of an approved application. Further, any OTC drug product subject to this monograph that is repackaged or relabeled after the effective date of the monograph must be in compliance with the monograph regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufacturers are encouraged to comply voluntarily with the monograph at the earliest possible date.

If the agency determines that any labeling for a condition included in the final monograph should be implemented sooner than the 12-month effective date, a shorter deadline may be established.

Similarily, if a safety problem is identified for a particular nonmonograph condition, a shorter deadline may be set for removal of that condition from OTC drug products.

All "OTC Volumes" cited throughout this document refer to the submissions made by interested persons pursuant 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), or to additional information that has come to the agency's attention since publication of the advance notice of proposed rulemaking. The volumes are on public display in the Dockets Management Branch (address above).

I. The Agency's Tentative Conclusions on the Comments

1. One comment requested that the agency make clear in all future publications that astringents applied to skin or mucous membrane to check oozing, discharge, or bleeding are "drug" products, and that astringent products used as cosmetics are not covered by this rulemaking. The comment stated that astringent products are well recognized as cosmetic products when used as skin cleansers and freshners; such uses are intended to produce temporary contractions of the skin surface resulting in a smoother and more aesthetically pleasing appearance. The comment stated that the Panel itself recognized that "there are several varied definitions for astringents," one of which is as "a liquid cosmetic for cleansing the skin and contracting the pores." (See the **Federal Register** of September 7, 1982; 47 FR 39427 and 39445.) The comment added that in the original skin protectant publication in this proceeding, the agency noted that skin protectant products are often components of cosmetics. (See the **Federal Register** of August 4, 1978; 43 FR 34628.)

The comment argued that it is well-established that the legal status of a product as a cosmetic or a drug, or both, is not determined by its ingredients or physical properties, but by reference to the representations made for the product by the vendor. The comment stated that this principle derives from the definitions for "cosmetic" and "drug" in the Federal Food, Drug, and Cosmetic Act (the act) and noted that these definitions in sections 201(i) and (g)(1) of the act (21 U.S.C. 321(i) and (g)(1)) both state "articles *intended* * * *" (emphasis added). The comment maintained that the intended use is determined by reference to the vendor's intent, usually as shown by the labeling and advertising for the product, and cited *National Nutritional Foods Assn.* v. *Mathews*, 557 F.2d 325, 333, 335 (2d Cir. 1977); *National Nutritional Foods Assn.* v. *FDA*, 504 F.2d 761, 789 (2d Cir. 1974); *United States* v. *"Sudden Change,"* 409 F.2d 734, 739 (2d Cir. 1969). The comment stated "The manufacturer of the article, through his representations in connection with its sale, can determine the use to which the article is to be put," and then cited S. Rep. No. 361, 74th Cong., 1st Sess. (1935), quoted in Dunn, *Federal Food, Drug, and Cosmetic Act* (Stechert & Co. 1938) at 240. The comment stated that at least one court has regarded products for which astringency claims are made as cosmetics and cited *United States* v. *Magic Secret*, 331 F.Supp. 912 (D. Md. 1971).

The comment also expressed concern that well recognized astringent cosmetic products not be inadvertently and improperly affected by the rulemaking for OTC astringent drug products. The comment suggested that the Panel's recommended monographs be amended to insert the words "drug product" after "astringent" wherever that term appears in the monograph. The comment contended that such a clarification is consistent with the agency's statement in the preamble to the tentative final monograph for OTC skin bleaching drug products that the OTC [drug] panels lack jurisdiction to review or make recommendations with respect to cosmetic claims (See the **Federal Register** of September 3, 1982; 47 FR 39109.) The comment concluded that the regulations (21 CFR Part 330) covering the OTC drug review program grant the agency and the expert panel authority to review drug claims only, not cosmetic claims.

The agency agrees that this rulemaking, which amends the tentative final monograph for OTC skin protectant drug products, applies only to astringent products that fall within the statutory definition of "drugs." In fact, in the tentative final monograph for OTC skin protectant drug products, the agency revised the scope of the rulemaking in order to make it clear that the rulemaking extends only to drug products. (See comment 6 at 48 FR 6822.) Based on that revision, which occurred after the advance notices or proposed rulemaking for OTC astringent drug products were published, the agency has already clarified that this rulemaking applies to drug products only and not to cosmetics. The agency concludes that there is no need to add the term "drug product" after the word "astringent" wherever that term appears in the monograph, as suggested by the comment.

Any product marketed solely as a cosmetic need not conform to the final monograph. However, a product marketed as both a cosmetic and a drug must conform to the requirements of the final monograph as relates to the drug aspects of the product. (See comment 6 at 48 FR 6822 to 6823.)

2. One comment requested that the Panel's Category II classification of borax and boric acid as "active" ingredients for use as an astringent be reconsidered and that these ingredients be redesignated as "inactive" ingredients. The comment noted that these ingredients are listed at 47 FR 39425 as *"Labeled ingredients contained in marketed products submitted to the Panel"* and at 47 FR 39428 as Category II astringent active ingredients because the Panel had no data. The comment stated that it has examined the OTC volumes (Refs. 1 through 11) submitted to the Panel for products containing boric acid and/or borax and these submissions did not disclose any claims for their use as active ingredients. The comment added that these ingredients are not active when used as buffering agents (Refs. 1 and 9) and that boric acid is present in concentrations of 0.012 percent and 2 percent in two submissions (Refs. 1 and 7) listed as astringent drug products. The comment stated that test data on boric acid in a number of submissions (Refs. 2, 4, 5, and 11) contradict the Panel's statement that it was not able to locate nor is it aware of data demonstrating the safety and effectiveness of boric acid when used as an OTC astringent active ingredient. The comment added that aluminum acetate (modified Burow's solution) was classified in Category I as an astringent based on three submissions for a product containing 0.012 percent boric acid (Refs. 1, 2, and 3). The comment contended that Burow's solution contains aluminum acetate and also contains boric acid as a buffering agent or preservative, neither of which uses make the boric acid an "active" ingredient. The comment concluded that some of the ingredients which the Panel considered to be "active" were not intended to be so classified within the meaning of the agency's definition of "active ingredient" in 21 CFR 210.3(b)(7) and that boric acid and borax in astringent drug products were inactive ingredients as defined in 21 CFR 210.3(b)(7) and (8).

The agency has reviewed the submissions referred to by the comment and determined that the labeling and information contained in the submissions represent boric acid as an ingredient for buffering and stabilizing

properties. These uses of boric acid are considered inactive uses of this ingredient. However, other submissions to the Panel represent borax or boric acid as active ingredients for astringent and/or other OTC drug uses (Refs. 4 through 9). Based on the labeling in those submissions, the Panel appropriately classified the ingredients as active ingredients for astringent use as well as for other OTC drug uses. Because the Panel had no data demonstrating the safety and effectiveness of these ingredients for use as an astringent, the Panel classified them in Category II. This Category II designation does not, of course, prevent the use of boric acid as a stabilizer or as a buffer at appropriate concentrations in OTC astringent or other drug products.

Boric acid is considered an inactive ingredient when used as part of a buffering system or stabilizer in OTC drug products. Inactive ingredients, although not included in OTC drug monographs, must meet the requirements of § 330.1(e) (21 CFR 330.1(e)) that they be suitable ingredients that are safe in the amounts administered and do not interfere with the effectiveness of the product or with tests to be performed on the product. Boric acid may be included as a buffering agent or stabilizer in the formulation of OTC drug products provided that it meets the above criteria.

References

(1) OTC Volume 160022.
(2) OTC Volume 160140.
(3) OTC Volume 160230.
(4) OTC Volume 160040.
(5) OTC Volume 160077.
(6) OTC Volume 160091.
(7) OTC Volume 160093.
(8) OTC Volume 160233.
(9) OTC Volume 160236.
(10) OTC Volume 160024.
(11) OTC Volume 160213.

3. One comment stated that the pharmacological action of OTC ingredients used on lesions amenable to treatment by external analgesics and astringents is well known, but that the Panel did not include the combination of these ingredients in its recommended monograph. The comment requested that § 348.20 (permitted combinations) of the tentative final monograph for OTC external analgesic drug products be amended to include combinations of ingredients listed in § 348.10 (a) and (b) of the advance notice of proposed rulemaking for OTC external analgesic drug products (published in the **Federal Register** of December 4, 1979 at 44 FR 69864) and an astringent listed in § 348.10(c) of the advance notice of proposed rulemaking for OTC astringent drug products at 47 FR 39432, provided that such products are appropriately labeled for both classes of ingredients. The comment also stated that the pharmacological action of OTC ingredients used on lesions amenable to treatment by skin protection and astringents is well known. The comment requested that § 347.20 (permitted combinations) of the tentative final monograph for OTC skin protectant drug products be amended to include combinations of a skin protectant listed in the tentative final monograph in proposed § 347.10 (48 FR 6832) and an astringent listed in the advance notice of proposed rulemaking for OTC astringent drug products in recommended § 347.12 (47 FR 39450).

In the advance notice of proposed rulemaking for OTC astringent drug products, the Panel stated that it concurred with the FDA guidelines for OTC combination drug products (Ref. 1), which state that Category I active ingredients from different therapeutic categories may be combined to treat different symptoms concurrently only if each ingredient is present within its established safe and effective dosage range and the combination meets the OTC combination policy in all other respects. (See 47 FR 39430 and 39448). Although stating that it was aware of products that combine various OTC ingredients with an astringent (47 FR 39429 and 39448), the Panel did not provide for any combinations in its recommended monograph nor did it specifically mention the combination of an external analgesic or a skin protectant with an astringent.

In response to the comment's request to include the combination of an external analgesic and an astringent in the tentative final monograph for OTC external analgesic drug products, the agency has surveyed the OTC drug marketplace to determine if there are any such combinations. The agency has determined that such combinations are currently being marketed with claims as for temporary relief of itching or for anal/perianal itching and discomfort (Refs. 2 and 3). These products contain Category I external analgesics with Category I astringents, such as menthol and camphor with aluminum acetate and pramoxine hydrochloride with witch hazel (Refs. 2 and 3).

In § 346.22(g) of the tentative final monograph for OTC anorectal drug products, the agency proposed the combination of an astringent and an external analgesic (analgesic, anesthetic, and antipruritic) in Category I based on the recommendations of the Advisory Review Panel on OTC Hemorrhoidal Drug Products (Hemorrhoidal Panel). (See the **Federal Register** of August 15, 1988; 53 FR 30756.) Thus, the agency has proposed that ingredients in the astringent and external analgesic therapeutic categories may be combined to treat anorectal symptoms, i.e., an astringent to relieve irritation and/or burning and an external analgesic to relieve pain and/or burning. (See 53 FR 30782.) In addition, the agency has proposed that the labeling for such products would be a combination of the respective monograph labeling for each ingredient and that the information may be combined in such a way to eliminate duplicative words or phrases so that the resulting information is clear and understandable.

In response to the comment's request to include the combination of a skin protectant and an astringent in the tentative final monograph for OTC skin protectant drug products, the agency has surveyed the OTC drug marketplaces to determine if there are any such combinations. The agency has determined that such combinations are currently being marketed with claims such as relief of anorectal and/or vaginal irritation, burning, and itching (Ref. 4). These products contain Category I skin protectants with Category I astringents, such as glycerin with witch hazel and white petrolatum with witch hazel (Ref. 4).

The rulemaking on OTC vaginal drug products does not address the combination of an astringent and a skin protectant because no such products were submitted for consideration. The agency invites comments or new data to support such combinations to be submitted to the rulemaking for OTC vaginal drug products following publication of the tentative final monograph for those drugs in a future issue of the **Federal Register**. However, data were submitted to the rulemaking for OTC anorectal drug products, and in the tentative final monograph for OTC anorectal drug products, the agency proposed this combination in Category I based on the recommendations of the Hemorrhoidal Panel. (See the **Federal Register** of August 15, 1988; 53 FR 30756.) Thus, the agency has proposed that ingredients in the astringent and skin protectant therapeutic categories may be combined to treat anorectal symptoms, i.e., an astringent to relieve irritation and/or burning and a protectant to protect inflamed perianal skin. In addition, the agency has proposed that the labeling for such products would be a combination of the respective monograph labeling for each ingredient and that the information may

be combined in such a way to eliminate duplicative words or phrases so that the resulting information is clear and understandable.

Because the comment provided no information on specific products containing an external analgesic or a skin protectant with an astringent, on the symptons/conditions to be treated concurrently, or on the proposed labeling for such combinations, the agency is proposing Category III status for these combinations at this time for any other uses other than those already proposed in Category I in the rulemaking for OTC anorectal drug products. The agency invites public comment and the submission of data, including product formulation, proposed labeling, any test data, and marketing history related to the appropriateness of such combinations containing an astringent for uses other than those already included in the rulemaking for OTC anorectal drug products.

References

(1) "General Guidelines for OTC Drug Combination Products—September 1978," Docket No. 78D–0322, Dockets Management Branch.

(2) Boyd, J. R., "Facts and Comparisons," Facts and Comparisons, Inc., St. Louis, p. 633, January, 1985.

(3) Billups, N.F., and S. M. Billups, "American Drug Index," 31st Ed., J. B. Lippincott Co., Philadelphia, pp. 272 and 465, 1987.

(4) "Physicians' Desk Reference—For Nonprescription Drugs," 9th Ed., Medical Economics Co., Inc., Oradell, NJ, pp. 604 and 633, 1988.

4. One comment requested clarification of the Panel's effectiveness recommendation for witch hazel. Referring to reference 8 (Ref. 1) of the Panel's discussion at 47 FR 39428, the comment stated anorectal the Panel failed to distinguish between witch hazel extract, which contains hamamelitannin, and witch hazel water, which contains no tannin because it is distilled. The comment contended that these two preparations contain different active ingredients but are discussed in a commingled and confusing way under the single title "Witch Hazel." Quoting one of the Panel's statements regarding distilled witch hazel extract, i.e., "The tannin of witch hazel bark on distillation remains in the residue and is absent from the distilled extracts," the comment contended that this statement was incompatible with another statement that the Panel made in discussing the effectiveness of witch hazel, i.e., "Literature reports have attributed the astringent action of witch hazel to its tannin content." The comment explained that both statements are correct, but they are incompatible because the first statement refers to the distilled witch hazel extract and the second statement refers to witch hazel extract (a nondistilled alcoholic extract). The comment added that the distilled witch hazel extract is used chiefly as an astringent in after-shave lotions and the nondistilled extract is used in preparations for relief of hemorrhoids. Because the Panel used the name "Witch Hazel" to refer to both preparations, the comment requested that the Panel's discussion be clarified as to which of the "witch hazel" preparations is effective.

The agency believes that the 2 statements in the Panel's report are general statements intended to provide background information concerning this ingredient and were not intended to be a definitive statement on witch hazel preparations. The Panel's recommended monograph clearly identifies "Witch hazel, NF XI" (Ref. 2) as the appropriate astringent active ingredient. NF XI refers to the ingredient as "Hamamlis Water," with synonyms of "Witch hazel Water" and "Distilled Witch-hazel Extract," and provides the method of preparation. Because this ingredient is no longer listed in an official compendium, the agency has determined that "Hamamelis water, NF XI" will be the accepted name for this ingredient in this tentative final monograph. In addition, in the tentative final monograph for OTC anorectal drug products (53 FR 30782), the agency also identified witch hazel water as Hamamelis water, NF XI" and not as witch hazel extract, as suggested by the comment.

References

(1) "Martindale. The Extra Pharmacopoeia," 26th Ed., edited by N. W. Blacow, The Pharmaceutical Press, London, p. 265, 1972.

(2) "The National Formulary," 11th Ed., Mack Publishing Co., Easton, PA, p. 158, 1960.

5. One comment contended that the Panel's report (47 FR 39412) erroneously classified aluminum sulfate in Category III as an OTC astringent ingredient in styptic pencils. Citing the transcript and minutes of the Panel's December 15, 1980 final meeting, the comment stated that the Panel by a five to two vote reclassified aluminum sulfate from Category III to Category I. The comment suggested that the Panel's published report may have been based on the Panel's November 15, 1980, Information Copy in which aluminum sulfate was tentatively classified in Category III. The comment requested that the published report be corrected in several places to reflect a Category I status.

The comment added that the Panel's report at 47 FR 39429 erroneously said that "In 75 years of marketing styptic pencils there have been reported instances of human toxicity." The comment stated that the Information Copy said that no instances of human toxicity were reported in 75 years of marketing styptic pencils and requested that the published report be corrected to read, "In 75 years of marketing styptic pencils there have been no reported instances of human toxicity."

In a letter dated November 15, 1982 (Ref. 1), the agency acknowledged that the requested corrections were valid, and stated that an apparent administrative error had occurred in that the Panel's vote at its final meeting to move aluminum sulfate to Category I was not incorporated into the final document.

Although one submission to the Panel (Ref. 2) indicated an average aluminum sulfate concentration of approximately 57 percent, which served as the basis for the Panel's recommendations, subsequent information from the manufacturer (Ref. 3) indicated that the 57-percent concentration was an average value based on the analysis of a limited number of samples and that subsequent assays over time have shown that there is a significant variation in concentration based on the amount of water physically bound to the aluminum sulfate. Experience from a larger number of batches of styptic pencils has shown concentrations ranging from 45.5 to 60.1 percent, with an average value of 53.9 percent. The manufacturer recommended a range of 46 to 61 percent anhydrous aluminum sulfate concentration for styptic pencils based on this actual manufacturing experience. Another submission (Ref. 4) provided a label claiming its product contained aluminum sulfate 90 percent; however, the submission contained no information to support the 90-percent concentration and stated that it adopted the content of the other submission (Ref. 2). Subsequent information (Ref. 5) from the latter manufacturer indicated that the concentration range of its product ranged from 51.7 to 62.3 percent (with an average value of 56.2 percent) anhydrous aluminum sulfate based on batches in its manufacturing experience.

Based on the Panel's recommendations, the information contained in the submissions (Refs. 2 and 4), and the additional information (Refs. 3 and 5), the agency has determined that a range of 46 to 63 percent aluminum sulfate (based on the anhydrous equivalent) is acceptable for use as a styptic pencil and this

concentration range is being proposed as Category I in this tentative final monograph. In addition, based on the same information, the agency is proposing the following indication: "Stops bleeding caused by minor surface cuts and abrasions as may occur during shaving"; warning: "For external use only. Avoid contact with the eyes"; and directions: "Moisten tip of pencil with water and apply to the affected area. Dry pencil after use."

References

(1) Letter from W. E. Gilbertson, FDA, to R. G. Pinco, Perito, Duerk, Carlson and Pinco, P. C., coded ANS, Docket No. 78N–0301, Dockets Management Branch.

(2) OTC Volume 160409.

(3) Letter from J. Geils, Requa, Inc., to W. E. Gilbertson, FDA, coded C00103, Docket No. 78N–0301, Dockets Management Branch.

(4) OTC Volume 160413.

(5) Letter from K. Rempell, Woltra Corporation, to W. E. Gilbertson, FDA, coded C00104, Docket No. 78N–0301, Dockets Management Branch.

6. Noting the Panel's reference to aluminum acetate solution as a "clear solution" (47 FR 39427), one comment stated that this reference was based on "The United States Pharmacopeia XIX" (U.S.P. XIX) (Ref. 1), which describes Burow's Solution (aluminum acetate solution) prepared de novo. The comment contended that the U.S.P. procedure does not pertain to modified aluminum acetate solutions prepared from tablets or powders, which do not result in a clear solution but do conform with all other requirements set forth in the Panel's recommended monograph. The comment requested that the reference to a clear aluminum acetate solution be deleted from the proposed monograph.

The reference to aluminum acetate topical solution being a clear solution was included as part of the Panel's discussion of a U.S.P. XIX dispensing requirement for this solution. (See 47 FR 39427.) This statement of the U.S.P. XIX dispensing requirement did not appear in the Panel's recommended monograph, nor will it appear as a requirement in this tentative final monograph. Therefore, no agency action is necessary in response to the comment's request.

The tentative final monograph proposes monograph status for aluminum acetate as an active ingredient in a use concentration of 0.13 to 0.5 percent. The final product may be prepared from tablets, powders, or liquid solutions. The tentative final monograph does not propose to address the clarity of the final solution that is prepared. However, any product that is marketed as Aluminum Acetate Topical Solution, U.S.P., would have to meet the compendial dispensing requirement of being a clear solution (Ref. 2).

References

(1) "The United States Pharmacopeia," 19th Revision, Mack Publishing Co., Easton, PA, p. 20, 1975.

(2) "United States Pharmacopeia XXI—National Formulary XVI," United States Pharmacopeial Convention, Inc., Rockville, MD, p. 29, 1985.

7. One comment contended that the Panel's recommended monograph contains several errors regarding aluminum acetate. The comment stated that Burow's Solution, which is a 5-percent aluminum acetate solution, is further diluted to yield a 1:20 to 1:40 solution for use as an astringent. Therefore, the comment suggested that § 348.10(c)(1) and all references in the monograph to aluminum acetate be revised to read "Aluminum acetate solution, 2.5 to 5 percent (equivalent to a 1:40 and 1:20 dilution, respectively)."

The agency agrees that the use concentration for aluminum acetate was incorrectly stated in the Panel's recommended monograph. Further, as discussed in Part III, paragraph B. 1, below, the agency has revised the use concentration for aluminum acetate for astringent use. The active ingredient listing being proposed for aluminum acetate in this tentative final monograph reads "Aluminum acetate, 0.13 to 0.5 percent (depending on the formulation and concentration of the marketed product, the manufacturer must provide adequate directions so that the resulting solution to be used by the consumer contains 0.13 to 0.5 percent aluminum acetate)." The 0.13 to 0.5 percent solutions correspond to 1/40 and 1/10 dilutions of a 5-percent aluminum acetate solution, respectively, and, therefore, include the concentrations mentioned by the comment. Because the rulemakings for the external analgesic and skin protectant uses of OTC astringent drug products have been combined (see discussion above), this information about aluminum acetate appears in proposed § 347.12(a) of this rulemaking on skin protectants and is being removed from the external analgesic rulemaking as it appeared in the Panel's recommended monograph in § 348.10(c)(1), published in the **Federal Register** of September 7, 1982 (47 FR 39412).

8. Referring to the Panel's recommended indication for products containing aluminum acetate, that states "For use as a wet dressing, compress, or soak for relief of inflammatory conditions and minor skin irritations due to allergies, insect bites, athlete's foot, poison ivy, or swelling associated with minor bruises and ulcerations of the skin," one comment proposed that the indication be revised to state more clearly the uses for aluminum acetate solution as follows: "A soothing wet dressing for relief of skin irritations caused by conditions such as insect bites, diaper rash, sunburn, or those caused by poison ivy, poison oak, poison sumac, soaps, detergents, cosmetics, and jewelry. A cleansing and drying agent to prepare the skin prior to the application of other medications for athlete's foot or hydrocortisone for rashes due to dermatitis and eczema. Helps to soften and remove crusts."

The agency has determined that some of the comment's suggestions are useful, while others are not. The agency does not normally include the word soothing in an indication for topical OTC drug products because many topical products can be soothing when applied but the "soothing" effect has no relationship to the pharmacologic action of the drug. In addition, the agency has previously stated that it considers the term "soothes" to be a cosmetic claim in the context of skin protectant products. (See comment 22 in the tentative final monograph for OTC skin protectant drug products at 48 FR 6827 to 6828). The agency does not consider the phrase "for use as a wet dressing (compress or soak)" to be an indication, and is including such information in the "Directions" section.

The agency agrees that "relief of inflammatory conditions and minor skin irritations" can be replaced with "relief of skin irritations" because the latter phrase is shorter and conveys the same meaning. However, the agency is including the word "minor" in this phrase for consistency with the indications for a number of other OTC topical drug products. The agency sees no need to replace the shorter phrase "due to" with the longer phrase "caused by conditions such as."

The Panel included "poison ivy" in its recommended indications for aluminum acetate. The agency concurs with this recommendation and is further extending the indications to also include "poison oak" and "poison sumac." The Panel also included "insect bites" in its recommended indications for aluminum acetate, and the agency concurs with this recommendation. The Panel did not include "diaper rash" in its recommended indications, and the agency is not aware of any data that support the use of aluminum acetate for the treatment of diaper rash. Therefore, the agency is not including "diaper rash" in the indications being proposed for aluminum acetate.

The agency agrees with the comment that the terms "soap, detergents, cosmetics, and jewelry" are informative to describe some of the likely sources of skin irritation that may be caused by allergies. However, because these products are being used by the relief of minor skin irritations, the agency believes that it would be more informative and understandable by consumers if the labeling stated that the products relieved "rashes" caused by these items, rather than "allergies" caused by these items. The "rash" is the physical manifestation of the allergy that the consumer is treating with the skin protectant astringent product.

Use of the term "sunburn" and the phrases "A cleansing and drying agent to prepare the skin prior to the application of other medications for athlete's foot or hydrocortisone for rashes due to dermatitis and eczema" and "helps to soften and remove crusts" as suggested by the comment are not being included in the revised indication because the comment did not provide any information or data to support these claims and no information on these claims has been submitted by any other interested person. The term "crusts" is unclear and appears to be an inappropriate term for consumer labeling. The claims relating to "cleansing" and "drying" used alone would be cosmetic claims and would not be subject to the monograph. These terms could appear outside of the indications section. Although the agency does not specifically prohibit commingled drug and cosmetic labeling separate from the indications section, the agency requests that such claims be appropriately described so that consumers will more readily be able to differentiate the drug aspects from the cosmetic aspects of such labeling. If commingled drug and cosmetic labeling claims are confusing or misleading, the agency may determine that the product's labeling is misleading within the meaning of the act and declare the product misbranded under sections 502(a) and 602(a) of the act.

Finally, the agency is deleting that portion of the Panel's recommended indication that reads "swelling associated with minor bruises and ulcerations of the skin." The Panel did not cite and the ageny is not aware of any data that show that aluminum acetate reduces swelling. Further, the word "ulcerations" is not a consumer term. In addition, the agency does not consider a number of the conditions which the Panel discussed at 47 FR 39427 and 39446, e.g., varicose ulcers, acute cutaneous inflammation, planter perforation ulcers, to be conditions which consumers should self-treat without a physician's supervision.

Because there are a number of conditions that aluminum acetate may be used for and manufacturers may not wish to include all of these conditions in their labeling, the agency is providing that manufacturers may select those conditions which they wish to include in the labeling for their product. Based on the above discussion, the revised indication proposed for aluminum acetate in this tentative final monograph reads as follows: "For temporary relief of minor skin irritations due to" (select one or more of the following: "poison ivy," "poison oak," "poison sumac," "insect bites," "athlete's foot," or "rashes caused by soaps, detergents, cosmetics, or jewelry").

II. The Agency's Evaluation of a Submission

9. Because the Panel inadvertently did not review a submission for the ingredient aluminum chloride hexahydrate (Ref. 1), the agency has evaluated the submission. The submission contained information on a marketed product containing aluminum chloride hexahydrate labeled to help relieve inflammation often associated with such common skin conditions as poison ivy, sunburn, athlete's foot, and insect bites. The product is marketed as a packet containing 12.9 grams (g) of aluminum chloride hexahydrate crystals for dissolving in approximately 12 ounces (oz) of water resulting in a 2-percent aluminum chloride solution for use as a wet dressing. The label states that a clean dressing or bandage soaked in the solution is to be applied loosely on inflamed skin and that such dressings are to be removed, remoistened, and reapplied every 10 to 15 minutes for 4 to 8 hours or as directed by a physician; the dressing should not be allowed to dry out; and the dressing material and used solution should be discarded daily and not reused. The label also cautions consumers that the product is for external use only; to avoid contact with the eyes; and if irritation occurs or persists, discontinue use and consult a physician.

The submission contained a study by Leyden and Kligman (Ref. 2) who used aluminum chloride hexahydrate as an astringent. The authors stated that astringency cannot be precisely defined and probably encompasses multiple actions involving the alterations of protein's ability to swell and to hold water and the production of dryness. The study (Ref. 2) used protein precipitation as a criterion for astringent activity. To each 2-milliliter (mL) portion of a 4-percent bovine albumin solution, 2 mL of the following were added: 30 percent, 20 percent, and 10 percent aluminum chloride hexahydrate, 30 percent aluminum acetate, 30 percent aluminum chlorohydrate, and 30 percent aluminum sulfate. Readings were made at 5 minutes, at 1 hour, and 24 hours.

The 30 percent aluminum chloride hexahydrate solution produced a thick precipitate within 5 minutes. With the 20 percent solution, there was turbidity at 5 minutes that became flocculent by 24 hours. The 10 percent solution had no effect. The 30 percent solutions of the other salts produced no precipitation except for 30 percent aluminum chlorohydrate, which became turbid in 24 hours.

Aluminum chloride was the only salt tested that possessed protein-precipitating properties to a high degree. From these results, the authors stated that one would expect aluminum chloride to be more drying than the other agents tested.

Two general references (Refs. 3 and 4) contained in the submission cited the use of aluminum chloride as an astringent at concentrations from 10 to 25 percent but provided no supporting data. A textbook (Ref. 5) cited the use of 2-percent aluminum chloride as an astringent and stated that it is a rare sensitizer but provided no supporting data. The remaining references in the submission were general textbook references on the use of wet dressings and did not mention the use of aluminum chloride. Several of the references describe the use of 1.5 to 2.5 percent aluminum chloride as an antimicrobial; and one reference described a sensitization study using 10 percent aluminum chloride. The majority of the references have no bearing on the effectiveness of aluminum chloride hexahydrate as an astringent.

The agency reviewed the data submitted and concludes that they are insufficient to establish the effectiveness of aluminum chloride hexahydrate as an OTC astringent drug product for use as a wet dressing for relief of inflammatory conditions.

Because aluminum chloride is classified in Category I at 15 percent or less concentration (calculated as the hexahydrate form) in the tentative final monograph for OTC antiperspirant drug products in the **Federal Register** of August 20, 1982 (47 FR 36504), the safety of a 2-percent aluminum chloride solution has been established.

Because some of the references in the submission are supportive of the effectiveness of aluminum chloride hexahydrate as an astringent, the

agency is classifying this ingredient in Category III at this time. Additional effectiveness data will be needed to upgrade the ingredient to Category I at a 2-percent aluminum chloride concentration.

The agency has not addressed specific guidelines for the testing of the effectiveness of topically applied astringents in this document. In revising the OTC drug review procedures relating to Category III, published in the **Federal Register** of September 29, 1981 (46 FR 47730), the agency advised that tentative final monographs will not include recommended testing guidelines for conditions that industry wishes to upgrade to monograph status. Instead, the agency will meet with industry representatives at their request to discuss testing protocols. The revised procedures also state the time in which test data must be submitted for consideration in developing the final monograph. (See also part III. paragraph A. 2. below—*Testing of Category II and Category III conditions.*)

References

(1) OTC Volume 160396.

(2) Leyden, J., and A. Kligman, "Aluminum Chloride in the Treatment of Symptomatic Athlete's Foot," *Archives of Dermatology*, 111:1004–1010, 1975.

(3) National Formulary XIV, American Pharmaceutical Association, Washington, pp. 33–34, 1975.

(4) A. Osol, et al., "The United States Dispensatory and Physicians' Pharmacology," J. B. Lipincott Co., Philadelphia, p. 47, 1967.

(5) A. A. Fisher, "Contact Dermatitis," Lea and Febiger, Philadelphia, p. 360, 1973.

III. The Agency's Tentative Conclusions and Adoption of the Panel's Recommendations

A. Summary of Ingredient Categories and Testing of Category II and Category III Conditions

1. Summary of ingredient categories

The agency has reviewed all claimed active ingredients submitted to the Panel, as well as other data and information available at this time. As a convenience to the reader, the following list is included as a summary of the categorization of active ingredients recommended by the Panel in both the external analgesic and skin protectant rulemakings and the proposed categorization by the agency in this document.

Astringent Active Ingredients	Panel	Agency
Acetone	II	II
Alcohol	II	II
Alcohol (14 percent)	II	II
Alum (powdered alum)	II	II
Aluminum acetate	I	I
Aluminum chlorhydroxy complex	II	II
Aluminum Chloride hexahydrate	N/A	III
Aluminum sulfate [1]	III	I
Ammonium alum	II	II
Aromatics	II	II
Benzalkonium chloride	II	II
Benzethonium chloride	II	II
Benzocaine	II	II
Benzoic acid	II	II
Borax	II	II
Boric acid	II	II
para-tertiary-Butyl-*meta*-cresol	II	II
Calcium acetate	II	II
Camphor (gum camphor)	II	II
Colloidal oatmeal	II	II
Cresol	II	II
Cupric sulfate	II	II
Eugenol	II	II
Ferric subsulfate	I	I
Hamamelis water, NF XI [2]	II	II
Honey	II	II
Isopropyl alcohol	II	II
Menthol	II	II
Oil of cloves	II	II
Oil of eucalyptus	II	II
Oil of peppermint	II	II
Oil of sage	II	II
Oil of wintergreen	II	II
Oxyquinoline sulfate	II	II
Phenol (carbolic acid)	II	II
Polyoxyethylene monolaurate	II	II
Potassium alum	II	II
Potassium ferrocyanide	II	II
Silver nitrate	II	II
Sodium diacetate	II	II
Starch	II	II
Talc	II	II
Tannic acid	II	II
Tannic acid glycerite	II	II
Thymol	II	II
Zinc chloride	II	II
Zinc oxide	II	II
Zinc phenolsulfonate	II	II
Zinc stearate	II	II
Zinc sulfate	II	II

[1] Appeared incorrectly in the Panel's recommended monograph as Category III.

[2] "Witch hazel, NF XI" was the name designated by the Panel for this ingredient. The name should have read "Hamamelis water" to reflect the title when it was officially recognized in the National Formulary XI.

2. Testing of Category II and Category III conditions

Interested persons may communicate with the agency about the submission of data and information to demonstrate the safety or effectiveness of any astringent ingredient or condition included in the review by following the procedures outlined in the agency's policy statement published in the **Federal Register** of September 29, 1981 (46 FR 47740), and clarified April 1, 1983 (48 FR 14050). That policy statement includes procedures for the submission and review of proposed protocols, agency meetings with industry or other interested persons, and agency communications on submitted test data and other information.

B. Summary of the Agency's Changes in the Panel's Recommendations

FDA has considered the comments and other relevant information and concludes that it will tentatively adopt the Panel's report with the changes described in FDA's responses to the comments above and with other changes described in the summary below.

1. The Panel had recommended directions for aluminum acetate as follows: the manufacturer must provide adequate directions so that the resulting solution to be used by the consumer contains 2.5 to 5 percent aluminum acetate. The Panel also stated "Based on the current literature and wide clinical usage, the Panel concludes that aluminum acetate solution 1:20 to 1:40 is safe and effective for topical use as an astringent." (See 47 FR 39428 and 39446.)

The agency finds that the above two statements are somewhat inconsistent. Aluminum acetate solution, more commonly known as Burow's solution, is an approximately 5 percent solution of aluminum acetate (Ref. 1). As the Panel noted, aluminum acetate solution has been used for many years as an astringent by dilution with 10 to 40 parts of water as a wet dressing (47 FR 39427 and 39445). In diluting the 5 percent solution 1/40 to 1/10, the actual use concentration of aluminum acetate is 0.13 to 0.5 percent. Because this use concentration may be prepared by dilution of aluminum acetate solution or from tablet or powder concentrates, the agency is revising § 347.12(a) to delete the percent of aluminum acetate recommended by the Panel and is proposing that this section read as follows: "Aluminum acetate, 0.13 to 0.5 percent (depending on the formulation and concentration of the marketed product, the manufacturer must provide adequate directions so that the resulting solution to be used by the consumer contains 0.13 to 0.5 percent aluminum acetate)." (See also comment 7 above.)

Reference

(1) "United States Pharmacopeia XXI—National Formulary XVI," United States Pharmacopeial Convention, Inc., Rockville, MD, p. 29, 1985.

2. The agency is revising the indication for aluminum acetate. (See comment 8 above.)

3. The agency is reclassifying aluminum sulfate 46 to 63 percent (based on the anhydrous equivalent) for use as a styptic pencil from Category III to Category I. (See comment 5 above.)

4. After reviewing a submission not reviewed by the Panel, the agency is classifying aluminum chloride

hexahydrate in Category III. (See comment 9 above.)

5. The agency is classifying the combinations of an external analgesic and an astringent and a skin protectant and an astringent in Category III at this time. (See comment 3 above.)

6. The agency is clarifying the Panel's recommended name for witch hazel and is proposing the name "Hamamelis water, NF XI" as the only witch hazel active ingredient. (See comment 4 above.) In addition, the agency is revising and combining the indications recommended for this ingredient by the Panel. The agency agrees with the Panel that hamamelis water may be used for treating insect bites. However, the terms "sunburn," "bruises," "contusions," and "sprains" as well as the claim "for relieving muscular pains" are not being included in the revised indication because the agency is not aware of any data to support these claims. The claim for external hemorrhoids is not being included in this rulemaking because the use of hamamelis water for anorectal conditions, including external hemorrhoids, is more fully covered in the rulemaking for OTC anorectal drug products. More extensive indications for hamamelis water are proposed in § 346.50(b) of the tentative final monograph for OTC anorectal drug products. (See the **Federal Register** of August 15, 1988; 53 FR 30756.) Manufacturers may label hamamelis water products with those claims and the claims proposed in this rulemaking provided the conditions of both monographs are fully met. After combining and revising the remaining indications, the new indication being proposed in § 347.52(b)(3) for hamamelis water reads as follows: "For temporary relief of minor skin irritations due to" (select one or more of the following: "insect bites," "minor cuts," or "minor scrapes"). As stated above (see comment 6), the agency is providing that manufacturers may select those conditions which they wish to include in the labeling for their product. The agency considers this revised indication to be more consistent with the indications proposed by the agency for OTC skin protectant drug products in § 347.50(b) of the tentative final monograph for OTC skin protectant drug products (48 FR 6832) and with the definition of an astringent being proposed in this document. (See paragraph 7 below.)

7. The agency is changing the Panel's recommended definition for an astringent drug to be consistent with the definition proposed in the tentative final monograph for OTC anorectal drug products in the **Federal Register** of (53 FR 30781).

The revised definition is as follows: "A drug that is applied to the skin or mucous membranes for a local and limited protein coagulant effect."

8. In an effort to simplify OTC drug labeling, the agency proposed in a number of tentative final monographs to substitute the word "doctor" for "physician" in OTC drug monographs on the basis that the word "doctor" is more commonly used and better understood by consumers. Based on comments to these proposals, the agency has determined that final monographs and any applicable OTC drug regulation will give manufacturers the option of using either the word "physician" or the word "doctor." This tentative final monograph proposes that option. (See § 347.52(c)(1)(i).)

9. The agency is not including in the tentative final monograph the Panel's recommended warning for aluminum acetate to "store in a cool dry place." The official compendium does not require such a storage condition for the only official aluminum acetate product, aluminum acetate topical solution (Ref. 1). Manufacturers of powder or tablet products containing aluminum acetate may include such a statement in the labeling of their products if they determine this type of storage is necessary to preserve the stability of the product. However, such a statement will not be a monograph requirement.

Reference

(1) "The United States Pharmacopeia XXI—The National Formulary XVI," United States Pharmacopeial Convention, Inc., Rockville, MD, p. 29, 1985.

10. The agency is revising and combining the warnings recommended by the Panel to be consistent with the format and style of other tentative final monographs.

In the **Federal Register** of May 1, 1986 (51 FR 16258), the agency published a final rule changing its labeling policy for stating the indications for use of OTC drug products. Under 21 CFR 330.1(c)(2), the label and labeling of OTC drug products are required to contain in a prominent and conspicuous location, either (1) the specific wording on indications for use established under an OTC drug monograph, which may appear within a boxed area designated "APPROVED USES"; (2) other wording describing such indications for use that meets the statutory prohibitions against false or misleading labeling, which shall neither appear within a boxed area nor be designated "APPROVED USES"; or (3) the approved monograph language on indications, which may appear within a boxed area designated "APPROVED USES," plus alternative language describing indications for use that is not false or misleading, which shall appear elsewhere in the labeling. All other OTC drug labeling required by a monograph or other regulation (e.g., statement of indentity, warnings, and directions) must appear in the specific wording established under the OTC drug monograph or other regulation where exact language has been established and identified by quotation marks, e.g., 21 CFR 201.63 or 330.1(g). The proposed rule in this document is subject to the labeling provisions in § 330.1(c)(2).

The agency has examined the economic consequences of this proposed rulemaking in conjunction with other rules resulting from the OTC drug review. In a notice published in the **Federal Register** of February 8, 1983 (48 FR 5806), the agency announced the availability of an assessment of these economic impacts. The assessment determined that the combined impacts of all the rules resulting from the OTC drug review do not constitute a major rule according to the criteria established by Executive Order 12291. The agency therefore concludes that no one of these rules, including this proposed rule for OTC external analgesic and skin protectant drug products used as an astringent, is a major rule.

The economic assessment also concluded that the overall OTC drug review was not likely to have a significant economic impact on a substantial number of small entities as defined in the Regulatory Flexibility Act, Public Law 96-354. That assessment included a discretionary Regulatory Flexibility Analysis in the event that an individual rule might impose an unusual or disproportionate impact on small entities. However, this particular rulemaking for OTC external analgesic and skin protectant drug products used as an astringent is not expected to pose such an impact on small businesses. Therefore, the agency certifies that this proposed rule, if implemented, will not have a significant economic impact on a substantial number of small entities.

The agency invites public comment regarding any substantial or significant economic impact that this rulemaking would have on OTC skin protectant drug products when used as an astringent. Types of impact may include, but are not limited to, costs associated with product testing, relabeling, repackaging, or reformulating. Comments regarding the impact of this rulemaking on OTC skin protectant drug products when used as an astringent

should be accompanied by appropriate documentation. Because the agency has not previously invited specific comment on the economic impact of the OTC drug review on external analgesic and skin protectant drug products used as an astringent, a period of 120 days from the date of publication of this proposed rulemaking in the **Federal Register** will be provided for comments on this subect to be developed and submitted. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this rulemaking in the preamble to the final rule.

The agency invited public comment in the advance notice of proposed rulemaking regarding any impact that this rulemaking would have on OTC external analgesic and skin protectant drug products used as an astringent. No comments on economic impacts were received. Any comments on the agency's initial determination of the economic consequences of this proposed rulemaking should be submitted by August 1, 1989. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this rulemaking in the preamble to the final rule.

The agency has determined under 21 CFR 25.24(c)(6) that this action is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Because the rulemakings for the external analgesic and skin protectant uses of OTC astringent drug products have been combined and are being proposed as part of the tentative final monograph for OTC skin protectant drug products (see 21 CFR Part 347 as proposed in the **Federal Register** of February 15, 1983; 48 FR 6820), the agency is removing in their entirety all paragraphs related to the external analgesic use of astringents that were included in the advance notice of proposed rulemaking for OTC external analgesic drug products. The paragraphs removed, which appeared in the **Federal Register** of September 7, 1982 (47 FR at 39432 and 39433), are § 348.3(h), § 348.10(c), and § 348.50(a)(3), (b) (4) and (5), (c) (7) and (8), and (d)(2) (i) and (ii).

Interested persons may, on or before June 2, 1989, submit to the Dockets Management Branch (address above), written comments, objections, or requests for oral hearing before the Commissioner on the proposed rulemaking. A request for an oral hearing must specify points to be covered and time requested. Written comments on the agency's economic impact determination may be submitted on or before August 1, 1989. Three copies of all comments, objections, and requests are to be submitted, except that individuals may submit one copy. Comments, objections, and requests are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Comments, objections, and requests may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. Any scheduled oral hearing will be announced in the **Federal Register**.

Interested persons, on or before April 3, 1990, may also submit in writing new data demonstrating the safety and effectiveness of those conditions not classified in Category I. Written comments on the new data may be submitted on or before June 4, 1990. These dates are consistent with the time periods specified in the agency's final rule revising the procedural regulations for reviewing and classifying OTC drugs, published in the **Federal Register** of September 29, 1981 (46 FR 47730). Three copies of all data and comments on the data are to be submitted, except that individuals may submit one copy, and all data and comments are to be identified with the docket number found in brackets in the heading of this document. Data and comments should be addressed to the Dockets Management Branch. Received data and comments may also be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

In establishing a final monograph for OTC skin protectant drug products used as an astringent, the agency will ordinarily consider only data submitted prior to the closing of the administrative record on June 4, 1990. Data submitted after the closing of the administrative record will be reviewed by the agency only after a final monograph for OTC skin protectant drug products is published in the **Federal Register**, unless the Commissioner finds good cause has been shown that warrants earlier consideration.

List of Subjects

21 CFR Part 347

Labeling, Over-the-counter drugs, Skin protectant drug products.

21 CFR Part 348

External analgesic drug products, Labeling, Over-the-counter drugs.

Therefore, under the Federal, Food, Drug, and Cosmetic Act and the Administrative Procedure Act, it is proposed that Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations be amended in Part 347 (proposed in the **Federal Register** of February 15, 1983; 48 FR 6820), and certain proposed amendments to Part 348 (proposed in the **Federal Register** of September 7, 1982; 47 FR 39412) are withdrawn to read as follows:

PART 347—SKIN PROTECTANT DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

1. The authority citation for 21 CFR Part 347 is revised to read as follows:

Authority: 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); 5 U.S.C. 553; 21 CFR 5.10 and 5.11.

2. Section 347.3 is amended by adding new paragraph (c), to read as follows:

§ 347.3 Definitions.

* * * * *

(c) *Astringent drug product.* A drug product that is applied to be skin or mucous membranes for a local and limited protein coagulant effect.

3. Section 347.12 is added, to read as follows:

§ 347.12 Astringent active ingredients.

The active ingredient of the product consists of the following within the specified concentration:

(a) Aluminum acetate, 0.13 to 0.5 percent (depending on the formulation and concentration of the marketed product, the manufacturer must provide adequate directions so that the resulting solution to be used by the consumer contains 0.13 to 0.5 percent aluminum acetate).

(b) Aluminum sulfate, 46 to 63 percent (the concentration is based on the anhydrous equivalent).

(c) Hamamelis water, NF XI.

4. Section 347.52 is added, to read as follows:

§ 347.52 Labeling of astringent drug products.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the product as an "astringent."

(b) *Indications.* The labeling of the product states, under the heading "Indications" any of the phrases listed in this paragraph (b), as appropriate. Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in this paragraph, may also be used, as provided in § 330.1(c)(2) of this chapter, subject to

the provisions of section 502 of the act relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act.

(1) *For products containing aluminum acetate identified in § 347.12(a).* "For temporary relief of minor skin irritations due to" (select one or more of the following: "poison ivy," "poison oak," "poison sumac," "insect bites," "athlete's foot," or "rashes caused by soaps, detergents, cosmetics, or jewelry").

(2) *For products containing aluminum sulfate identified in § 347.12(b) for use as a styptic pencil.* "Stops bleeding caused by minor surface cuts and abrasions as may occur during shaving."

(3) *For products containing hamamelis water identified in § 347.12(c).* (i) "For relief of minor skin irritations due to" (select one or more of the following: "insect bites," "minor cuts," or "minor scrapes").

(c) *Warnings.* The labeling of the product contains the following warnings under the heading "Warnings:"

(1) "For external use only. Avoid contact with the eyes."

(2) *For products containing aluminum acetate identified in § 347.12(a) or hamamelis water identified in § 347.12(c).* "If condition worsens or symptoms persist for more than 7 days, discontinue use of the product and consult a" (select one of the following: "physician" or "doctor.")

(3) *For products containing aluminum acetate identified in § 347.12(a) used as a compress or wet dressing.* "Do not cover compress or wet dressing with plastic to prevent evaporation."

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions:"

(1) *For products containing aluminum acetate identified in § 347.12(a)*—(i) *For products used as a soak.* "For use as a soak: Soak affected area in the solution for 15 to 30 minutes. Repeat 3 times a day. Discard remaining solution after use."

(ii) *For products used as a compress or wet dressing.* "For use as a compress or wet dressing: saturate a clean, soft, white cloth (such as a diaper or torn sheet) in the solution, gently squeeze, and apply loosely to the affected area. Saturate the cloth in the solution every 15 to 30 minutes and apply to the affected area. Repeat as often as necessary. Discard remaining solution after use."

(2) *For products containing aluminum sulfate identified in § 347.12(b) for use as a styptic pencil.* "Moisten tip of pencil with water and apply to the affected area. Dry pencil after use."

(3) *For products containing hamamelis water identified in § 347.12(c).* "Apply to the affected area as often as necessary."

PART 348—EXTERNAL ANALYGESIC DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

5. The authority citation for 21 CFR Part 348 (proposed in the **Federal Register** of September 7, 1982; 47 FR 39412) is revised to read as follows:

Authority: 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); 5 U.S.C. 553; 21 CFR 5.10 and 5.11.

§§ 348.6, 348.10, 348.50 [Amended]

6. In § 348.3 paragraph (h), in § 348.10 paragraph (c), and in § 348.50 paragraphs (a)(3), (b)(4) and (5), (c)(7) and (8), and (d)(2)(i) and (ii) are withdrawn.

Dated: February 27, 1989.

Frank E. Young,

Commissioner of Food and Drugs.

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