DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 347

[Docket No. 78N–021A]

RIN 0910–AA01

Skin Protectant Drug Products for Over-the-Counter Human Use; Astringent Drug Products; Final Monograph; Proposed Rule

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to amend the regulation that established conditions under which over-the-counter (OTC) skin protectant astringent drug products are generally recognized as safe and effective and not misbranded. This action would revise some labeling for astringent drug products to be consistent with the final rule for OTC skin protectant drug products (68 FR 33362, June 4, 2003) and would add labeling for certain small packages (styptic pencils). This action is part of FDA's ongoing review of OTC drug products. This proposed rule is a companion document to the direct final rule published elsewhere in this issue of the **Federal Register**.

DATES: Submit written comments on the proposed rule by August 27, 2003.

ADDRESSES: Submit written comments on the proposed rule to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments*.

FOR FURTHER INFORMATION CONTACT: Gerald M. Rachanow, Center for Drug Evaluation and Research (HFD–560), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–2307.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of October 21, 1993 (58 FR 54458), FDA published a final monograph for OTC skin protectant astringent drug products in part 347 (21 CFR part 347), subpart A. In the **Federal Register** of June 4, 2003 (68 FR 33362), FDA published a final rule for OTC skin protectant drug products and revised the format of part 347. Subpart A was redesignated as ''General Provisions,'' and the astringent active ingredients (§ 347.10) and labeling (§ 347.50) were redesignated as §§ 347.12 and 347.52, respectively.

Two ingredients (colloidal oatmeal and sodium bicarbonate) added to the skin protectant monograph are used as a soak, compress, or wet dressing similar to the astringent active ingredient aluminum acetate. In the skin protectant final monograph, the agency included a warning about soaking too long (§ 347.50(c)(7)) and included directions for colloidal oatmeal (§ 347.50(d)(2)) and sodium bicarbonate (§ 347.50(d)(3)) that are shorter than the directions for aluminum acetate (§ 347.52(d)(1)) and that are in the new OTC drug labeling format. In this proposed rule, the agency is adding this warning, shortening the directions for aluminum acetate drug products, and stating these directions in the new OTC drug labeling format.

Section 201.66(d)(10) (21 CFR 201.66(d)(10)) of the OTC drug labeling rule (64 FR 13254 at 13286, March 17, 1999) establishes a modified labeling format for small packages that need more than 60 percent of their total surface area available to bear labeling to meet the requirements of § 201.66(c)(1) through (c)(9) and (d)(1) through (d)(9). The agency stated in that rule that it would consider additional approaches for accommodating certain products in their respective monographs, taking into consideration the risks and benefits of the drug, the intended use, and the need to communicate limitations or restrictions about the use of the product to the target population (64 FR 13254 at 13270, March 17, 1999). The 2003 skin protectant final monograph included additional labeling exemptions for certain small packages (lip protectant products) that meet the size criteria established in § 201.66(d)(10). The agency determined that lip protectant/lip balm products are typically packaged in small amounts, applied to limited areas of the body, have a high therapeutic index, carry extremely low risk in actual consumer use situations, provide a favorable public health benefit, require no specified dosage limitation, and require few specific warnings and no general warnings (e.g., pregnancy or overdose warnings).

Consequently, the agency is now proposing to include additional labeling exemptions for certain small packages of skin protectant astringent drug products (styptic pencils) that meet the criteria established in § 201.66(d)(10), taking into consideration the risks and benefits of the drug, the intended use, and the need to communicate limitations or restrictions about the use of the product to the target population. For the safety profile of styptic pencils, the agency considered the recommendations of the Advisory Review Panel on OTC Miscellaneous External Drug Products (the Panel). The Panel noted that ''In 75 years of marketing styptic pencils there have been [no] reported instances of human toxicity'' (47 FR 39412 at 39429, September 7, 1982). (The word ''no'' was inadvertently left out of the September 7, 1982, publication, and the agency corrected this error in its notice of proposed rulemaking for OTC skin protectant astringent drug products (54 FR 13490 at 13493, April 3, 1989).) The Panel also stated that aluminum sulfate (the active ingredient in styptic pencils) ''has little, if any, cell permeability and exerts its effect on the cell surface.'' The only side effect the Panel noted was that application of the styptic pencil on a cut may result in some stinging. Thus, these products have an extremely low risk in actual consumer use situations, and the monograph only requires two general warnings (§ 347.50(c)(1)) and no ingredient specific warnings.

The agency also considered the factors listed above that were the basis for labeling modifications for OTC lip protectant/lip balm drug products. Like those products, styptic pencils are packaged in small amounts, have a high therapeutic index and a favorable public health benefit (stop bleeding), would be used infrequently and on very limited areas of the body to stop bleeding of minor cuts from shaving, require minimal warnings (there is no pregnancy warning because this is a topical product), and have no specified dosage limitation (the directions for use are to apply to the affected area). For these reasons, the agency is including specific labeling provisions for certain small packages of skin protectant astringent drug products (styptic pencils) in this proposed rule.

II. Description of the Labeling Revisions

The warning in § 347.50(c)(7), when the colloidal oatmeal or sodium bicarbonate product is labeled for use as a soak, compress, or wet dressing, states: ''When using this product [bullet] in some skin conditions, soaking too long may overdry.'' The agency is proposing to add this warning in new § 347.52(c)(4) for products containing aluminum acetate when labeled for use as a soak, compress, or wet dressing. Our decision to revise the warning set forth in this direct final rule is based upon a finding that bathing can dry the skin out and exacerbate some conditions (as discussed in the 2003 skin protectant final monograph (68 FR 33362 at 33367). Mandating a warning does not require a finding that any or all of the astringent drug products actually caused

an adverse event, and FDA does not so find. Nor does FDA's mandate of a warning repudiate the OTC drug monograph under which the affected drug products have been lawfully marketed. Rather, as a consumer protection agency, FDA has determined that this revised warning is necessary to ensure that these OTC drug products continue to be safe and effective for their labeled indications under ordinary conditions of use as those terms are defined in the Federal Food, Drug, and Cosmetic Act.

FDA's decision to act in an instance such as this one need not meet the standard of proof required to prevail in a private tort action (*Glastetter* v. *Novartis Pharmaceuticals, Corp.*, 252 F.3d 986, 991 (8th Cir. 2001)). To mandate a warning, or take similar regulatory action, FDA need not show, nor do we allege, actual causation.

The agency is proposing to revise the directions in § 347.52(d)(1)(i) for aluminum acetate used as a soak to read: ''For use as a soak: [bullet] soak affected area for 15 to 30 minutes as needed, or as directed by a doctor [bullet] repeat 3 times a day or as directed by a doctor [bullet] discard solution after each use''. The agency is proposing to revise the directions in § 347.52(d)(1)(ii) for aluminum acetate used as a compress or wet dressing to read: ''For use as a compress or wet dressing: [bullet] soak a clean, soft cloth in the solution [bullet] apply cloth loosely to affected area for 15 to 30 minutes [bullet] repeat as needed or as directed by a doctor [bullet] discard solution after each use''. The agency is also proposing to shorten the directions in § 347.52(d)(3) for products containing witch hazel to read: ''apply as often as needed''.

The agency is proposing to add new § 347.52(e) for products containing aluminum sulfate formulated as a styptic pencil. This section allows products that meet the criteria established in § 201.66(d)(10) to be marketed with reduced labeling.

III. Additional Information

This proposed rule is a companion to the direct final rule published in the final rules section of this issue of the **Federal Register**. This companion proposed rule and the direct final rule are identical. This companion proposed rule will provide the procedural framework to finalize the rule in the event the direct final rule receives significant adverse comments and is withdrawn. The comment period for this companion proposed rule runs concurrently with the comment period of the direct final rule. Any comments received under the companion proposed rule will be treated as comments regarding the direct final rule.

If no significant adverse comment is received in response to the direct final rule, no further action will be taken related to this proposed rule. Instead, FDA will publish a confirmation document stating that the direct final is effective as of 135 days after the date of publication in the **Federal Register**. If FDA receives significant adverse comments, the agency will withdraw the direct final rule. FDA will proceed to respond to all of the comments received regarding the rule and, if appropriate, the rule will be finalized under this companion rule using usual notice-and-comment procedures.

For additional information, see the corresponding direct final rule published in the final rules section of this issue of the **Federal Register**. FDA will not provide additional opportunity for comment. A significant adverse comment is one that explains why the rule would be inappropriate, including challenges to the rule's underlying premise or approach, or would be ineffective or unacceptable without a change. A comment recommending a rule change in addition to this rule will not be considered a significant adverse comment, unless the comment states why this rule would be ineffective without the additional change.

IV. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (2 U.S.C. 1501 *et seq.*). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Under the Regulatory Flexibility Act, if a rule has a significant economic impact on a substantial number of small entities, an agency must analyze regulatory options that would minimize any significant impact of the rule on small entities. Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement and economic analysis before proposing any rule that may result in an expenditure in any one year by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million (adjusted annually for inflation).

The agency concludes that this proposed rule is consistent with the principles set out in the Executive order and in these two statutes. The proposed rule is not a significant regulatory action as defined by the Executive order and so is not subject to review under the Executive order. FDA has determined that the proposed rule does not have a significant economic impact on a substantial number of small entities. The Unfunded Mandates Reform Act does not require FDA to prepare a statement of costs and benefits for this proposed rule, because the proposed rule is not expected to result in any 1–year expenditure that would exceed $100 million adjusted for inflation. The current inflation adjusted statutory threshold is about $110 million.

The purpose of this proposed rule is to make some minor labeling revisions in the previously issued astringents portion of the skin protectant drug products monograph to make the labeling consistent with the rest of the monograph and to add small package labeling provisions for aluminum sulfate marketed as a styptic pencil.

Current manufacturers of these products should incur only minor costs to relabel their products to meet the monograph. Some manufacturers will have to add a warning and revise the directions in their labeling. The agency will provide either 24 months from the date of publication of a final rule or the date of the first major labeling revision after the effective date of the final rule, whichever occurs first, for the manufacturers to use up existing labeling and to print new labeling that incorporates the labeling included in any final rule that may publish based on this proposal. Further, the labeling in the proposed rule is in the new OTC drug labeling format. Therefore, no additional professional skills are needed and manufacturers will not incur expenses determining how to state the product's labeling.

The agency believes that relabeling costs of the type required by this proposed rule generally average about $2,000 to $3,000 per stock keeping unit (SKU) (individual products, packages, and sizes). Assuming that there are about 25 affected OTC SKU's in the marketplace, total one-time costs of relabeling would be $50,000 to $75,000. The agency believes that the actual cost could be lower for the reasons stated in the previous paragraph.

For the reasons stated above and under the Regulatory Flexibility Act (5 U.S.C. 605(b)), the Commissioner certifies that this proposed rule will not have a significant economic impact on a substantial number of small entities.

V. Paperwork Reduction Act of 1995

FDA concludes that the labeling requirements in this document are not subject to review by the Office of Management and Budget because they do not constitute a ''collection of information'' under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 *et seq.*). Rather, the labeling statements are a ''public disclosure of information originally supplied by the Federal government to the recipient for the purpose of disclosure to the public'' (5 CFR 1320.3(c)(2)).

VI. Environmental Impact

The agency has determined under 21 CFR 25.31(a) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VII. Request for Comments

This comment period runs concurrently with the comment period for the direct final rule; any comments received will be considered as comments regarding the direct final rule. Interested persons may submit to the Dockets Management Branch (see **ADDRESSES**) written or electronic comments regarding this document. Submit a single copy of electronic comments to *http://www.fda.gov/dockets/ecomments* or three hard copies of any written comments, except that individuals may submit one hard copy. Comments are to be identified with the docket number forund in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday. In the event the direct final rule is withdrawn, all comments received will be considered comments on this proposed rule.

List of Subjects in 21 CFR Part 347

Labeling, Over-the-counter drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 347 be amended 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 continues to read as follows:

Authority: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371.

2. Section 347.52 is amended by adding paragraphs (c)(4) and (e) and by revising paragraphs (d)(1)(i), (d)(1)(ii), and (d)(3) to read as follows:

§ 347.52 Labeling of astringent drug products.

* * * * *

(c) * * *

(4) *For products containing aluminum acetate identified in § 347.12(a) when labeled for use as a soak, compress, or wet dressing.* ''When using this product [bullet] in some skin conditions, soaking too long may overdry''.

(d) * * *

(1) * * *—(i) *For products used as a soak.* ''For use as a soak: [bullet] soak affected area for 15 to 30 minutes as needed, or as directed by a doctor [bullet] repeat 3 times a day or as directed by a doctor [bullet] discard solution after each use''.

(ii) *For products used as a compress or wet dressing.* ''For use as a compress or wet dressing: [bullet] soak a clean, soft cloth in the solution [bullet] apply cloth loosely to affected area for 15 to 30 minutes [bullet] repeat as needed or as directed by a doctor [bullet] discard solution after each use''.

* * * * *

(3) *For products containing witch hazel identified in § 347.12(c).* ''Apply as often as needed''.

(e) *Products formulated and labeled as a styptic pencil and that meet the criteria established in § 201.66(d)(10) of this chapter.* The title, headings, subheadings, and information described in § 201.66(c) of this chapter shall be printed in accordance with the following specifications:

(1) The labeling shall meet the requirements of § 201.66(c) of this chapter except that the headings and information described in § 201.66(c)(3) and (c)(7) may be omitted, and the headings, subheadings, and information described in § 201.66(c)(4) and (c)(5) may be presented as follows:

(i) The heading and indication required by § 201.66(c)(4) of this chapter may be limited to: ''Use [in bold type] stops bleeding of minor cuts from shaving''.

(ii) The ''external use only'' warning in § 347.52(c)(1) and in § 201.66(c)(5)(i) of this chapter may be omitted. The second warning in § 347.52(c)(1) may state: ''Avoid contact with eyes''. The warning in § 201.66(c)(5)(x) may be limited to the following: ''Keep out of reach of children.'' The subheadings in § 201.66(c)(5)(iii) through (c)(5)(vii) may be omitted, provided the information after the heading ''Warning'' contains the warnings in this paragraph.

(2) The labeling shall be printed in accordance with the requirements of § 201.66(d) of this chapter, except that any requirements related to § 201.66(c)(3) and (c)(7) and the horizontal barlines and hairlines described in § 201.66(d)(8), may be omitted.

Dated: May 27, 2003.

Jeffrey Shuren,

Assistant Commissioner for Policy.

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ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 62

[FRL–7511–5]

Approval and Promulgation of State Plans for Designated Facilities and Pollutants: Louisiana, New Mexico, Oklahoma and Bernalillo County, NM; Negative Declarations

AGENCY: Environmental Protection Agency (EPA).

ACTION: Proposed rule.

SUMMARY: EPA is proposing to approve negative declarations submitted by the States of Louisiana, New Mexico, Oklahoma, and the City of Albuquerque (Bernalillo County), New Mexico, which certify that there are no existing small municipal waste combustion units in Louisiana, New Mexico, and Oklahoma subject to the requirements of sections 111(d) and 129 of the Clean Air Act (CAA). EPA is also proposing to approve negative declarations submitted by the State of New Mexico and the City of Albuquerque (Bernalillo County) which certify that there are no existing hospital/medical/infectious waste incinerators subject to the requirements of sections 111(d) and 129 of the CAA. In addition, EPA is proposing to approve a negative declaration submitted by the City of Albuquerque (Bernalillo County) which certifies that there are no existing large municipal waste combustion units subject to the requirements of sections 111(d) and 129 of the CAA. Finally, EPA is proposing to approve a negative declaration submitted by the State of New Mexico which certifies that there are no existing commercial and industrial solid waste incineration units subject to the requirements of sections 111(d) and 129 of the CAA.

DATES: Written comments must be received by July 14, 2003.