DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 310

[Docket No. 78N-301D]

RIN 0905-AA06

External Analgesic Drug Products for Over-the-Counter Human Use; Diaper Rash Labeling Claims

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule establishing that any over-the-counter (OTC) external analgesic drug product for use in the treatment and/or prevention of diaper rash is not generally recognized as safe and effective and is misbranded. FDA is issuing this final rule after considering public comments on the agency's notice of proposed rulemaking, and all new data and information on external analgesic drug products for use in the treatment and/or prevention of diaper rash that have come to the agency's attention. This final rule is part of the ongoing review of OTC drug products conducted by FDA.

EFFECTIVE DATE: June 18, 1993.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD-810), 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), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking and reopened the administrative record for the rulemaking for OTC external analgesic drug products, to allow for consideration of a statement on OTC drug products for the treatment of diaper rash prepared by the Advisory Review Panel on OTC Miscellaneous External Drug Products (the Panel), which was the advisory review panel responsible for evaluating data on the active ingredients used for the treatment of diaper rash. 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 the Federal Register of December 28, 1982 (47 FR 57738), in response to a request for an extension of time, the comment period and reply comment period for OTC external analgesic drug products were extended to February 4, 1983, and to March 7, 1983, respectively.

In accordance with § 330.10(a)(10), the data and information considered by the Panel, after deletion of a small amount of trade secret information, were placed on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration, rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857.

The agency's notice of proposed rulemaking for OTC external analgesic drug products for the treatment and/or prevention of diaper rash was published in the Federal Register of June 20, 1990 (55 FR 25234). Interested persons were invited to file by December 17, 1990, written comments, objections, or requests for oral hearing before the Commissioner of Food and Drugs regarding the proposal. Interested persons were invited to file comments on the agency's economic impact determination by December 17, 1990. New data could have been submitted until June 20, 1991 and comments on the new data until August 20, 1991. Final agency action occurs with the publication of this final rule on OTC external analgesic drug products for the treatment and/or prevention of diaper rash.

In response to the notice of proposed rulemaking for OTC external analgesic drug products for the treatment and/or prevention of diaper rash, one manufacturer submitted two comments. Neither comment discussed active ingredients or labeling claims that would be pertinent to external analgesic diaper rash drug products. Both comments were also submitted to the three other rulemakings that include OTC diaper rash ingredients: OTC topical antifungal, topical antimicrobial, and skin protectant drug products. The comments addressed skin protectant active ingredients and labeling claims and will be discussed in the final monograph for OTC skin protectant drug products for the treatment and/or prevention of diaper rash. Copies of the comments received are on public display in the Dockets Management Branch (address above).

In the notice of proposed rulemaking for OTC external analgesic drug products, published in the Federal Register of February 8, 1983 (48 FR 5852 at 5868 and 5869), the agency stated that drug products containing external analgesic active ingredients, which are intended for the relief of pain and/or itching or for the relief of minor aches and pains, should not be used on children under 2 years of age except as recommended by a physician. The agency discussed the possibility of cutaneous absorption due to occlusion of the skin, as from a diaper, and mentioned that analgesic drugs can be corrosive to infants' skin under occlusion (48 FR 5864). The agency added that children at the age of 2 years are just beginning to learn to communicate verbally in expressing their symptoms to a parent, whereas children below the age of 2 years (a major portion of the target population for diaper rash drug products) are more passive and less able to express and localize symptoms to a parent.

The agency reiterated these views in the notice of proposed rulemaking for OTC external analgesic drug products for the treatment and/or prevention of diaper rash and concluded that external analgesic active ingredients should not be present in OTC diaper rash drug products (55 FR 25234 at 25236 and 25237). No comments were submitted in opposition to the agency's proposal.

In the Federal Register of August 25, 1992 (57 FR 38568 at 38573), the agency published a notice of proposed rulemaking stating that certain ingredients in OTC drug products are not generally recognized as safe and effective or are misbranded. The ingredients listed in this proposal included any external analgesic ingredients labeled with claims or directions for use in the treatment and/or prevention of diaper rash. No comments were received on this diaper rash portion of the proposal.

Based on the above, the agency concludes that no OTC external analgesic drug product labeled for the treatment and/or prevention of diaper rash is generally recognized as safe and effective. Accordingly, the agency is declaring that OTC drug products labeled for use in the treatment and/or prevention of diaper rash should not be formulated to contain any external analgesic active ingredients.

The agency emphasizes that this final rule for OTC external analgesic drug products, as it relates to OTC diaper rash drug products, does not apply to: (1) Active ingredients included in the external analgesic final monograph, to be published in a future issue of the Federal Register, that are Category I antipruritics for claims other than diaper rash; and (2) active ingredients included in both the external analgesic and skin protectant rulemakings where the ingredient is a Category I skin protectant making allowable diaper rash skin protectant claims, e.g., sodium bicarbonate.

Any OTC external analgesic drug product bearing any claims or directions

for use of the product for the treatment and/or prevention of diaper rash may not continue to be initially introduced or delivered for introduction into interstate commerce unless it is the subject of an approved application or abbreviated application (hereinafter called application). The agency is amending 21 CFR part 310 by adding to subpart E, new § 310.545(a)(10)(iv) (21 CFR 310.545(a)(10)(iv)) to include any external analgesic drug products labeled for use in the treatment and/or prevention of diaper rash. Any claims or directions for using an OTC external analgesic drug product in the treatment and/or prevention of diaper rash should be eliminated from OTC drug products by June 18, 1993, regardless of whether further testing is undertaken to justify future use. Thereafter, any OTC drug product containing any external analgesic active ingredient and labeled or intended for use in the treatment and/or prevention of diaper rash will be considered nonmonograph and misbranded under section 502 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 352) and a new drug under section 201(p) of the act (21 U.S.C. 321(p)) for which an approved application under section 505 of the act (21 U.S.C. 355) and 21 CFR part 314 of the regulations is required for marketing. Therefore, on or after June 18, 1993, no OTC drug product containing any external analgesic active ingredient labeled or intended for use in the treatment and/or prevention of diaper rash 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 containing any active ingredient subject to this final rule that is repackaged or relabeled after the effective date of this final rule must be in compliance with the final rule regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufacturers are urged to comply voluntarily with this final rule at the earliest possible date.

The agency points out that publication of this final rule does not preclude a manufacturer's testing an external analgesic ingredient for diaper rash uses. New, relevant data can be submitted to the agency at a later date as the subject of an application that may provide for prescription or OTC marketing status. (See 21 CFR part 314.) As an alternative, where there are adequate data establishing general recognition of safety and effectiveness for these uses such data may be submitted in an appropriate citizen petition to amend the final monograph for OTC external analgesic drug products. (See 21 CFR 10.30.) However, marketing of products containing external analgesic active ingredients and bearing diaper rash claims or directions for use may not begin or continue while the data are being evaluated by the agency.

No comments were received in response to the agency's request for specific comment on the economic impact of this rulemaking (55 FR 25234 at 25237). The agency concludes that there is no basis for the continued marketing of any OTC external analgesic drug products with claims or directions for use in the treatment and/or prevention of diaper rash. As a result of this final rule, manufacturers will need to relabel some external analgesic drug products to delete these claims and/or directions for use prior to promulgation of the final monograph for OTC external analgesic drug products and/or reformulate and relabel some OTC skin protectant drug products prior to promulgation of the final monograph for OTC skin protectant drug products for the treatment and/or prevention of diaper rash, where such products contain both an external analgesic and a skin protectant active ingredient. The final rule for OTC skin protectant drug products for the treatment and/or prevention of diaper rash will be published in a future issue of the Federal Register.

Early finalization of the nonmonograph status of external analgesic active ingredients having diaper rash claims will benefit both consumers and manufacturers. Consumers will benefit from the early removal from the marketplace of product claims for which safety and effectiveness have not been established. This will result in a direct economic savings to consumers. Manufacturers of diaper rash drug products will benefit from being able to continue to market products containing other ingredients that have been proposed by the agency as being generally recognized as safe and effective, without manufacturers incurring additional expense of clinical testing to support these claims. (See proposed § 347.10, 48 FR 6820 at 6832 (February 15, 1983), and § 347.10, 55 FR 25204 at 25232.) In addition, external analgesic active ingredients will remain available for other claims that have been proposed by the agency as being generally recognized as safe and effective, without manufacturers incurring additional expense of clinical testing to support these claims. (See proposed § 348.50(b), 48 FR 5852 at 5868.) As noted above, some product reformulation and/or relabeling may be needed. The agency is aware of a limited number of diaper rash drug products that contain external analgesic active ingredients. Based on the above, the agency certifies that this final rule will not have a significant economic impact on a substantial number of small entities.

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 effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

List of Subjects in 21 CFR Part 310

Administrative practice and procedure, Drugs, Labeling, Medical devices, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 310 is amended as follows:

PART 310—NEW DRUGS

1. The authority citation for 21 CFR part 310 continues to read as follows:

Authority: Secs. 201, 301, 501, 502, 503, 505, 506, 507, 512–516, 520, 601(a), 701, 704, 705, 706 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 360b–360f, 360j, 361(a), 371, 374, 375, 376); secs. 215, 301, 302(a), 351, 354–360F of the Public Health Service Act (42 U.S.C. 216, 241, 242(a), 262, 263b–263n).

2. Section 310.545 is amended by adding new paragraph (a)(10)(iv), by revising the introductory text of paragraph (d), and by adding new paragraph (d)(9), to read as follows:

§ 310.545 Drug products containing certain active ingredients offered over-the-counter (OTC) for certain uses.

(a) * * *

(10) * * *

(iv) *Diaper rash drug products.* Any ingredient(s) labeled with claims or directions for use in the treatment and/or prevention of diaper rash.

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(d) Any OTC drug product that is not in compliance with this section is subject to regulatory action if initially introduced or initially delivered for introduction into interstate commerce after the dates specified in paragraphs (d)(1) through (d)(9) of this section.

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(9) June 18, 1993, for products subject to paragraph (a)(10)(iv) of this section.

Dated: October 9, 1992.

Michael R. Taylor,

Deputy Commissioner for Policy.

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