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Part II

Department of  
Health and Human  
Services

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Food and Drug Administration

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21 CFR Part 347

Skin Protectant Drug Products for Over-  
the-Counter Human Use; Diaper Rash  
Products; Proposed Rule

individually classified by either Panel for use in diaper rash.

Several submissions (Ref. 5) were for products containing stabilized aloe vera for topical use for numerous indications including diaper rash, and one submission (Ref. 6) was for a product containing vitamin E for numerous skin conditions, including diaper rash. Subsequently, the manufacturers withdrew all of these submissions (Refs. 7, 8, and 9). Accordingly, the agency is not evaluating stabilized aloe vera and vitamin E in this rulemaking.

#### References

(1) OTC Volumes 160021, 160025, 160027, 160036, 160041, 160053, 160077, 160091, 160150, 160179, 160221, 160235, 160243, 160245, and 160357.

(2) OTC Volumes 160021, 160025, 160027, and 160179.

(3) OTC Volumes 160028, 160041, 160067, and 160179.

(4) OTC Volumes 160052 and 160086.

(5) OTC Volumes 160252, 160273, 160274, 160422, and 160423.

(6) OTC Volume 160067.

(7) Letter from B.C. Coats, Aloe Vera of America, Inc., to W. E. Gilbertson, FDA, dated April 5, 1983, in OTC Volume 06DRSTFM, Docket No. 78N-021D, Dockets Management Branch.

(8) Letter from A.J. Davis, Aloe Vera of America, Inc., to W. E. Gilbertson, FDA, dated October 24, 1986, in OTC Volume 06DRSTFM, Docket No. 78N-021D, Dockets Management Branch.

(9) Letter from S. Most, Block Drug Co., Inc., to Division of OTC Drug Evaluation, FDA, dated November 6, 1986, in OTC Volume 06DRSTFM, Docket No. 78N-021D, Dockets Management Branch.

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

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

##### 1. Summary of Ingredient Categories

Although the Panel discussed the use of skin protectant ingredients for the treatment of diaper rash, it did not review or classify any individual ingredients. All ingredients in marketed products submitted to the Panel or ingredients that appeared in the call-for-data notices were simply listed in the Panel's statement on OTC drug products for the treatment of diaper rash (47 FR 39436 at 39439). The Panel recommended that the use of skin protectant ingredients included in this list be referred to the rulemaking for OTC skin protectant drug products and requested comments from any interested person on the use of any of these ingredients for the treatment of diaper rash.

The agency has reviewed all claimed active ingredients submitted to the Miscellaneous External Panel, the

recommendations of the Topical Analgesic Panel on OTC skin protectant drug products (43 FR 34628), the tentative final monograph on OTC skin protectant drug products (48 FR 6820), and other data and information available at this time. Based upon this information, the agency is proposing the following categorization of skin protectant active ingredients for the treatment and prevention of diaper rash:

Ingredient	Category
Aldicarb	III
Allantoin	I
Aloe vera <sup>1</sup>	N/A
Aluminum acetate	III
Aluminum hydroxide	III
Bismuth subnitrate	III
Boric acid	II
Calamine	I
Casein (calcium caseinate) <sup>1</sup>	N/A
Cellulose, microporous	III
Cholecalciferol	III
Cocoa butter	III
Cod liver oil (in combination)	I
Colloidal oatmeal	III
Cysteine hydrochloride	III
Dexpantrolol	III
Dimethicone	I
Glycerin	III
Kaolin	I
Lanolin (in combination)	I
Live yeast cell derivative	III
Mineral oil	I
Peruvian balsam	III
Peruvian balsam oil	III
Petrolatum	I
Protein hydrolysate (1-leucine, 1-isoleucine, 1-methionine, 1-phenylalanine, and 1-tyrosine)	III
Racemethionine	III
Shark liver oil	III
Sodium bicarbonate	III
Sulfur	II
Talc	I
Tannic acid	II
Topical starch	I
Vitamin A	III
Vitamin E <sup>1</sup>	N/A
White petrolatum	I
Zinc acetate	III
Zinc carbonate	III
Zinc oxide	I

<sup>1</sup> Not classified—withdrawn from review.

##### 2. Testing of Category II and Category III Conditions

The agency is not proposing specific testing guidelines in this document. Interested persons may communicate with the agency about the submission of data and information to demonstrate the safety or effectiveness of any skin protectant 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 Agency's Changes

FDA has considered the comments and other relevant information and concludes that it will tentatively adopt the substance of the Panel's statement. In the absence of a specific monograph recommendation from the Panel, the agency has developed a monograph based on its evaluations of the data and its responses to the comments above and below.

The agency has revised the Panel's definition of diaper rash, which was as follows:

Diaper rash is a common skin problem of infancy, caused by contact with urine and feces, worsened by occlusion with plastic pants, and often secondarily infected with *Candida albicans*. (See 47 FR 39440.)

One comment noted that diaper rash is perhaps best viewed as a group of disorders rather than a specific diagnosis. The comment stated that the condition commonly referred to as diaper rash is an acute, inflammatory reaction of the skin in the diaper area, which may range from mild (characterized by mild erythema with or without chafing) to severe (characterized by vesicles, pustules, or bullae). The comment added that mild diaper rash is primarily caused by one or more diverse chemical and mechanical irritants. The comment stated that a major cause of diaper rash is the exposure of tender skin for relatively long periods of time to moisture from urine and to feces, with this exposure taking place in an enclosed, humid area. The skin is hydrated and susceptible to frictional irritation as well as chemical irritation.

In reviewing numerous articles on diaper rash that have appeared in the literature (Refs. 1 through 12), the agency notes that various authors have defined diaper rash in different ways. The agency has evaluated these, the Panel's, and the comment's definitions and is proposing the following definition in § 347.3 of this tentative final monograph:

*Diaper rash or diaper dermatitis.* An inflammatory skin condition in the diaper area (perineum, buttocks, lower abdomen, and inner thighs) caused by one or more of the following factors: moisture, occlusion, chafing, continued contact with urine or feces or both, or mechanical or chemical irritation. Mild conditions appear as simple erythema. More severe conditions include papules, vesicles, oozing, and ulceration.