

Alpha-hydroxycaprylic acid, alpha-hydroxyoctanoic acid, alpha-hydroxyethanoic acid and ammonium alpha-hydroxyetanoate, alpha hydroxy and botanical complex, glycolic acid, glycolic acid and ammonium glycolate, glycomer in crosslinked fatty acids alpha nutrium, hydroxycaprylic acid, L-alpha hydroxy acid, lactic acid, mixed fruit acid, sugar cane extract, tri-alpha hydroxy fruit acids, triple fruit acid

Beta hydroxy acids
Beta hydroxybutanoic acid, salicylic acid¹, trethocanic acid, tropic acid
Alpha and beta hydroxy acids
Citric acid, malic acid
Other ingredients

Egg albumin, magnesium aluminum silicate, protein, sodium silicate

¹ From a chemist's perspective, based on its chemical structure, salicylic acid is not a true beta hydroxy acid. However, cosmetic companies often refer to this ingredient as a beta hydroxy acid. Consequently, many consumers think of it as one as well.

III. Categories That Will Not Be Reviewed

A. Categories Reclassified or Considered as Foods

The categories "salt substitutes," "salt tablets," and "sweeteners" were included in the 1975 call-for-data notice (40 FR 38179 at 38183). These types of products are currently regulated as foods and will not be further considered as part of the OTC drug review. During the course of the review, several parties inquired whether "oral electrolyte replacement" products and "weight increasing" products would be included in the review because these product categories were not mentioned in the 1973 and 1975 call-for-data notices. Oral electrolyte replacement products intended to treat diarrhea are regulated as medical foods under section 529(b)(3) of the act (21 U.S.C. 360ee(b)(3) and 21 CFR 101.9(j)(8)), and products for "weight gain" are considered foods (21 U.S.C. 301 *et seq.*).

B. Categories Reclassified or Considered as Medical Devices

In several instances, since 1975, FDA determined that certain types of products previously regulated as drugs should be regulated as medical devices and changed its regulatory approach accordingly (Ref. 4). These products include a spray-on dressing that does not contain a drug component and a "device incorporating a drug component with the combination product having the primary intended purpose of fulfilling a device function." This latter group of products includes a skin closure or bandage with an

antimicrobial agent and a wound dressing with an antimicrobial agent. These products are considered combination products regulated by the Center for Devices and Radiological Health (CDRH), using device authorities under the act.

A liquid bandage⁵ is defined in 21 CFR 880.5090 as "a sterile device that is a liquid, semiliquid, or powder and liquid combination used to cover an opening in the skin or as a dressing for burns. The device is also used as a topical skin protectant." A medical adhesive tape and adhesive bandage is defined in 21 CFR 880.5240 as:

"* * * a device intended for medical purposes that consists of a strip of fabric material or plastic, coated on one side with an adhesive, and may include a pad of surgical dressing without a disinfectant. The device is used to cover and protect wounds, to hold together the skin edges of a wound, to support an injured part of the body, or to secure objects to the skin."

FDA is not including any of these device products in this current call for data.

IV. Request for Data and Information

FDA invites the submission of data, published and unpublished, and other information, pertinent to all active ingredients in these and other eligible unreviewed OTC drug categories (see section II of this document). Interested persons should include any consumer comprehension data relating to the OTC use of drug products containing these ingredients. These data and information will contribute to the following objectives:

- Facilitate FDA's review and aid in its determination of whether these OTC drugs for human use are generally recognized as safe and effective and not misbranded under their recommended conditions of use, and

- Provide all interested persons an opportunity to present for consideration the best data and information available to support the stated claims for these products. Any relevant data and information on these drug products that may have been submitted to earlier rulemakings or in response to earlier call-for-data notices should be updated and resubmitted to facilitate FDA's review of these products.

FDA also requests manufacturers to identify other OTC drug products that still need to be reviewed to determine

⁵The categories "liquid bandages (sprays)—protective skin preparations" and "medicated bandages" were in the 1975 call-for-data notice (40 FR 38179 at 38181), which listed 23 active ingredients possibly used in these products. These ingredients in products for these specific uses would not be considered OTC drug active ingredients.

if they are GRAS/E for OTC use. For OTC drug products that should have been submitted for review but for which data and information have not been received, FDA may not consider those products to be GRAS/E for OTC use. In accordance with section 201(p) of the act, such drug products would be considered new drugs and would need an NDA to be marketed.

In the **Federal Register** of January 23, 2002 (67 FR 3060), FDA published a final rule providing additional criteria and procedures for classifying OTC drugs as GRAS/E and not misbranded. The procedures identified in that rule apply to OTC drugs initially marketed in the United States after the OTC drug review began in 1972 and to OTC drugs without any U.S. marketing experience. This notice is not intended to apply to ingredients covered by the additional criteria and procedures identified in that rule.

This notice also does not apply to new chemical entities that have not previously been marketed for OTC use, regardless of the claims. These products should be submitted to FDA for evaluation in an NDA under 21 CFR part 314.

Manufacturers submitting data and information in response to this call for data should include any information (e.g., information showing when the product was first marketed in the United States) relating to the regulatory status of their product under the general regulatory policy described in the next section of this document. If such information does not exist or is found to be inadequate, such products may be at risk of regulatory action by FDA.

V. General Regulatory Policy

In order for a product to be eligible for the OTC drug review that began on May 11, 1972, the product or similarly formulated and labeled products had to be marketed as OTC drugs at the inception of the OTC drug review, which date was later extended to on or before December 4, 1975. Prescription drug products were also eligible for the review, as long as they continued to be marketed on a prescription basis while FDA evaluated data to ascertain whether the ingredient or combination of ingredients in the product could be proposed as GRAS/E for OTC use.

FDA may exercise its enforcement discretion to permit OTC drug products that do not have an approved NDA during the pendency of the OTC drug review to be marketed provided the following conditions are met:

1. The product or similarly formulated and labeled products were marketed as OTC drugs at the inception