FDA Publishes Proposed Rule in Federal Register Classifying Certain Ingredients and Categories of OTC Drug Products as Not “Generally Recognized as Safe and Effective”

On Thursday, June 19, 2008, the U.S. Food and Drug Administration (FDA) published a response to a 2003 Request for Data and Information in the form of a Proposed Rule. 73 Fed. Reg. 34895 (June 19, 2008). In the Proposed Rule, FDA proposes to classify certain over-the-counter (OTC) drug product categories and active ingredients as not “generally recognized as safe and effective” or as misbranded unless they are approved by FDA through the new drug approval (NDA) procedures.

FDA’s 2003 Request for Data and Information

The Proposed Rule responds to a 2003 Request for Data and Information (Call for Data) published in the Federal Register. See 68 Fed. Reg. 75585 (December 31, 2003). At that time and in accordance with the OTC drug review procedures, FDA identified several new OTC drug product categories and asked that interested parties submit data and information to show that the active ingredients used in these drug products are “generally recognized as safe and effective” (GRASE) for the identified OTC drug uses.

FDA also requested data and information on the use of two ingredients, aloe vera and urea, in existing OTC drug product categories, namely, use of aloe vera as an active ingredient in topical antimicrobials and use of aloe vera and urea as active ingredients in external analgesics.

Some products and claims identified in the Proposed Rule and original Call for Data have until now been considered to be cosmetic or non-medicated categories. If finalized as published, the Proposed Rule would cause these products to be regulated as unapproved new drugs. At the very least, compliance with the Proposed Rule as currently written will require relabeling and possible reformulation to avoid new drug status.

Proposed Rule Restricting the Use of Certain Ingredients and Product Categories

In the preamble to the Proposed Rule, FDA reports it received no submissions in support of the safe and effective use of most of the ingredients and drug categories listed in its 2003 Call for Data. Accordingly, for those ingredients and categories, the agency proposal identifies

1) the active ingredients considered Class II (nonmonograph) for uses identified in the Proposed Rule,

2) the product categories considered not GRASE and thus subject to NDA approval, and

3) the product claims and intended uses considered not GRASE and which cause products bearing such claims to be subject to NDA approval.
Active Ingredients Impacted by the Proposed Rule

- Any external analgesic drug products containing aloe vera or urea
- Any topical antimicrobial drug products containing aloe vera
- Any drug products containing urea for any labeled claims
- Ammonia as a reflex stimulant

Product Categories Impacted by the Proposed Rule

If finalized as proposed, the following drug product categories and product claims or intended uses would be considered misbranded without prior NDA approval.

Product Categories:

- Any skin protectant drug product with blister guard claims.
- Any skin protectant drug products labeled with claims or directions for use as a nipple protectant (previously referred to as breast creams) for use when nursing, except those containing lanolin, which will be considered as an active ingredient in a later Notice. Under the Proposed Rule, manufacturers will be prohibited from using the following active ingredients in such products: cetyl alcohol, cocoa butter, cod liver oil, dimethicone, glycerin, glycercyl monostearate, hard fat, mineral oil, petrolatum and white petrolatum.
- Any drug products formulated as wet dressings other than skin protectant and astringent drug products formulated and labeled in accordance with 21 CFR part 347 (Skin Protectant Drug Products for Over-the-Counter Human Use).

Product Claims or Instructions for Use for:

- Bed-wetting deterrents.
- Blemish remedies, other than topical acne drug products in compliance with 21 CFR 333 part D.
- Bunion remedies.
With respect to vaginal moisturizers, FDA requested data and information supporting the use of these products for indications such as “safe immediate relief for vaginal dryness,” which it apparently considers to be a drug indication.

Nasal Moisturizers:
FDA indicated its position that nasal moisturizers should be regulated under the OTC cough-cold or miscellaneous internal drug products monographs. FDA requested data and information supporting the safety and effectiveness of these products for claims such as “provides soothing moisture to dry, inflamed nasal membranes due to colds, allergies, low humidity, and other minor nasal irritations” or “use for dry nasal membranes caused by chronic sinusitis, allergy, asthma, dry air or oxygen therapy.”

Urinary Analgesics/Antiseptics:
FDA requested data on urinary analgesics/antiseptics and products for too frequent, burning, and painful urination. Specifically, FDA stated its intent to consider the use of phenazopyridine HCl in such products. Some of the issues for which FDA requested data included whether this condition is appropriate for self-medication, whether the product label should mention the need for treatment with an antibacterial drug, permissible ingredient strengths, neoplasia findings, carcinogenesis labeling statements and the existence of updated safety data.

Wrinkle Removers:
FDA sought information on the use of alpha hydroxyl acids and beta hydroxyl acids in such products.

Lanolin as a Nipple Protectant:
FDA received data and information on the safe use of lanolin in nipple protectant products. It did not receive any data or information on the following ingredients that were previously listed for use in nipple protectant products: cetyl alcohol, cocoa butter, cod liver oil, dimethicone, glycerin, glyceryl monostearate, hard fat, mineral oil, petrolatum, and white petrolatum. But for lanolin, FDA proposes prohibiting the use of these ingredients in nipple protectant products. Lanolin as a nipple protectant ingredient will be considered in a future Federal Register Notice.

Ichthammol as a Drawing Salve:
FDA received data on the safety of ichthammol for this use. It, however, did not receive data or information on the other drawing salve ingredients listed in the 2003 Call for Data including ergot fluid extract, juniper tar (oil of cade), magnesium sulfate, pine tar, rosin, rosin cerate, and sulfur. Ichthammol as a drawing salve ingredient will be considered in a future Federal Register Notice.

**Comments May Be Submitted Through September 17, 2008**

FDA will be accepting written or electronic comments on the Proposed Rule through September 17, 2008. Please do not hesitate to contact us if you would like additional information about the Proposed Rule and its potential impact, or would like to discuss submitting comments on the Proposed Rule or preparing a Citizen’s Petition in support of an ingredient or product category.

A link to FDA’s Proposed Rule is provided below:

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