
Guidance for Industry

Drug Products Containing Ensulizole, Hypromellose, Meradimate, Octinoxate, and Octisalate — Labeling Enforcement Policy

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
May 2003**

Procedural

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I. INTRODUCTION

This guidance discusses how FDA plans to exercise its enforcement discretion after September 1, 2002, with regard to drug products whose labeling does not use the established names for ensulizole, hypromellose, meradimate, octinoxate, and octisalate.

II. BACKGROUND

A series of actions related to the need for labeling changes for certain drug products has led to the development of this guidance. The actions are outlined briefly here.

A. USP Monograph Title Changes

In the May and June 2000 *Pharmacopeial Forum*, Volume 26, No. 3, the United States Pharmacopeial Convention proposed changes to several United States Pharmacopeia (USP) monographs. These title changes, which shortened the names of certain substances, were made to harmonize USP usage with World Health Organization (WHO) and, in some cases, *European Pharmacopoeia* usage. These changes were finalized on January 2, 2001, in the 3rd *USP 24-NF 19 Supplement*. The Supplement generally went into effect March 1, 2001. However, the

¹ This guidance has been prepared by the Office of Regulatory Policy in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

monograph title changes discussed in this guidance were given a delayed effective date of September 1, 2002. The following title changes were made:

- *hydroxypropyl methylcellulose* to *hypromellose*
- *menthyl anthranilate* to *meradimate*
- *octyl methoxycinnate* to *octinoxate*
- *octyl salicylate* to *octisalate*
- *phenylbenzimidazole sulfonic acid* to *ensulizole*

Ensulizole, meradimate, octinoxate, and octisalate are active ingredients used in sunscreen drug products for over-the-counter (OTC) human use. Hypromellose is a widely used inactive ingredient and is used to a lesser extent as an active ingredient in pharmaceutical products.

B. Established Names

Section 502(e)(1)(A) of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 352(e)(1)(A)) generally requires the label of a drug product to bear the established name of the drug product's active and inactive ingredients. Section 502(e)(3) (21 U.S.C. 352(e)(3)) defines the established name as:

(A) the applicable official name designated pursuant to section 508 [of the Act], or (B) if there is no such name and such drug, or such ingredient, is an article recognized in an official compendium, then the official title thereof in such compendium, or (C) if neither clause (A) nor clause (B) of this subparagraph applies, then the common or usual name, if any, of such drug or of such ingredient
* * *

The USP is one of the official compendia recognized in the Act (section 201(j), 21 U.S.C. 321(j)).

Section 508 of the Act (21 U.S.C. 358) authorizes us to designate an official name for any drug if we determine "that such action is necessary or desirable in the interest of usefulness and simplicity." We do not, however, routinely designate official names for drug products under section 508 of the Act. In the absence of designation by FDA of an official name, the current compendial name will ordinarily be used as the established name (or if there is no compendial name, the common and usual name would be considered to be the established name). See 21 CFR 299.4(e). Because we have not designated official names for these substances, their compendial names (i.e., *ensulizole*, *hypromellose*, *meradimate*, *octinoxate*, and *octisalate*) would be the established names of the substances.

C. Citizen Petitions

On July 26, 2002, the Cosmetic, Toiletry, and Fragrance Association (CTFA) submitted a petition requesting that we publish a rule amending §§ 352.10 and 352.20 to provide a September 1, 2003, effective date for the active ingredient name changes to *ensulizole*,

meradimate, *octinoxate*, and *octisalate*.² As an alternative, the CTFA requested that we provide notice to industry that we will exercise enforcement discretion and not enforce the requirement that labeling of drug products subject to the OTC sunscreen monograph bear the new names until September 1, 2003.

On August 2, 2002, Bayer Health Care, Consumer Health Division also submitted a petition essentially requesting us to stay, until September 1, 2003, any enforcement action based on a manufacturer's or distributor's failure to bring its products' labeling into compliance with the USP monograph title change from *hydroxypropyl methylcellulose* to *hypromellose*.³

III. EXERCISE OF ENFORCEMENT DISCRETION

As we discuss in further detail in our response to CTFA's petition, we determined that industry could have experienced uncertainty regarding our timing for implementation of the USP name changes for sunscreen products. In addition, we have determined that exercising our enforcement discretion regarding all of the labeling changes discussed in this guidance is appropriate to avoid the need for drug manufacturers and distributors to incur extraordinary expenses in implementing the labeling changes immediately or to cease marketing certain drug products whose labeling cannot be changed in a timely manner. As the petitioners state, these ingredients are found in numerous sunscreen and other pharmaceutical products.

While harmonization of drug names with WHO and the *European Pharmacopoeia* is an important goal of both USP and FDA, this limited use of enforcement discretion should not lead to any significant confusion. Most pharmacists or other individuals who are knowledgeable about inactive ingredients or active ingredients in sunscreen and ophthalmic products are familiar with the names *hydroxypropyl methylcellulose*, *menthyl anthranilate*, *octyl methoxycinnate*, *octyl salicylate*, and *phenylbenzimidazole sulfonic acid*. These names have been used for years, and the continued use of the names for one more year should not cause any significant problems.

Accordingly, we intend to exercise our enforcement discretion by not initiating any enforcement action based on a firm's failure to bring its products' labeling into compliance, before September 1, 2003, with the USP monograph title changes for ensulizole, hypromellose, meradimate, octinoxate, and octisalate.

We note, however, that the USP is currently considering a large number of similar changes. Manufacturers and distributors are responsible for keeping up to date on these changes and any other changes being considered for, or made to, the USP. The *USP-NF* and the *Pharmacopeial Forum* are available by purchase or subscription. The changes will be first proposed in the *Pharmacopeial Forum*. Interested parties have opportunities to comment on proposed changes and request appropriate effective dates. While we intend to exercise our enforcement discretion in relation to the established names discussed in this guidance, manufacturers should

² See docket number 78N-0038/PSA3.

³ See docket number 02P-0357/PSA1.

not assume we will exercise such discretion in the future with respect to other established name changes.