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BY HAND DELIVERY

Dockets Management Branch
Food and Drug Administration (HFA-305)
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Proposed Rule; Reopening of the Administrative Record for Topical Antimicrobial Drug Products for Over-the-Counter Human Use; Health-Care Antiseptic Drug Products. 68 Fed. Reg. 32003 (May 29, 2003). [Docket No. 75N-183H]

Dear Sir or Madam:

Hyman, Phelps & McNamara, P.C. (HPM) hereby submits these comments in response to the Food and Drug Administration's (FDA's) reopening of the administrative record regarding the tentative final monograph for Over-the-Counter (OTC) Health-Care Antiseptic Drug Products, 59 Fed. Reg. 31402 (June 17, 1994) (Antiseptic TFM). HPM is a law firm that represents a number of manufacturers of OTC products that are affected by the Antiseptic TFM. These comments address the labeling requirements proposed for health-care antiseptic drug products, which may be improperly interpreted to require the duplicative listing of the established name of the active ingredient on the principal display panel of an OTC drug product and in the Drug Facts box. HPM requests that FDA state clearly and formally that the statement of identity for an OTC antiseptic drug product must include any established name for the drug itself but does not require inclusion of the established name of the active ingredient.[1]

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[1] Inasmuch as similar language appears in other OTC monographs, these comments are intended to apply to all such stated requirements.

Specifically, the proposed labeling for health-care antiseptic drug products in the Antiseptic TFM includes a statement of identity which "contains the established name of the drug, if any, and identifies the product as an 'antiseptic' and/or with the appropriate statement of identity described in [subsequent sections]." Proposed 21 C.F.R. § 333.450(a) (emphasis added).[2] Under FDA's general OTC drug labeling regulations, the statement of identity must appear on the principal display panel of the drug, 21 C.F.R. § 201.61(c).

Although the proposed requirement expressly applies only to "the established name of the drug" and only "if any" such established name exists, there is reason to believe that FDA incorrectly interprets that requirement to apply to the established name of the active ingredient for an OTC drug that contains only one such ingredient. This apparently has arisen from the language of the general OTC drug labeling requirement, 21 C.F.R. § 201.61(b), which provides, in pertinent part:

> Such statement of identity shall be in terms of the established name of the drug, if any there be, followed by an accurate statement of the general pharmacological category(ies) of the drug or the principal intended action(s) of the drug. In the case of an [OTC] drug that is a mixture and that has no established name, this requirement shall be deemed satisfied by a prominent and conspicuous statement of the general pharmacological action(s) of the mixture or of its principal intended action(s) in terms that are meaningful to the layman.

That provision has reportedly been interpreted to mean that the statement of identity for a single entity OTC drug must include the established name of its active ingredient, while the statement of identity for a combination OTC drug need not do so. That interpretation is wrong as a matter of law and of the plain reading of the current and proposed regulations. However, to avoid any misunderstanding, FDA should state the proper interpretation on the record here.

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[2] Similar requirements exist in virtually all of the current final monographs (see, e.g., id. at § 333.250(a), labeling for antifungal drug products).

The FDC Act clearly distinguishes the requirement for the established name between a drug and an active ingredient. Section 502(e)(1)(A)(i) of the FDC Act, 21 U.S.C. § 352(e)(1)(A)(i), requires that the label of a drug bear "the established name . . . of the drug, if there is such a name." Section 502(e)(1)(A)(ii) requires that the label also bear "the established name and quantity . . . of each active ingredient." Thus, the established name of a drug – if any – is distinct from the established name of an active ingredient under the law. The established name of the drug refers to the entire drug product, including the active and inactive ingredients.

The requirement for a "statement of identity," as well as its placement on the principal display panel, actually arises under the Fair Packaging and Labeling Act, 15 U.S.C. § 1453(a)(1). That provision authorized FDA to promulgate regulations for OTC drugs which "specify the identity of the commodity." Id. (emphasis added). And see 15 U.S.C. § 1459(a)(3) (excluding prescription drugs). FDA merged that requirement with the FDC Act requirement for declaring the established name of the drug.

FDA's regulations respecting OTC drug labeling in general and in specific monographs correctly follow the statute in requiring the statement of identity to include the established name of the drug, if one exists. Those regulations literally do not require the statement of identity to include the established name of the active ingredient, even though one must exist. The latter is correctly identified in the Drug Facts box, as required by the law and FDA regulations. FDC Act § 502(e)(1)(A)(ii), 21 U.S.C. § 352(e)(1)(A)(ii); 21 C.F.R. § 201.66(e)(2).

Despite the clear language of both the law and regulations, the preamble to the Antiseptic TFM appears to misinterpret the requirements in discussing the statement of identity for antiseptics. 59 Fed. Reg. at 31404-5. Using antiseptics that contain povidone-iodine as the example, FDA listed the "[e]stablished name" of the drug as "povidone-iodine." Id. at 31405. Rather confusingly, this is followed by a "statement of identity" that describes acceptable uses. Id. However, it appears from that discussion that FDA would require the statement of identity for an OTC drug product to include the "established name" of the ingredient, not the drug itself. As noted above, that is nowhere required in the law or FDA's regulations; indeed, the example contradicts the law and regulations.

The confusion may be due, in part, to the general labeling regulation's reference to "a mixture . . . that has no established name." 21 C.F.R. § 201.61(b). Although, to our knowledge, FDA has never formally defined the word, "mixture." However, neither FDA nor other medical or pharmaceutical references define the term to apply only to combinations of active ingredients. Indeed, the agency has used the term to refer to OTC drug products that contain both active and inactive drug components. For example, in the preamble to the final monograph for OTC combination Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products, FDA refers to a decongestant combination as containing an "aromatic mixture" of "camphor, menthol . . . [and] bornyl acetate," where bornyl acetate is an inactive ingredient. 67 Fed. Reg. 78163 (Dec. 23, 2002). Similarly, the final monograph for OTC Skin Protectant Drug Products identifies a combination of sodium bicarbonate and water as a "mixture." 68 Fed. Reg. 33378 (June 4, 2003). Certainly, if FDA had intended "mixture" to mean combination drug, the agency would have so stated in the regulation.

The distinction between "established name" and "mixture" is especially important for OTC drugs. Unlike prescription drugs, OTC drugs do not usually have established names and are more likely to be mixtures. Prescription drugs are virtually always marketed under approved new drug applications, which specify the established name of those drugs. 21 U.S.C. § 355; 21 C.F.R. § 314.50(a)(1).

In contrast, most OTC drugs – especially topical products – are mixtures, in which one or more active ingredients may be mixed (or combined) with various inactive ingredients. The OTC Drug Review regulations make clear that the OTC drug monograph describes only active ingredients which may contain unidentified "suitable inactive ingredients which are safe in the amounts administered." 21 C.F.R. § 330.1(e). Thus, OTC monograph drugs can be differing mixtures that do not bear an established name, even if their active ingredients do have such names. In fact, very few OTC drugs have established names. Therefore, the law and FDA's regulations require only that the label of most OTC drugs list their pharmacological categories or principal actions on the principal display panel.

In that regard, an interpretation that would require a single active ingredient to be named in the identity statement, while no ingredients would be named in a combination drug could confuse consumers, who might interpret these differences as implying some special strength or benefit from the specific identification.

Nor does the proper application of the law create any disadvantage to professional healthcare workers or ordinary consumers, particularly in light of the availability of all pertinent information to them under the new OTC Drug labeling format. 21 C.F.R. § 201.66. The consumer is (or will become) familiar with the uniform location of the active ingredients and other information in the Drug Facts box. The consumer is fully informed as to the purpose of the OTC drug by the statement of identity on the principal display panel (e.g., "antiseptic handwash") and by the list of active ingredients in the Drug Facts box.

In conclusion, HPM requests that FDA clearly state that the appropriate statement of identity for healthcare antiseptic (and, indeed, most OTC drugs) is a statement of the pharmacological category (e.g., "antiseptic") or principal intended action, "in terms that are meaningful to the layman," 21 C.F.R. § 201.61(b), unless there is an established name for the drug itself and not simply its active ingredient(s).

Respectfully Submitted,

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