

Producers of Quality
Nonprescription Medicines and
Dietary Supplements for Self-Care

CONSUMER HEALTHCARE PRODUCTS ASSOCIATION

Formerly Nonprescription Drug Manufacturers Association

September 8, 2000

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

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CITIZEN PETITION

The undersigned submits this petition under applicable sections of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 371] and 21 CFR 10.30 to request the Commissioner of Food and Drugs to amend the 21 CFR 201.66 to permit a manufacturer or distributor of nonprescription (over-the-counter, OTC) medicines to use the phrase "may contain," the phrase "may also contain," or the phrase "and/or" on a finished product label to list inactive ingredients which may or may not be present because they are sourced from multiple suppliers.

A. Action requested

The Consumer Healthcare Products Association (CHPA)¹ asks that FDA amend the final regulation on OTC label content and format, 21 CFR 201.66, to allow an OTC drug manufacturer or distributor who sources inactive ingredients or bulk products from multiple suppliers to use the phrase "may contain," the phrase "may also contain," or the phrase "and/or" on the finished OTC drug product label to list those inactive ingredients where mixtures, composite ingredients, or bulk products are obtained from more than one supplier.

CHPA requests this action by FDA so that manufacturers and distributors can fulfill the requirement to disclose product ingredients, but have the needed flexibility to source ingredients and product from more than one supplier without the expense of separate inventories and costly label changes.

CHPA's petition supports a similar Citizen Petition submitted on June 2, 2000, by Arnall

Golden & Gregory, LLP.

98N-0337

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¹ CHPA is the 119-year-old trade organization representing dietary supplements and nonprescription drugs, including over 200 members across the manufacturing, distributing, supply, research testing, and advertising sectors of the self-care industry.

B. Statement of grounds

1. Background

a. Overview of Relevant Characteristics of OTC Drug Production

An OTC drug product is individually prepared and labeled to disclose the ingredients, distributor and other information specific to that product. Typically, OTC drugs are produced and shipped in short periods of time, with the principle of just-in-time inventory.

An OTC drug company may often use multiple suppliers for inactive ingredients in some products in order to maintain an uninterrupted supply of product to its customers. Short-term demands on suppliers can disrupt production schedules, thereby interrupting the flow of products and components from supplier to producer, resulting in delays and extra costs.

The specific makeup of composite inactive ingredients can vary slightly from supplier to supplier. For example, different suppliers may use different lubricants or binders that are specific to their particular processes.

b. Regulatory Considerations

In 1984, CHPA adopted a voluntary inactive ingredient labeling program that stipulated the disclosure of inactive ingredients on all OTC drug labels (see Appendix A). As part of the voluntary program on OTC inactive ingredient labeling, the industry guidelines permitted the use of the terms "or" and "may also contain" to account for inactive ingredients that may differ according to source. Specifically, the CHPA voluntary program stated:

Ingredients which may be but are not always present in a product should be identified by words such as "or" or "may also contain."

Many times FDA has commended the industry on this program, stating, "The agency commends these voluntary efforts and urges all other OTC drug manufacturers to voluntarily label their products in accordance with NDMA's guidelines."^{2 3}

² Oral Health Care Drug Products for Over-the-Counter Human Use; Amendment to Tentative Final Monograph to Include OTC Relief of Oral Discomfort Drug Products [56 F.R. 48314 (9/24/91)].

³ Vaginal Drug Products for Over-the-Counter Human Use; Withdrawal of Advance Notice of Proposed Rulemaking; Notice [59 F.R. 5231 (2/3/94)].

In 1997, passage of the Food and Drug Administration Modernization Act (FDAMA) added section 502(e)(1)(A)(iii) to the FDA Act, 21 USC 352(e)(1)(A)(iii), requiring all drugs to bear "the established name of each inactive ingredient listed in alphabetical order on the outside of the retail package" and if deemed appropriate by FDA, also on the immediate container. Shortly after FDAMA passed, FDA finalized the OTC label format and content rule (Federal Register 64: 13254, March 17, 1999; 21 CFR 201.66), whereby the agency requires an "Inactive Ingredients" section that lists the established name of each inactive ingredient [21 CFR 201.66(c)(8)].

As part of the final rule on OTC label content and format, FDA stipulates that the agency may exempt or defer one or more of the specific requirements of the rule on the basis that it is "inapplicable, impracticable, or contrary to the public health or safety" [21 CFR 201.66(e)]. A separate request must be submitted for each drug product under this exemption procedure. However, the exemption process is not a practical approach to addressing this issue relating to inactive ingredient labeling. A Citizen Petition is, as explained below.

2. Rationale for Requested Change via Amendment of the Final Rule on Label Content and Format

CHPA requests an across-the-board amendment to the final rule on OTC label content and format for the following reasons:

- From a consumer health and product use standpoint, inactive ingredient labeling is included on OTC labeling to alert consumers to ingredients which might cause a consumer to have an allergic reaction or other adverse effect which the consumer wishes to avoid on the basis of personal preference. The only drawback to labeling containing the phrase, "may contain" (or "may also contain" or "and/or") would be that the consumer would not purchase a drug because of a listed ingredient, even though the product may not contain the ingredient of concern. However, in this case the consumer would not be without appropriate self-care alternatives, as most, if not all, OTC drug products are marketed against competing products with different formulations, thereby allowing consumers to self-select to their needs.
- "May contain" has been a phrase that has had practical use in the OTC marketplace through the successful voluntary inactive ingredient program that was in use over a

period of 13 years. As noted earlier, FDA has commended the industry for this voluntary labeling effort.

- FDA has recently granted the Zee Medical, Inc. Application for Exemption relating to the listing of inactive ingredients on PainAid Pain Relief Tablets, allowing the use of the phrase "may contain" to list inactive ingredients that may or may not be present in the product, since Zee Medical, Inc. sources bulk tablets from three sources whose formulations contain different inactive ingredients;
- Use of the phrase "may contain" is analogous to and entirely consistent with FDA regulations that permit its use for cosmetic ingredient label declarations. Under certain circumstances, FDA permits the label of a cosmetic to declare the presence of an ingredient that may not be present in the product, if prefaced by the phrase "may contain." 21 CFR § 701.3(g). The use of the phrase "may contain" is commonly used in cosmetic ingredient labeling where different colors are used for color matching, or for a line or assortment of cosmetics similar in composition that are intended for the same use. The agency has by regulation also long recognized the need to permit cosmetic labeling of alternative ingredients where there is a current or anticipated shortage of a cosmetic ingredient. 21 CFR § 701.3 (m). In the case of many OTC inactive ingredients, the existence of multiple suppliers is pervasive, which means that differences in certain OTC inactives is the rule rather than the exception.
- Because of the large number of products that are potentially affected by the requested use of "may contain," "may also contain," or "and/or" in the "Inactive Ingredients" section of OTC labeling, it would be inefficient, cumbersome, time-consuming, resource-intensive and cost-ineffective to require an exemption for every product label, as FDA did for Zee Medical, Inc.
- Without the ability to use the phrases "may contain," "may also contain," or "and/or," a company would incur excessive costs through impractical use of resources. Specifically, were a company not able to use these phrases, it would:
 - Have to purchase from only one supplier, running the risk of product shortages due to the supplier's problems with its production process or with meeting higher than forecasted retail demands; or

- Have to carry separate inventories of packaging and labeling materials for the same product, with attendant substantial economic impact of maintaining adequate warehouse space to store all the materials, establishing new shelf keeping units (SKU's) and inventory controls, creating and retaining the supportive documentation as well as supporting additional personnel to maintain duplicate labeling and packaging inventories. This also increases the potential for labeling mix-ups.
- The effect of not amending the final rule is a de facto requirement that different suppliers have to manufacture inactive ingredients to the same, exact formula. This is impractical, since each supplier has specific experience with its own equipment, raw material sources, and methods of compounding and processing these materials, any and all of which may differ from those of another suppliers.

C. Environmental Impact

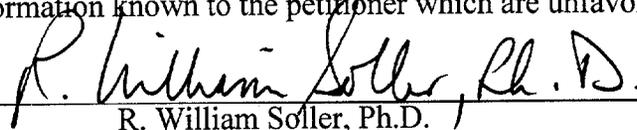
Under 21 CFR 25.31, this petition qualifies for a categorical exemption from the requirement to submit an environmental assessment

D. Lack of Economic Impact and Compliance Date

FDA specifies that specific economic information is to be submitted only when requested by the Commissioner following review of the petition.

E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.



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Appendix A: 1984 CHPA Voluntary Inactive Ingredient Labeling Program (reprinted 1996)

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Guidelines for OTC Labeling

..... *Disclosure of Inactive Ingredients*

The manufacture of nonprescription, over-the-counter (OTC) medicines is a science which requires the use of both active and inactive ingredients. Active ingredients produce the therapeutic effect. Inactive ingredients provide the "delivery system." Among other necessary functions, inactive ingredients serve as flavors, colors, binders, lubricants and preservatives.

OTC labels are required by law to identify all active ingredients and to identify and list quantities of certain ingredients, such as alcohol, whether active or not. The Nonprescription Drug Manufacturers Association (NDMA) in 1984 adopted a voluntary program to identify for the consumer inactive ingredients used in OTC medicines. This identification is not required by law.

Inactive ingredients in OTC medicines have established histories of safe use. But a small percentage of people are sensitive to particular substances no matter how safe they are for the vast majority. The NDMA voluntary program for listing of inactive ingredients is a further effort by industry to enable these persons to identify the presence or absence of substances in OTC medicines which they may wish to avoid.

The guidelines for disclosure of inactive ingredients are as follows:

1. The package of an OTC medicine intended for retail sale (but including samples and institutional packages) should contain an alphabetical listing of its inactive ingredients, including colors. The listing should be prefaced by language such as "also contains," "other ingredients" or "inactive ingredients" so as to distinguish clearly between active and inactive ingredients.
2. The listing should be legible and visible to consumers at point of purchase.
3. A small product container (one with a total surface area of less than 12 square inches and which is not contained in an outer container, such as a carton) may list its

inactive ingredients in accompanying labeling.

4. Flavors and fragrances may be listed as "flavors" and "fragrances."
5. Ingredients which may be but are not always present in a product should be identified by words such as "or" or "may also contain."
6. An ingredient whose identity is a trade secret need not be disclosed if the inactive ingredients list states "and other ingredients." For purposes of this guideline, an ingredient constitutes a trade secret if its presence confers a significant competitive advantage on its manufacturer and the identity of the ingredient cannot be determined using modern analytical technology.
7. The name of an inactive ingredient should be taken from the most current edition of the following reference works:
 - (a) United States Pharmacopeia (USP)/ National Formulary;
 - (b) United States Adopted Names (USAN) and USP Dictionary of Drug Names;
 - (c) CTFA (The Cosmetic, Toiletry, and Fragrance Association) Cosmetic Ingredient Dictionary; and
 - (d) Food Chemicals Codex.

An ingredient not listed in any of the above references should be identified by the name generally recognized by consumers or, if none, the chemical or other technical name.

8. Incidental ingredients which are present in the product at insignificant levels and that have no technical or functional effect need not be identified, unless the omission of the incidental ingredient would constitute a failure to reveal a material fact.

The effective date for voluntary compliance with these guidelines was December 1, 1985.

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