

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 310 and 341

[Docket No. 2004N-0289]

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**Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use; Proposed Amendment of Final Monograph for Over-the-Counter Nasal Decongestant Drug Products**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Proposed rule.

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**SUMMARY:** The Food and Drug Administration (FDA) is proposing to amend the final monograph for over-the-counter (OTC) nasal decongestant drug products (drug products used to relieve nasal congestion due to a cold, hay fever, or other upper respiratory allergies) to remove the indication “for the temporary relief of nasal congestion associated with sinusitis” and to prohibit use of the terms “sinusitis” and “associated with sinusitis” elsewhere on the labeling. This proposal is part of FDA’s ongoing review of OTC drug products.

**DATES:** Submit written or electronic comments on the document and comments on the agency’s economic impact determination by *[insert date 90 days after date of publication in the Federal Register]*. See sections V and X of this document for the proposed effective and compliance dates of any final rule that may publish based on this proposal.

**ADDRESSES:** You may submit comments, identified by [Docket No. 2004N-0289 and/or RIN number 0910-AF34], by any of the following methods:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments.
- Agency Web site: <http://www.fda.gov/dockets/ecomments>. Follow the instructions for submitting comments on the agency Web site.
- E-mail: [fdadockets@oc.fda.gov](mailto:fdadockets@oc.fda.gov). Include [Docket No.2004N–0289 and/or RIN number 0910–AA01] in the subject line of your e-mail message.
- FAX: 301–827–6870.
- Mail/Hand delivery/Courier [For paper, disk, or CD–ROM submissions]:  
Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the agency name and Docket No. or Regulatory Information Number (RIN) for this rulemaking. All comments received will be posted without change to <http://www.fda.gov/dockets/ecomments>, including any personal information provided. For detailed instructions on submitting comments and additional information on the rulemaking process, see the “Comments” heading of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: For access to the docket to read background documents or comments received, go to <http://www.fda.gov/dockets/ecomments> and/or the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

**FOR FURTHER INFORMATION CONTACT:** Michael T. Benson, Center for Drug Evaluation and Research (HFD–560), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–2222.

**SUPPLEMENTARY INFORMATION:**

## I. Background

### A. Advance Notice of Proposed Rulemaking

In the **Federal Register** of September 9, 1976 (41 FR 38312), the Advisory Review Panel on OTC Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products (the Panel) recommended the following as one of 13 labeling indications for OTC nasal decongestant drug products: “For temporary relief of nasal congestion associated with sinusitis.” (See 41 FR 38312 at 38422.) The Panel recommended 13 indications for OTC nasal decongestant drug products (41 FR 38312 at 38403 to 38404). Only one of these indications involved the term “sinusitis,” i.e., “For temporary relief of nasal congestion associated with sinusitis.” The Panel did not provide any explanation for this indication in its general discussion of OTC nasal decongestants (41 FR 38312 at 38396 to 38397) or in its Category I labeling discussion.

### B. Tentative Final Monograph

In the **Federal Register** of January 15, 1985 (50 FR 2220), FDA concurred with the Panel’s recommendation and proposed a similar indication in the tentative final monograph for OTC nasal decongestant drug products. That indication in proposed § 341.80(b)(1) (50 FR 2220 at 2238) stated: “For the temporary relief of nasal congestion due to the common cold (cold), hay fever” (which may be followed by any of the following: “(allergic rhinitis),” “or other upper respiratory allergies,” or “or other upper respiratory allergies (allergic rhinitis)”) “or associated with sinusitis.”

### C. Final Monograph

In the **Federal Register** of August 23, 1994 (59 FR 43386), FDA published a final monograph with a similar indication included in § 341.80(b)(1)(iii). The

complete indication for OTC nasal decongestant drug products in § 341.80(b)(1) states:

(Select one of the following: “For the temporary relief of nasal congestion” or “Temporarily relieves nasal congestion”) (which may be followed by any of the following in paragraphs (b)(1)(i), (ii), and (iii) of this section):

(i) “due to” (select one of the following: “the common cold” or “a cold”).

(ii) “due to” (select one of the following: “hay fever,” “hay fever (allergic rhinitis),” “hay fever or other upper respiratory allergies,” or “hay fever or other upper respiratory allergies (allergic rhinitis)”); and

(iii) “associated with sinusitis.”

## **II. Sinusitis**

### *A. General Discussion*

Sinusitis is characterized by inflammation of the paranasal passages (Ref. 1). Primary care providers and subspecialists often recommend antibiotics for the management of acute sinusitis and chronic sinusitis because these conditions often have a bacterial etiology (Refs. 1 through 4). Other nasal diseases may have symptoms similar to those of sinusitis. These include allergic and nonallergic rhinitis, the common cold or influenza, Wegener’s granulomatosis, acquired and congenital immunodeficiency diseases, nasal polyposis, sarcoidosis, fungal sinusitis, or neoplasm (Refs. 1 and 3). Further, sinusitis and asthma often occur together in the same person. As many as 40 to 70 percent of people with asthma have accompanying sinusitis (Ref. 1). Moreover, complications of acute bacterial sinusitis include infections of the orbit (bony cavity that contains the eyeball), the central nervous system, or both. These complications are rare, but have the potential to result in blindness or death (Ref. 2).

### *B. Recent Developments*

Recent publications (Refs. 1 and 2) indicate that prospective studies on the role of nasal decongestants in the treatment of sinusitis are lacking, and the data on their use as an adjunct in the treatment of sinusitis are limited and controversial. Despite the lack of evidence for their use, nasal decongestants are recommended or prescribed by health care providers as adjunctive therapy for sinusitis. This treatment occurs within a physician-patient relationship and should not be construed as evidence that consumers should self-diagnose and self-manage sinusitis. In addition, there is preclinical evidence that topical nasal decongestants may have a negative effect on the resolution of sinusitis, as they may increase the degree of sinus inflammation (Ref. 3).

Sinusitis develops in approximately 31 million Americans each year. Acute sinusitis typically follows a viral infection of the upper respiratory tract or occurs as a complication of allergic rhinitis. Swelling of the nasal mucous membranes may obstruct the sinus ostia (openings), resulting in retained secretions, impaction of mucus, decreased oxygenation, and changes in pressure within the sinus cavities. Retained secretions and impacted mucus may become infected and produce increased congestion and inflammation of the sinus mucosa, and may lead to the clinical symptoms associated with acute sinusitis, such as nasal discharge containing pus, postnasal drip, facial pain and headache, and nasal congestion. Treatment is directed towards curing the infection and restoring normal sinus openings and drainage. Health care providers often recommend nasal decongestants as adjunctive therapy for acute sinusitis (Ref. 1).

### III. FDA's Concerns

Due to the current labeling, FDA is concerned that consumers use OTC nasal decongestant drug products (both oral and topical) to treat symptoms associated with sinusitis, rather than seeking medical evaluation and definitive treatment. The delay in medical evaluation could also result in a lost opportunity for early diagnosis of another serious medical condition in patients who have symptoms similar to those of sinusitis. Consumers who have bacterial sinusitis could potentially have their condition worsen by delaying treatment with appropriate antibiotic medications, possibly resulting in serious complications. Consumers who have both sinusitis and accompanying asthma could have complications from both diseases if there is a delay in appropriate evaluation and treatment of their asthma. Due to the data contained in recent publications and the potential medical harms described in this section, FDA now considers the indication “for the temporary relief of nasal congestion associated with sinusitis” inappropriate and potentially misleading in the labeled uses for OTC nasal decongestant drug products. Consumers could interpret this indication to mean that the product can be used for self-treating sinusitis. Likewise, use of the term “sinusitis” on the product’s principal display panel could cause the same misunderstanding.

### IV. FDA's Proposal

#### A. *What is Included?*

FDA is proposing to remove the partial labeling indication “associated with sinusitis” from the monograph for OTC nasal decongestant drug products by removing § 341.80(b)(1)(iii). FDA is also including both “sinusitis” and “associated with sinusitis” as nonmonograph conditions in proposed § 310.545(a)(6)(ii)(C).

## *B. What Is Not Included?*

This proposal does not affect other “sinus” claims in the monograph.

These claims include:

- “Helps decongest sinus openings and passages” (§ 341.80(b)(2)(iv)),
- “Temporarily relieves sinus congestion and pressure” (§ 341.80(b)(2)(iv) and (b)(2)(v)), and
- “Promotes nasal and/or sinus drainage” (§ 341.80(b)(2)(v)).

## **V. Analysis of Impacts**

FDA has examined the impacts of this proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity).

Under the Regulatory Flexibility Act, if a rule has a significant impact on a substantial number of small entities, an agency must analyze regulatory options that would minimize any significant impact of the rule on small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits before proposing “any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year.”

FDA believes that this proposed rule is consistent with the principles set out in Executive Order 12866 and in these two statutes. FDA has determined that the proposed rule is not a significant regulatory action as defined by the Executive order and so is not subject to review under the Executive order. As discussed later in this section, FDA believes that the proposed rule, if finalized, will not have a significant economic impact on a substantial number of small entities. The Unfunded Mandates Reform Act of 1995 does not require FDA to prepare a statement of costs and benefits for this proposed rule, because the proposed rule is not expected to result in any 1-year expenditure that would exceed \$100,000,000 adjusted for inflation. The current inflation adjusted statutory threshold is about \$110,000,000.

The purpose of this proposed rule is to remove a labeling claim for OTC nasal decongestant drug products. Removal of this claim should reduce possible misuse and improve consumers' self-use of these products. FDA does not anticipate that removal of this claim will significantly affect OTC sales of these products.

The proposed rule would require relabeling of some OTC nasal decongestant drug products, i.e., those products that currently have a claim for sinusitis in their labeling. FDA's drug listing system identifies about 1,121 manufacturers and 381 marketers of approximately 1,960 stockkeeping units (SKUs) (individual products, packages, and sizes) of OTC nasal decongestant drug products. These numbers include some products marketed under a new drug application (NDA) or abbreviated new drug application (ANDA). In addition, there may be a few additional marketers and products that are not identified in the sources FDA reviewed. FDA is using 2,000 SKUs as an

approximate number of products in the marketplace that would be affected by this proposed rule.

FDA has reviewed the labeling of some of these nasal decongestant drug products and found that 74 of 100 products did not have a sinusitis claim. Extrapolating these numbers to approximately 2,000 SKUs of these products, the agency estimates that approximately 520 products (26 percent) would have to be relabeled. FDA estimates (based on information provided by OTC drug manufacturers) that the proposed rule would impose total one-time compliance costs on industry for relabeling of about \$3,000 to \$4,000 per SKU, for a total cost for 520 SKUs of \$1,560,000 to \$2,080,000.

FDA believes the actual cost could be lower for several reasons. First, as FDA explained in the final rule for OTC drug product labeling requirements (64 FR 13254 at 13280, March 17, 1999), most of the labeling changes will be made by private label small manufacturers that tend to use simpler and less expensive labeling. Second, FDA is proposing a period of 18 months (24 months for products with annual sales less than \$25,000) after the date of publication of a final rule based on this proposal for manufacturers to implement the new labeling. Thus, manufacturers should be able to use up existing labeling stocks and to make the labeling changes in the normal course of business. Further, manufacturers will not incur any expenses determining how to state the product's labeling because the proposed amendment (and any final rule based on this proposal) provides that information. Any final rule that publishes based on this proposal will not be expected to require any new reporting and recordkeeping activities. Therefore, no additional professional skills would be needed.

FDA considered, but rejected several labeling alternatives: (1) A shorter or longer implementation period and (2) an exemption from coverage for small entities. While FDA believes that consumers would benefit from having this proposed labeling in place as soon as possible, FDA also acknowledges that a shorter implementation period could significantly increase the compliance costs and these costs could be passed through to consumers. A longer time period would unnecessarily delay the benefit of new labeling to consumers who self-medicate with these drug products. FDA rejected an exemption for small entities because the new labeling information is also needed by consumers who purchase products marketed by those entities. However, a longer compliance date (24 months) is being provided for products with annual sales less than \$25,000.

OTC nasal decongestant drug products are not the sole products produced by manufacturers affected by this rule. FDA believes the incremental costs of this proposed rule will be less than 1 percent of any manufacturer's total sales. Thus, this economic analysis, together with other relevant sections of this document, serves as FDA's initial regulatory flexibility analysis, as required under the Regulatory Flexibility Act.

#### **VI. Paperwork Reduction Act of 1995**

FDA tentatively concludes that the labeling requirement proposed in this document is not subject to review by the Office of Management and Budget because it does not constitute a "collection of information" under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520).

Rather, the proposed removal of a labeling claim is a "public disclosure of information originally supplied by the Federal government to the recipient for the purpose of disclosure to the public" (5 CFR 1320.3(c)(2)).

## **VII. Environmental Impact**

FDA has determined under 21 CFR 25.31(a) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

## **VIII. Federalism**

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the proposed rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, FDA tentatively concludes that the proposed rule does not contain policies that have federalism implications as defined in the Executive order, and consequently, a federalism summary impact statement has not been prepared.

## **IX. Request for Comments**

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. Submit one paper copy of electronic comments or three paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

## **X. Proposed Effective and Compliance Dates**

FDA is proposing that any final rule based on this proposal become effective 18 months after the date of its publication in the **Federal Register**.

FDA is proposing the following compliance dates for nasal decongestant drug products marketed under the monograph:

- 24 months after the date of publication of a final rule in the **Federal Register** for products with annual sales less than \$25,000 and
- 18 months after the date of publication in the **Federal Register** for all other such drug products.

## XI. References

The following references are on display in the Division of Dockets Management (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Parameters for the Diagnosis and Management of Sinusitis, supplement to *The Journal of Allergy and Clinical Immunology*, 102 (6 Part 2): S107–S144, December 1998.
2. American Academy of Pediatrics Subcommittee on Management of Sinusitis and Committee on Quality Improvement, “Clinical Practice Guideline: Management of Sinusitis,” *Pediatrics*, 108(3): 798–808, 2001.
3. “Report of the Rhinosinusitis Task Force Committee Meeting,” *Otolaryngology-Head and Neck Surgery*, 117 (3 Part 2): S1–S68, 1997.
4. Snow, V., et al., “Principles of Appropriate Antibiotic Use for Acute Sinusitis in Adults,” *Annals of Internal Medicine*, 134 (6): 495–497, 2001.

## List of Subjects

### 21 CFR Part 310

Administrative practice and procedure, Drugs, Labeling, Medical devices, Reporting and recordkeeping requirements.

### 21 CFR Part 341

Labeling, Over-the-counter drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR parts 310 and 341 be amended as follows:

**PART 310—NEW DRUGS**

1. The authority citation for 21 CFR part 310 continues to read as follows:

**Authority:** 21 U.S.C. 321, 331, 351, 352, 353, 355, 360b-360f, 360j, 361(a), 371, 374, 375, 379e; 42 U.S.C. 216, 241, 242(a), 262, 263b-263n.

2. Section 310.545 is amended by adding paragraph (a)(6)(ii)(C) to read as follows:

**§ 310.545 Drug products containing certain active ingredients offered over-the-counter (OTC) for certain uses.**

(a) \* \* \*

(6) \* \* \*

(ii) \* \* \*

(C) Approved as of [Date 18 months after date of publication of the final rule in the Federal Register]; [date 24 months after date of publication of the final rule in the Federal Register], for products with annual sales less than \$25,000. Any ingredient(s) labeled with claims or directions for use for sinusitis or for relief of nasal congestion associated with sinusitis.

\* \* \* \* \*

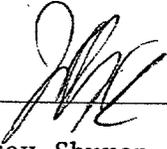
**PART 341—COLD, COUGH, ALLERGY, BRONCHODILATOR, AND ANTI-ASTHMATIC DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE**

3. The authority citation for 21 CFR part 341 continues to read as follows:

**Authority:** 21 U.S.C. 321, 351, 352, 353, 355, 360, 371.

4. Section 341.80 is amended by removing paragraph (b)(1)(iii).

Dated: 7/23/04  
July 23, 2004.



Jeffrey Shuren,  
Assistant Commissioner for Policy.

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