XM—Manitoba
XN—Nova Scotia
XO—Ontario
XP—Prince Edward Island
XQ—Quebec
XS—Saskatchewan
XT—Northwest Territories
XW—Newfoundland
XY—Yukon Territory

Dated: March 29, 1996.

Martha Farnsworth Riche,

Director, Bureau of the Census.

[FR Doc. 96–8925 Filed 4–5–96; 4:14 pm]

BILLING CODE 3510–07–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 2

[Docket No. 92P–0403]

Chlorofluorocarbon Propellants in Self-Pressurized Containers; Addition to List of Essential Uses

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) has granted the petition of Boehringer Ingelheim Pharmaceuticals, Inc. (BIPI), to add metered-dose albuterol sulfate and ipratropium bromide in combination for oral inhalation to the list of products containing a chlorofluorocarbon (CFC) propellant for an essential use. Essential use products are exempt from FDA's ban on the use of CFC propellants in FDA-regulated products and the Environmental Protection Agency's (EPA's) ban on the use of CFC's in pressurized dispensers. This document amends FDA's regulations governing use of CFC's to include metered-dose albuterol sulfate and ipratropium bromide in combination for oral inhalation as an essential use.

EFFECTIVE DATE: April 9, 1996.

FOR FURTHER INFORMATION CONTACT: Wayne H. Mitchell, Center for Drug Evaluation and Research (HFD–097), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–594–1049.

SUPPLEMENTARY INFORMATION:

I. Background

In response to a citizen petition submitted by BIPI, in the Federal Register of October 17, 1995 (60 FR 53725), FDA published a proposed rule to amend 1A2.125 (21 CFR 2.125) to add metered-dose albuterol sulfate and ipratropium bromide in combination for oral inhalation to the list of productscontaining a CFC propellant for an essential use.

Under 1A2.125, any food, drug, device, or cosmetic in a self-pressurized container that contains a CFC propellant for a nonessential use is adulterated or misbranded, or both, under the Federal Food, Drug, and Cosmetic Act. This prohibition is based on scientific research indicating that CFC's may reduce the amount of ozone in the stratosphere and thereby increase the amount of ultraviolet radiation reaching the earth. An increase in ultraviolet radiation may increase the incidence of skin cancer, change the climate, and produce other adverse effects of unknown magnitude on humans, animals, and plants. Section 2.125(d) exempts from the adulteration and misbranding provisions of 1A2.125(c) certain products containing CFC propellants thatFDA determines provide unique health benefits that would not be available without the use of a CFC. These products are referred to in the regulation as essential uses of CFC's and are listed in 1A2.125(e).

Under 1A2.125(f), any person may petition the agency to request additions to the list of uses considered essential. To demonstrate that the use of a CFC is essential, the petition must be supported by an adequate showing that: (1) There are no technically feasible alternatives to the use of a CFC in the product; (2) the product provides a substantial health, environmental, or other public benefit unobtainable without the use of the CFC; and (3) the use does not involve a significant release of CFC's into the atmosphere or, if it does, the release is warranted by the consequence if the use were not permitted.

EPA regulations implementing provisions of the Clean Air Act contain a general ban on the use of CFC's in pressurized dispensers, such as metered-dose inhalers (MDI's) (40 CFR 82.64(c) and 82.66(d)). These regulations exempt from the general ban ''medical devices'' that FDA considers essential and that are listed in 1A2.125(e). Section 601(8) of the Clean Air Act (42 U.S.C. 7671(8)) defines ''medical device'' as any device (as defined in the Federal Food, Drug, and Cosmetic Act), diagnostic product, drug (as defined in the Federal Food, Drug, and Cosmetic Act), and drug delivery system, if such device, product, drug, or drug delivery system uses a class I or class II ozone-depleting substance for which no safe and effective alternative has been developed (and where necessary, approved by the Commissioner of Food and Drugs (the Commissioner)); and if such device, product, drug, or drug delivery system has, after notice and opportunity for public comment, been approved and determined to be essential by the Commissioner in consultation with the Administrator of EPA (the Administrator). Class I substances include CFC's, halons, carbon tetrachloride, methyl chloroform, methyl bromide, and other chemicals not relevant to this document (see 40 CFR part 82, appendix A to subpart A). Class II substances include hydrochlorofluorocarbons (HCFC's)(see 40 CFR part 82, appendix B to subpart A).

II. Petition Received by FDA

BIPI submitted a petition under 1A2.125(f) and 21 CFR part 10 requesting an addition to the list of CFC uses considered essential. The petition is on file under the docket number found in brackets in the heading of this document and may be seen in the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 10923, Rockville, MD 20857. The petition requested that metered-dose albuterol sulfate and ipratropium bromide in combination for oral inhalation be included in 1A2.125(e) as an essential use of CFC's. The petition contained a discussion supporting the position that there are no technically feasible alternatives to the use of CFC's in the product. It included information showing that no alternative delivery systems (e.g., the dry powder inhaler) or other substitute propellants (e.g., compressed gases) can dispense the drug for effective inhalation therapy as safely and uniformly, in all situations, as CFC propellants. Also, the petition stated that the product provides a substantial health benefit that would not be obtainable without the use of CFC's. In this regard, the petition contained information to support the use of this product as a combination bronchodilator. The petition asserted that metered-dose albuterol sulfate andipratropium bromide in combination potentially reduces the amount of CFC's released into the atmosphere attributable to patients using one MDI for the combination product, rather than two MDI's, one for each of the two active ingredients.

The agency has determined that, for some chronic obstructive pulmonary disease patients, the use of metered-dose albuterol sulfate and ipratropium bromide in combination provides a special benefit that would be unavailable without the use of CFC's,

and that the use of the drugs in combination has the potential to reduce the amount of CFC's released into the atmosphere. In this regard, FDA notes that albuterol sulfate and ipratropium bromide are currently listed separately (i.e., not in combination) in 1A2.125(e) as essential uses of CFC's. Based on the evidence currently before it, FDA also agrees that the use of a metered-dose delivery system for this product does not involve asignificant release of CFC's into the atmosphere. Therefore, FDA is amending 1A2.125(e) to include metered-dose albuterol sulfate and ipratropium bromide in combination for oral inhalation in the list of essential uses of CFC propellants.

A copy of the proposed rule was provided to the Administrator.

III. Comments on the Proposed Rule

Interested persons were given 30 days to comment on the proposed rule. FDA received one comment regarding the proposed rule. The comment pointed out that CFC-free MDI's for albuterol sulfate and other drugs are generally expected to be developed and marketed in the near future, and that the availability of alternative propellants will undercut the factual basis for FDA's determination that the use of CFC's in MDI's is medically necessary. The comment suggested that FDA's determination be made conditionally, and that FDA reexamine the ''medical essentiality'' of the MDI if and when a CFC-free albuterol sulfate MDI is approved. The comment also suggested that future rulemaking may be necessary to provide for the transition between MDI's containing CFC's and CFC-free MDI's.

FDA is aware of the development of CFC-free MDI's and shares the comment's concerns that proper provision should be made for the transition between MDI's containing CFC's and CFC-free MDI's. FDA, working with EPA, is developing a policy on this matter at this time, and anticipates that a rulemaking procedure may be necessary to implement that policy. Section 2.125 does not provide for a ''conditional'' listing as an essential use and to provide for such a ''conditional'' listing in this rule would be beyond the scope of the proposal. Any phase-out or reformulation requirement for MDI's containing albuterol sulfate and ipratropium bromide in combination undertaken because of the availability of alternative propellants will be undertaken as part of a properly implemented general policy on the elimination of CFC's from MDI's and other similar products.

IV. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (Pub. L. 96–354). 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). The agency believes that this final rule is consistent with the regulatory philosophy and principles identified in the Executive Order. In addition, the final rule is not a significant regulatory action as defined by the Executive Order and so is not subject to review under the Executive Order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the agency is not aware of any adverse impact this final rule will have on any small entities, the agency certifies that the final rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

List of Subjects in 21 CFR Part 2

Administrative practice and procedure, Cosmetics, Devices, Drugs, Foods.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 2 is amended as follows:

PART 2—GENERAL ADMINISTRATIVE RULINGS AND DECISIONS

1. The authority citation for 21 CFR part 2 continues to read as follows:

Authority: Secs. 201, 301, 305, 402, 408, 409, 501, 502, 505, 507, 512, 601, 701, 702, 704 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 335, 342, 346a, 348, 351, 352, 355, 357, 360b, 361, 371, 372, 374); 15 U.S.C. 402, 409.

2. Section 2.125 is amended by adding new paragraph (e)(14) to read as follows:

§ 2.125 Use of chlorofluorocarbon propellants in self-pressurized containers.

* * * * *

(e) * * *

(14) Metered-dose ipratropium bromide and albuterol sulfate, in combination, administered by oral inhalation for human use.

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Dated: March 29, 1996.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 96–8826 Filed 4–8–96; 8:45 am]

BILLING CODE 4160–01–F

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21 CFR Part 341

[Docket No. 76N–052G]

RIN 0910–AA01

Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use; Products Containing Diphenhydramine Citrate or Diphenhydramine Hydrochloride; Enforcement Policy

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule; enforcement policy.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule, and a statement of its enforcement policy, providing for the use of diphenhydramine citrate or diphenhydramine hydrochloride as an antitussive and an antihistamine for treating concurrent symptoms in either single-ingredient or combination drug products. The agency will include the permitted combination products that may include diphenhydramine citrate or diphenhydramine hydrochloride in the final monograph for over-the-counter (OTC) cold, cough, allergy, bronchodilator, and antiasthmatic (cough-cold) combination drug products. The OTC marketing of combination drug products containing diphenhydramine citrate or diphenhydramine hydrochloride is being permitted pending completion under the OTC drug review of the final monograph for OTC cough-cold combination drug products. This final rule is part of the ongoing review of OTC drug products conducted by FDA.

EFFECTIVE DATE: April 9, 1996.

ADDRESSES: Written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD–105), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–2304.