**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

**21 CFR Parts 310 and 341**

**[Docket No. 95N–0205]**

**RIN 0905–AA06**

# Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use; Proposed Amendment of Monograph for OTC Bronchodilator Drug Products

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

**ACTION:** Notice of proposed rulemaking.

**SUMMARY:** The Food and Drug Administration (FDA) is proposing to amend the final monograph for over-the-counter (OTC) bronchodilator drug products to remove the ingredients ephedrine, ephedrine hydrochloride, ephedrine sulfate, and racephedrine hydrochloride and to classify these ingredients as not generally recognized as safe and effective for OTC use. This action is being taken in response to a request from the U.S. Department of Justice, Drug Enforcement Administration (DEA) to restrict OTC availability of ephedrine because of its illicit use as the primary precursor utilized in the synthesis of the controlled substances methamphetamine and methcathinone. This action is also based on new information that shows that the misuse and abuse of OTC ephedrine drug products has the potential for causing harm and on comments made by FDA's Pulmonary-Allergy Drugs Advisory Committee and the Nonprescription Drugs Advisory Committee on November 14, 1994. This proposal is part of the ongoing review of OTC drug products conducted by FDA.

**DATES:** Written comments or objections by August 28, 1995; written comments on the agency's economic impact determination by August 28, 1995. FDA is proposing that any final rule that may issue based on this proposal become effective 30 days after its date of publication in the **Federal Register**.

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

**FOR FURTHER INFORMATION CONTACT:** William E. Gilbertson, Center for Drug Evaluation and Research (HFD–810), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–5000.

**SUPPLEMENTARY INFORMATION:**

## I. Background

In the **Federal Register** of September 9, l976 (41 FR 38312), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC cold, cough, allergy, bronchodilator, and antiasthmatic drug products, together with the recommendations of the Advisory Review Panel on OTC Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products (the Panel), which was the advisory review panel responsible for evaluating data on the active ingredients in this drug class. The Panel recommended that ephedrine preparations be Category I (generally recognized as safe and effective) for OTC bronchodilator use (41 FR 38312 at 38370 and 38371, September 9, 1976). The agency concurred with the Panel in the bronchodilator tentative final monograph (47 FR 47520 at 47527, October 26, 1982) and included ephedrine preparations in the final monograph for OTC bronchodilator drug products (51 FR 35326 at 35339, October 2, 1986).

## II. Recent Developments

Since publication of the final monograph for OTC bronchodilator drug products, the agency's views about OTC ephedrine-containing bronchodilator drug products have changed for several reasons: (1) A large-scale diversion of OTC ephedrine-containing drug products to illicit use in the manufacture of the controlled substances methamphetamine and methcathinone, (2) new information that ephedrine may be unsafe for OTC use and has the potential for causing harm as a result of misuse and abuse, due to widespread and easy availability as an OTC drug, and (3) the consensus of FDA's Pulmonary-Allergy Drugs Advisory Committee and the Nonprescription Drugs Advisory Committee (the Committee) on November 14, 1994, that the use of oral ephedrine drug products as an OTC bronchodilator to relieve the symptoms of asthma can no longer be justified when the drug's potential for illicit use and misuse is considered.

## III. Illicit Use of OTC Ephedrine Drug Products

FDA has received correspondence and inquiries from consumers, U.S. Senators, DEA, and others (Ref. 1) concerning the need for additional controls on the distribution of OTC ephedrine-containing drug products. The ''Domestic Chemical Diversion Control Act of 1993, Pub. L. 103–200'' was signed into law on December 17, 1993, to control the diversion of certain chemicals (e.g., ephedrine) used in the illicit production of controlled substances such as methcathinone and methamphetamine. The law became effective on April 16, 1994, and removed the exemption from the definition of a ''regulated transaction'' that had existed for single entity ephedrine drug products legally marketed under the Federal Food, Drug, and Cosmetic Act (the act). Thus, drugs that were previously marketed lawfully under the act are no longer exempt from chemical precursor controls. The new law was intended to close this loophole and help eliminate the availability of ephedrine as a raw material source in the clandestine synthesis of methamphetamine and methcathinone.

In the **Federal Register** of October 11, 1994 (59 FR 51365), DEA issued a final rule eliminating the threshold for ephedrine and subjecting all transactions involving bulk ephedrine and single entity ephedrine drug products to the applicable provisions of the Controlled Substances Act (21 U.S.C. 801). The final rule eliminated the threshold (an amount of a listed chemical that determines if a transaction such as receipt or sale of the chemical is a regulated transaction under part 1310 (21 CFR part 1310)) for single entity ephedrine drug products. The final rule established that all transactions involving ephedrine, regardless of size, are subject to recordkeeping and reporting requirements set forth in part 1310 and the notification provisions of part 1310 (21 CFR part 1313). However, the final rule did not apply to combination drug products containing ephedrine.

At the Committee meeting on November 14, 1994, the Committees discussed OTC bronchodilator drug products. DEA had submitted a comment (Ref. 2) to the Committee expressing its concern that, although the recent legislation and proposed regulations (59 FR 12562, March 17, 1994) (now final regulations (59 FR 51365)) adequately address the ability to control single ingredient ephedrine products, DEA is aware that laboratories may turn to combination drug products containing ephedrine and guaifenesin that would be exempt from the final rule.

The comment stated that the illicit use of OTC ephedrine drug products is contributing to a serious public health problem that is an extremely critical