Constitution Avenue, NW., Washington, DC, to solicit further input from interested members of the importing community, in order to better inform and assist the agency in fashioning a final rule document which complies with the law and maintains effective Customs control over the subzone refineries, while minimizing interference with their efficient operation. In this regard, matters already raised by several refinery subzones expressing concern over the proposed rule, on which Customs is especially interested in receiving additional guidance are as follows:

1. Any factual and/or legal basis for including in the definition of "petroleum refinery" a plant that does not refine petroleum.

2. Quantitative examples illustrating the concept of "producibility".

3. A quantitative description illustrating the attribution of product to feedstock using the producibility concept specifically under a 30-day manufacturing period.

4. Reasons to support the view that volume measurement would provide accurate feedstock balance data, assuming that weight were not used as a measurement of feedstock inventories.

5. A definition for "protection of the revenue", with a legal justification and quantitative examples provided therefor.

Since the meeting, as noted, is scheduled for December 15 and 16, 1992, Customs has also determined that an extension of the comment period for an additional 60 days is warranted (until February 8, 1993).

Parties interested in attending the meeting are requested to inform Customs of their intention to do so, in order to assure that adequate accommodations are provided. Notice of this intention should be received by December 8, 1992. Such notice may be given in writing or telephonically. Written notices should be sent to U.S. Customs Service, room 2311, 1301 Constitution Avenue, NW., Washington, DC 20229. Telephone replies may be made to Mr. Hryniw at (202) 927–1100.

Dated: November 18, 1992.

Samuel H. Banks,

Assitant Commissioner, Office of Commercial Operations.

FR Doc. 92–28464 Filed 11–23–92; 8:45 am]

BILLING CODE 4820-02-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 355

[Docket No. 80N–0042]

RIN 0905–AA06

Anticaries Drug Products for Over-the-Counter Human Use; Tentative Final Monograph; Reopening of Administrative Record

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of proposed rulemaking; reopening of administrative record.

SUMMARY: The Food and Drug Administration (FDA) is reopening the administrative record for the proposed rulemaking for over-the-counter (OTC) anticaries drug products to obtain public comment on whether the labeling of OTC fluoride-containing drug products should include the quantity of fluoride, i.e., the specific amount of fluoride present in the product. The issue was raised by a Department committee that was considering ways of establishing optimal fluoride levels in dental products, as a means of reducing dental caries while minimizing dental fluorosis (discoloring of the teeth). This action is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments by January 25, 1993.

ADDRESSES: Written comments 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, 301–295–8000.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of March 28, 1980 (45 FR 20666), 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 anticaries drug products, together with the recommendations of the Advisory Review Panel on OTC Dentifrice and Dental Care Drug Products (the Panel), which was the advisory review panel responsible for evaluating data on the active ingredients in this class. The Panel recommended that the labeling of dental products state the name and quantity of each active ingredient in appropriate units (45 FR 20666 at 20674).

The agency's proposed regulation, in the form of a tentative final monograph, for OTC anticaries drug products was published in the **Federal Register** of September 30, 1985 (50 FR 39854). Under that proposal, the labeling for fluoride toothpaste drug products would not have to list the quantity of fluoride (i.e., the specific amount of a fluoride salt or ion in a fluoride toothpaste product) (50 FR 39854 at 39868). The agency stated that although section 502(e) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 352(e)) required disclosure of all active ingredients, there is no requirement that quantities of active ingredients in OTC drug products be listed, except for specific drugs designated in the act.

In February 1991, the Public Health Service Ad Hoc Subcommittee on Fluoride of the Committee to Coordinate Environmental Health and Related Programs (Subcommittee) issued a report entitled "Review of Fluoride: Benefits and Risks" (Ref. 1). In the executive summary of the report, the Subcommittee recommended that the U.S. Public Health Service sponsor a scientific conference(s) to recommend both the optimal level of fluoride exposure from all sources combined (including drinking water) and the appropriate usage of fluoride-containing dental products. The Subcommittee's goal was to achieve the benefits of reduced caries while minimizing dental fluorosis (Ref. 2).

In considering the Subcommittee's recommendations, the agency sent letters in April 1991, to three professional associations asking for suggestions on the possibility of having OTC fluoride-containing drug products labeled to identify their fluoride levels, in order to provide consumers with information to make informed decisions about using these products (Refs. 3, 4, and 5).

In response, one association (dental group) submitted information in support of having fluoride levels listed in the labeling of OTC fluoride-containing drug products (Refs. 6 and 7). The association stated that as of September 1991, it required the following labeling for fluoride-containing dentifrice products that it found acceptable for its endorsement: (1) Fluoride ion levels as percent-by-volume, and (2) the statement "Do not swallow—use only a pea-sized amount for children under six." The association stated that listing fluoride concentration in percent weight/volume (w/v) would provide consumers with useful information about the relative concentration of anticaries active ingredients among the

different dentifrice brands. The association pointed out that although two dentifrices might contain different percentages of active ingredient that would be difficult for consumers to compare, the products would contain the same amount of fluoride. The association provided the following example: a 0.76-percent sodium monofluorophosphate dentifrice with a density of 1.5 grams/milliliter (g/mL) would contain 0.10 percent weight/weight (w/w) fluoride and 0.15 percent w/v fluoride active ingredient, while a 0.24-percent sodium fluoride dentifrice with a density of 1.4 g/mL would contain 0.11 percent w/w fluoride and 0.15 percent w/v of fluoride active ingredient. The association mentioned that the percentage differences between fluoride compound concentrations could be confusing to consumers, who may think that there is more fluoride in a 0.76-percent sodium monofluorophosphate dentifrice compared to a 0.24-percent sodium fluoride dentifrice. The association added that toothpaste is dispensed by volume and not by weight; thus, the labeling of fluoride concentration in percent w/v would be more meaningful to consumers. The association stated that by identifying dentifrice fluoride levels in percentage w/v, all dentifrice products on the market that contain theoretical total fluorine at concentrations between 1,000 and 1,100 parts per million (ppm) will contain between 0.14 percent and 0.15 percent fluoride. Dentifrice products containing 1,500 ppm theoretical total fluorine would contain 0.20 percent fluoride. The association noted that this type of labeling terminology has been used by FDA to express the concentration of active ingredients for other topical OTC drug products.

The other two associations (trade groups) responded in opposition to changing the labeling of OTC fluoride-containing drug products to identify fluoride levels. They provided the following reasons: (1) There is a lack of scientific support for a cause and effect relationship between the ingestion of fluoride from dentifrice products and the subsequent development of enamel fluorosis; (2) the reported increase in fluorosis (very mild to mild) appears to be a result of factors other than dentifrice use; (3) current manufacturing changes to reduce the fluoride content in baby formula has already been initiated and may counteract the reported increase in fluorosis; and (4) professional labeling to physicians regarding the administration of fluoride supplements to young children may reduce the increase of the "very mild to mild" forms of fluorosis that have been reported. The associations discussed 10 studies conducted over the past 10 years to assess exposure to various fluoride sources and the occurrence of enamel fluorosis (Ref. 8).

The trade associations further maintained that clinical and epidemiologic studies do not support an association between the use of fluoride dentifrices and the increase in "very mild and mild" fluorosis. The associations made the following recommendations: (1) There should be no changes in the formulation of current fluoride-containing dentifrices; and (2) there should be no changes in the labeling of fluoride-containing dentifrices with respect to specific fluoride content. The associations also expressed concern that stating the precise quantity of fluoride on dentifrice products might unjustifiably raise concerns by consumers about use of fluoride-containing dentifrices, thereby leading to their decreased use and resulting in an increase in the incidence of dental caries.

The agency has considered this concern about decreased use and is not presently aware of any data or information that providing this specific additional information in the labeling of dentifrice products would lead to a decreased use of these products. Comments or data on this issue are requested.

While considering the three associations' responses, the agency asked the dental association to comment on two additional ways that might be used to identify the level of fluoride per serving of a dentifrice: (1) "—— parts per million (ppm)" (e.g., "1,000 ppm") and (2) "—— milligrams per inch (mg/in)" (e.g., "2.4 mg/in") (Ref. 9). The agency stated that the term ppm would represent the content of fluoride in the dentifrice product, while the term "mg/in" would represent the mg of fluoride ion per inch (e.g., serving) of dentifrice. The agency mentioned that these alternatives might be considered for two reasons. First, fluoride concentrations have been expressed in ppm in drinking water and been recognized over the years for anticaries drug products. Second, mg per serving has been used for many years to label the fluoride content of oral vitamin/mineral products and oral fluoride tablets. The agency also noted that consumers are already familiar with the use of the term mg in food labeling (e.g., infant formulas, sodium levels, vitamin supplements, and other additives) and that consumers and health professionals are accustomed from food labeling to computing sodium intake in mg. The agency added that the term mg is also uniformly used to describe the amount of active ingredient(s) in OTC and prescription drug products.

The dental association responded that a consensus of its members preferred that the percentage of fluoride ion per w/v be used because it would be more meaningful to consumers (Ref. 10). The association mentioned that this method of expressing fluoride concentration is now used in Europe and would assist the agency in its efforts to achieve international harmonization of regulatory standards. The association added that this method would be consistent with the FDA's own method of expressing concentrations of active ingredients for other topical OTC drugs, e.g., 0.5 percent hydrocortisone. The association felt that an expression of mg/in has shortcomings because all toothpaste brands do not have the same tube orifice size. For this reason, two products could have the same fluoride concentration, but different fluoride levels in mg/in. The association contended that mg/in would result in a wide variation of values that would merely confuse consumers. Accordingly, the association concluded that expressing fluoride concentration as percent w/v would offer the most uniform means of expressing concentration and enable consumers to make intelligent decisions about their choice of products.

The agency believes that the labeling of fluoride concentration in the form of percent weight of fluoride per unit volume (w/v) has merit. However, this labeling format would not provide information that is consistent with sodium content, vitamin, or food labeling that consumers are familiar with. Also, this labeling format would not be consistent with the labeling of fluoride supplements, e.g., tablets, drops, or vitamin products, that are labeled to state the amount of fluoride per tablet or milliliter. The agency believes that use of the terms ppm and/or mg might provide a more uniform approach to labeling of different types of products that contain fluoride. The agency believes it is important to achieve a consistent labeling approach among fluoride-containing products to ensure that optimal levels of fluoridation are not exceeded, while preventing dental caries and minimizing the occurrence of dental fluorosis.

The agency is currently considering the three associations' views on this matter and, before proceeding further, is seeking full public comment on this

issue. Is there consumer benefit in having OTC fluoride-containing drug products labeled to state their fluoride levels? If the answer is yes, what is the best way(s) to provide this information to consumers. The agency particularly invites comments on the fluoride labeling options discussed above, as well as any other possible labeling options that might be used. Would a combination of labeling options (e.g., percent w/v and mg/in) provide consumers with the most useful information?

The agency is currently developing the final rule for OTC anticaries drug products. The agency believes that it would be appropriate to reopen the administrative record to consider comments on these fluoride labeling issues. The agency also needs to respond to the Subcommittee's request for recommendations on the labeling of OTC fluoride-containing drug products. The agency therefore finds that good cause exists to reopen the administrative record. The agency plans to discuss identification of fluoride levels in the labeling of OTC drug products containing fluoride in the final rule.

Interested persons may on or before January 25, 1993, submit to the Dockets Management Branch (address above) written comments regarding the labeling of OTC fluoride-containing drug products to identify their fluoride levels. Three copies of any comments are to be submitted except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

References

(1) Department of Health and Human Services, "Review of Fluoride Benefits and Risks: Report of the Ad Hoc Subcommittee on Fluoride of the Committee to Coordinate Environmental Health and Related Programs," February, 1991, in OTC Vol. No. 08FLTFM, Docket No. 80N–0042, Dockets Management Branch.

(2) Department of Health and Human Services, "Executive Summary of the Review of Fluoride Benefits and Risks," February, 1991, in OTC Vol. No. 08FLTFM, Docket No. 80N–0042, Dockets Management Branch.

(3) Letter from W. E. Gilbertson, FDA, to C. Whall, Council on Dental Therapeutics of the American Dental Association, coded LET15, Docket No. 80N–0042, Dockets Management Branch.

(4) Letter from W. E. Gilbertson, FDA, to J. D. Cope, Nonprescription Drug Manufacturers Association, coded LET16, Docket No. 80N–0042, Dockets Management Branch.

(5) Letter from W. E. Gilbertson, FDA, to E. E. Kavanaugh, The Cosmetic, Toiletry and Fragrance Association, coded LET17, Docket No. 80N–0042, Dockets Management Branch.

(6) Comment No. C0086, Docket No. 80N–0042, Dockets Management Branch.

(7) Comment No. C0087, Docket No. 80N–0042, Dockets Management Branch.

(8) Comment No. C0085, Docket No. 80N–0042, Dockets Management Branch.

(9) Letter from W. E. Gilbertson, FDA, to K. H. Burrell, Council on Dental Therapeutics of the American Dental Association, coded LET19, Docket No. 80N–0042, Dockets Management Branch.

(10) Comment No. C0088, Docket No. 80N–0042, Dockets Management Branch.

Dated: November 3, 1992.

Michael R. Taylor,

Deputy Commissioner for Policy.

[FR Doc. 92–28431 Filed 11–23–92; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

Schedules of Controlled Substances; Proposed Placement of Zolpidem into Schedule IV

AGENCY: Drug Enforcement Administration, Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: This proposed rule places the drug, zolpidem, into Schedule IV of the Controlled Substances Act (CSA). The Administrator of the Drug Enforcement Administration (DEA) has received a recommendation from the Department of Health and Human Services (DHHS) that zolpidem be controlled in Schedule IV.

DATES: Comments must be submitted on or before December 24, 1992.

ADDRESSES: Comments and objections should be submitted to: Administrator, Drug Enforcement Administration, Washington, DC 20537. Attention: DEA Federal Register Representative/CCR.

FOR FURTHER INFORMATION CONTACT: Howard McClain, Jr., Chief, Drug and Chemical Evaluation Section, Drug Enforcement Administration, Washington, DC 20537, Telephone: (202) 307–7183.

SUPPLEMENTARY INFORMATION: On September 15, 1992, the Administrator of the DEA received a letter from the Assistant Secretary for Health, acting on behalf of the Secretary of the DHHS, recommending that zolpidem be placed in Schedule IV of the CSA (Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 801–996)). Enclosed with this letter from the Assistant Secretary was a document which listed the factors which the Act requires the Secretary to consider and the summarized considerations of the Secretary in recommending control for zolpidem. In his letter, the Assistant Secretary recommended, further, that this scheduling action become effective if and when the zolpidem New Drug Application (NDA) receives final approval by the Food and Drug Administration (FDA).

The factors considered by the Assistant Secretary for zolpidem were:

(1) Its actual or relative potential for abuse;

(2) Scientific evidence of its pharmacological effect, if known;

(3) The state of current scientific knowledge regarding the drug or other substance;

(4) Its history and current pattern of abuse:

(5) The scope, duration, and significance of abuse;

(6) What, if any, risk there is to the public health;

(7) Its psychic or physiological dependence liability; and

(8) Whether the substance is an immediate precursor of a substance already controlled under the CSA.

Relying on the scientific and medical evaluation and the recommendation of the Assistant Secretary of Health, received in accordance with section 201(f) of the Act (21 U.S.C. 811(f)), the Administrator of the DEA, pursuant to sections 201(a) and 201(b) of the Act (21 U.S.C. 811(a) and 811(b)), finds that:

(1) Based on information now available, zolpidem has a low potential for abuse relative to the drugs or other substances currently listed in Schedule III;

(2) Zolpidem will, upon issuance of a NDA by the FDA, have a currently accepted medical use in treatment in the United States; and

(3) Abuse of zolpidem may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in Schedule III.

Interested persons are invited to submit their comments, objections or requests for a hearing, in writing, with regard to this proposal. Requests for a hearing should state, with particularity, the issues concerning which the person desires to be heard. All correspondence regarding this matter should be submitted to the Administrator, Drug Enforcement Administration, Washington, DC 20537. Attention: DEA Federal Register Representative.

In the event that comments, objections or requests for a hearing raise one or more issues which the Administrator finds warrant a hearing, the