§ 381.304 [Amended]

4. In § 381.304, paragraph (a) is amended by removing ''$ 10,640'' and inserting ''$ 10,990'' in its place.

§ 381.305 [Amended]

5. In § 381.305, paragraph (a) is amended by removing ''$ 3,990'' and inserting ''$ 4,120'' in its place.

§ 381.403 [Amended]

6. Section 381.403 is amended by removing ''$ 6,920'' and inserting ''$ 7,140'' in its place.

§ 381.505 [Amended]

7. In § 381.505, paragraph (a) is amended by removing ''$ 11,960'' and inserting ''$ 12,340'' in its place and by removing ''$ 13,540'' and inserting ''$ 13,970'' in its place.

§ 381.801 [Amended]

8. Section 381.801 is amended by removing ''$ 1,560'' and inserting ''$ 1,620'' in its place.

[FR Doc. 98–22582 Filed 8–21–98; 8:45 am]

BILLING CODE 6717–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 310

[Docket No. 98N–0636]

RIN 0910–AA01

Status of Certain Additional Over-the-Counter Drug Category II and III Active Ingredients

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule stating that certain ingredients in over-the-counter (OTC) drug products are not generally recognized as safe and effective or are misbranded. FDA is issuing this final rule after considering the reports and recommendations of various OTC drug advisory review panels and public comments on proposed agency regulations, which were issued in the form of a tentative final monograph (proposed rule). Based on the absence of any submissions on these ingredients to the panels, as well as the failure of interested parties to submit new data or information to FDA under the proposed regulations, the agency has determined that the presence of these ingredients in an OTC drug product would result in that drug product not being generally recognized as safe and effective for its intended use or would result in misbranding. This final rule is part of the ongoing review of OTC drug products conducted by FDA.

EFFECTIVE DATE: February 22, 1999.

FOR FURTHER INFORMATION CONTACT: Gerald M. Rachanow, Center for Drug Evaluation and Research (HFD–560), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–2307.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of November 7, 1990 (55 FR 46914), FDA published under § 330.10(a)(7)(ii) (21 CFR 330.10(a)(7)(ii)) a final rule on the status of certain OTC drug Category II and III active ingredients. That final rule declared as not generally recognized as safe and effective certain active ingredients that had been proposed as nonmonograph (Category II or Category III) under the agency's OTC drug review. The periods for submission of comments and new data following the publication of a notice of proposed rulemaking (NPRM) had closed and no significant comments or new data had been submitted to upgrade the status of these ingredients. In each instance, a final rule for the class of ingredients involved had not been published to date.

In the **Federal Register** of May 10, 1993 (58 FR 27636), FDA published a final rule establishing that certain additional active ingredients in OTC drug products are not generally recognized as safe and effective or are misbranded. That final rule included active ingredients from a number of OTC drug rulemakings that were not covered by the November 7, 1990, final rule (see Table I of the May 10, 1993, final rule (58 FR 27636 at 27639 to 27641) for a list of OTC drug rulemakings and active ingredients covered by that final rule). The final rule included a number of active ingredients found in OTC internal analgesic and orally administered menstrual drug products. Those ingredients are listed in § 310.545(a)(23) and (a)(24) (21 CFR 310.545(a)(23) and (a)(24)), respectively.

The ingredients listed in these sections do not include ephedrine, ephedrine salts (ephedrine hydrochloride, ephedrine sulfate, racephedrine hydrochloride), atropine, or atropine salts (atropine sulfate). The agency is aware of several combination drug products marketed for OTC internal analgesic or menstrual use that include ephedrine sulfate and atropine sulfate among their ingredients, in addition to aspirin or acetaminophen (Ref. 1). No submissions of data supporting the use of ephedrine or atropine singly or in combination were made to the advisory review panels that reviewed these classes of OTC drug products. No information was provided following publication of the tentative final monographs for OTC orally administered menstrual drug products or internal analgesic, antipyretic, and antirheumatic drug products on November 16, 1988 (53 FR 46194 and 46204, respectively). A final rule has not been published to date for either of these classes of OTC drug products.

FDA is not aware of any information that supports the use of ephedrine or atropine as active ingredients in OTC orally administered menstrual or internal analgesic, antipyretic, and antirheumatic drug products. Accordingly, these active ingredients will not be included in the relevant final monographs because they have not been shown to be generally recognized as safe and effective for their intended use(s). These ingredients should be eliminated from OTC drug products 180 days after the date of publication in the **Federal Register** of this final rule, regardless of whether further testing is undertaken to justify future use.

Publication of a final rule under this proceeding does not preclude a manufacturer's testing an ingredient. New, relevant data can be submitted to the agency at a later date as the subject of a new drug application (NDA) that may provide for prescription or OTC marketing status (see part 314 (21 CFR part 314)). As an alternative, where there are adequate data establishing general recognition of safety and effectiveness, such data may be submitted in an appropriate citizen petition to amend a monograph (see § 10.30 (21 CFR 10.30)).

II. The Agency's Final Conclusions on Certain OTC Drug Category II and III Ingredients

The agency notes that no comments or data have been submitted to the OTC drug review to support any ephedrine or atropine ingredient as being generally recognized as safe and effective for any OTC uses in orally administered menstrual or internal analgesic, antipyretic, and antirheumatic drug products. The agency has determined that these ingredients should be deemed not generally recognized as safe and effective for OTC use before a final monograph for each respective drug category is established. Accordingly, any drug product containing any of these ingredients and labeled for OTC

oral menstrual or internal analgesic, antipyretic, and antirheumatic use will be considered nonmonograph and misbranded under section 502 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 352) and a new drug under section 201(p) of the act (21 U.S.C. 321(p)) for which an approved application under section 505 of the act (21 U.S.C. 355) and part 314 of the regulations is required for marketing. As an alternative, where there are adequate data establishing general recognition of safety and effectiveness, such data may be submitted in a citizen petition to amend the appropriate monograph to include any of these ingredients in OTC drug products (see § 10.30). Any OTC drug product containing any of these ingredients and labeled for the uses discussed in this document that is initially introduced or initially delivered for introduction into interstate commerce after the effective date of this final rule and that is not the subject of an approved application will be in violation of sections 502 and 505 of the act and, therefore, subject to regulatory action. Further, any OTC drug product subject to the final rule that is repackaged or relabeled after the effective date of the rule would be required to be in compliance with the rule regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufacturers are encouraged to comply voluntarily with the rule at the earliest possible date.

III. Reference

(1) American Pharmaceutical Association, *Handbook of Nonprescription Drugs*, 10th ed., pp. 646, 648, and 667, 1993.

IV. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612). 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.

Title II of the Unfunded Mandates Reform Act (2 U.S.C. 1501 *et seq.*) requires that agencies prepare a written statement and economic analysis before proposing any rule that may result in an expenditure in any 1 year by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million (adjusted annually for inflation).

The agency believes that this final rule is consistent with the principles set out in the Executive Order and in these two statutes. The purpose of this final rule is to act on the nonmonograph status of certain ingredients in advance of finalization of other monograph conditions in order to expedite completion of the OTC drug review. There are a limited number of products currently marketed that will be affected by this rule. The agency is aware of at least three products, although there may be more. These products are marketed by three different manufacturers, all of which are considered small entities, using the U.S. Small Business Administration designation for this industry (750 employees).

Manufacturers of these products will no longer be able to market products containing the ephedrine or atropine ingredients included in this final rule after its effective date. However, the manufacturers will be able to reformulate these products and continue to market them with proposed monograph ingredients. The cost of reformulation and relabeling to any one manufacturer should be minimal as only one product per manufacturer appears to be affected. Total costs should be minimal ($500,000 to $1 million) as only a limited number of products appear to be affected. The lost sales from the products containing nonmonograph ingredients may be offset by sales of the substitute products containing monograph ingredients. In addition, manufacturers have been aware of the status of these products since 1988 and have not submitted any safety and effectiveness data to the agency.

The agency considered but rejected not acting on these ingredients in advance of the finalization of other monograph conditions. The final monographs for OTC orally administered menstrual and internal analgesic, antipyretic, and antirheumatic drug products are not expected to be completed for a period of time. The agency also considered publishing an additional notice alerting manufacturers that the ingredients in this final rule would be removed earlier. However, safety and effectiveness have not been established for these ingredients and manufacturers have not submitted the necessary data. Based on past experience, FDA has found that manufacturers do not submit the necessary data after a proposed rule is published when no data or petitions have been submitted in response to prior requests. In addition, consumers will benefit from the early removal from the marketplace of products containing ingredients for which safety and effectiveness have not been established. Consumers can then purchase products containing only ingredients proposed for monograph status. Manufacturers who choose to reformulate or replace affected products will be able to use alternative ingredients that are proposed as monograph conditions without incurring any additional expense of clinical testing for those ingredients.

While this final rule may cause manufacturers to discontinue marketing or to reformulate some products prior to issuance of the applicable final monograph, these manufacturers have known for some time that if adequate data were not submitted to support safety and effectiveness, cessation of marketing of the current products would be required, in any event, when the final monographs are published. Because this rule imposes no additional reporting or recordkeeping requirements, no additional professional skills are necessary to comply.

The analysis shows that this final rule is not economically significant under Executive Order 12866 and that the agency has considered the burden to small entities. Based on the above analysis, the agency does not believe that the few affected manufacturers will incur a significant economic impact, although there may be some reformulation costs or inventory losses. Thus, this economic analysis, together with other relevant sections of this document, serves as the agency's regulatory flexibility analysis, as required under the Regulatory Flexibility Act. Finally, this analysis shows that the Unfunded Mandates Act does not apply to the final rule because it would not result in an expenditure in any 1 year by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million.

V. Paperwork Reduction Act of 1995

This final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

VI. Environmental Impact

The agency has determined under 21 CFR 25.30(h) that this action is of a type that is categorically excluded from the preparation of an environmental assessment because these actions, as a

class, will not result in the production or distribution of any substance and therefore will not result in the production of any substance into the environment.

List of Subjects in 21 CFR Part 310

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

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 310 is 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, 357, 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 redesignating the text of paragraphs (a)(23) and (a)(24) as paragraphs (a)(23)(i) and (a)(24)(i), respectively; by adding paragraphs (a)(23)(i) and (a)(24)(i) headings, by adding paragraphs (a)(23)(ii), (a)(24)(ii), and (d)(26); and by revising paragraph (d)(11) to read as follows:

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

(a) * * *

(23) *Internal analgesic drug products*—(i) *Approved as of November 10, 1993.* * * *

(ii) *Approved as of* February 22, 1999.

Any atropine ingredient

Any ephedrine ingredient

(24) *Orally administered menstrual drug products*—(i) *Approved as of November 10, 1993.* * * *

(ii) *Approved as of* February 22, 1999.

Any atropine ingredient

Any ephedrine ingredient

* * * * *

(d) * * *

(11) November 10, 1993, for products subject to paragraphs (a)(8)(ii), (a)(10)(v) through (a)(10)(vii), (a)(18)(ii) (except products that contain ferric subsulfate) through (a)(18)(vi), (a)(22)(ii), (a)(23)(i), (a)(24)(i), and (a)(25) of this section.

* * * * *

(26) February 22, 1999, for products subject to paragraphs (a)(23)(ii) and (a)(24)(ii) of this section.

Dated: August 11, 1998.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 98–22568 Filed 8–21–98; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 892

[Docket No. 96N–0320]

Radiology Devices; Classifications for Five Medical Image Management Devices; Correction

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule; correction.

SUMMARY: The Food and Drug Administration (FDA) is correcting a final rule that appeared in the **Federal Register** of April 29, 1998 (63 FR 23385). The document classified, along with other devices, the medical image storage device and medical image communications device. These devices were classified into Class I and were exempted from the requirement of premarket notification when they do not use irreversible data compression. The document was published with an incomplete device identification and description of the conditions for exemption from premarket notification. This document corrects those errors.

EFFECTIVE DATE: August 24, 1998.

FOR FURTHER INFORMATION CONTACT: Loren A. Zaremba, Center for Devices and Radiological Health (HFZ–470), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301–594–1212.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of April 29, 1998 (63 FR 23385), FDA published a final rule classifying certain medical image management devices. Under the final rule, the medical image storage device and medical image communications device were classified into Class I and exempted from the requirement of premarket notification when they do not use irreversible data compression. Although the preamble of the final rule, as well as the proposal upon which the final rule is based, correctly identifies the devices and describes the limitation of the exemption from premarket notification, an editorial change was mistakenly made in the regulatory language of the final rule. As it currently reads, the device identification, not the exemption provision, is limited to those devices that do not perform irreversible data compression. This has the effect of leaving unclassified the medical image storage device and medical image communications device that do not perform irreversible data compression. This document corrects the error by removing the limiting language form the device identification paragraph and reinserting the appropriate language in the classification paragraph.

Furthermore, the agency also notes that in response to the comments in the preamble of the April 29, 1998, final rule, the agency erroneously stated that ''* * * the class I devices will be exempt from the design controls requirement in accordance with § 820.30 (21 CFR 820.30). FDA believes that design controls are not necessary for class I devices in this rule.'' However, under § 820.30(a)(2)(i), devices automated with computer software are specifically identified as devices which are subject to design controls. Because the medical image storage device and medical image communications device described by the classification regulation are digital, they are by definition, ''automated with computer software.'' The agency is therefore clarifying that these devices are subject to design controls.

In FR Doc. 98–11317 appearing on page 23385 in the **Federal Register** of April 29, 1998, the following corrections are made:

§ 892.2010 [Corrected]

1. On page 23387, in the first column, in § 892.2010 *Medical image storage device*, paragraph (a) is corrected by removing the phrase ''without irreversible data compression'' and paragraph (b) is corrected by adding the phrase ''only when the device stores images without performing irreversible data compression'' at the end of the paragraph.

§ 892.2020 [Corrected]

2. On the same page, in the same column, in § 892.2020 *Medical image communications device*, paragraph (a) is corrected by removing the phrase ''without irreversible data compression'' and paragraph (b) is corrected by adding the phrase ''only when the device transfers images without performing irreversible data compression'' at the end of the paragraph.

Dated: August 7, 1998.

D.B. Burlington,

Director, Center for Devices and Radiological Health.

[FR Doc. 98–22571 Filed 8–21–98; 8:45 am]

BILLING CODE 4160–01–F