DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 201, 310, and 314

[Docket No. 92N-0076]

RIN 0905-AA06

Labeling of Drug Products for Over-the-Counter Human Use Subject to an Approved Application or Abbreviated Application

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing that the alternative labeling policy that applies to over-the-counter (OTC) drug products that are marketed under an OTC drug monograph be extended, in part, to OTC drug products that are marketed under an approved new drug or an abbreviated new drug application (hereinafter collectively called an application). The label and labeling of OTC drug products approved under an application would be permitted to contain, in a prominent and conspicuous location, either the designation "APPROVED USES," together with the specific wording on indications for use established under an approved application, all of which must appear within a boxed area; or the designation "APPROVED INFORMATION," together with the specific wording on indications for use and other applicable labeling (e.g., statement of identity, warnings, and directions) established under an approved application, all of which must appear within a boxed area. FDA is issuing this proposal to make the labeling of OTC drug products consistent, whether the products are marketed under an approved application or under an OTC drug monograph.

DATES: Written comments by January 10, 1994.

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, 301-594-5000.

SUPPLEMENTARY INFORMATION: In the Federal Register of May 1, 1986 (51 FR 16258), FDA issued a final rule in § 330.1(c)(2) (21 CFR 330.1(c)(2)) establishing alternate labeling for OTC drug products marketed under an OTC drug monograph. (OTC drug products that follow all conditions for marketing set out in an OTC drug monograph are deemed generally recognized as safe and effective and not misbranded.) The final rule established three alternatives for the "Indications" portion of OTC drug product labeling. The label and labeling of OTC drug products marketed under an OTC drug monograph are required to contain, in a prominent and conspicuous location, the "Indications" that have been established in a final monograph. At the option of the manufacturer, this labeling may be designated "APPROVED USES," or given a similar permitted designation. If the "APPROVED USES" designation is used, the labeling must appear within a boxed area. Other labeling in the monograph may also be placed within the boxed area, in which case the labeling is designated "APPROVED INFORMATION," rather than "APPROVED USES." All information must be in the exact language established in the monograph. In addition, there must be a statement that the boxed information was published by FDA. In lieu of this latter statement, the designation of the boxed area may be modified to read "FDA APPROVED USES" or "FDA APPROVED INFORMATION," or similar wording.

As a second alternative, "Indications" labeling may contain other truthful and nonmisleading statements, describing only those indications for use that have been established in an applicable monograph. In this case, the "APPROVED USES" or "APPROVED INFORMATION" designation may not be used.

Under a third alternative, the labeling may meet the boxed area requirement, described above, and in addition use other truthful and nonmisleading substitute or alternate language describing indications for use. This additional language must appear elsewhere in the labeling (outside the boxed area).

OTC drug labeling other than indications for use (e.g., statement of identity, warnings, and directions) must use the specific wording established under the monograph.

During the time that the final rule was being developed, several comments requested that the "FDA APPROVED USES" designation be permitted for OTC drug products marketed under an approved application as well as for those marketed under a monograph. The agency agreed in principle, stating that it would promote consistency in the labeling of OTC drug products if all products, whether approved under an application or included in a monograph, were permitted to use the terms "FDA APPROVED USES" or "FDA APPROVED INFORMATION" in their labeling. However, since § 330.1(c) was in a portion of the FDA regulations that applied only to OTC drugs covered by a monograph, a separate regulation would be required to address labeling of OTC drug products subject to an application. Accordingly, the agency is now proposing regulations under parts 310 and 314 (21 CFR parts 310 and 314) for alternate labeling of OTC drug products that are subject to an approved application.

I. OTC Drug Products Subject to an Application

There are several classes of OTC drug products that are subject to an application. Examples include:

1. Products containing ingredients that are approved in monographs but the products are nonetheless subject to an application because the ingredient is formulated in a sustained-release dosage form. Examples include chlorpheniramine maleate (antihistamine) and pseudoephedrine hydrochloride (nasal decongestant).

2. Products containing ingredients that have been approved in a monograph for some indications but are not included in a monograph for the use covered by the approved application. An example of such an ingredient is doxylamine succinate, which has been proposed for inclusion in the antihistamine drug products monograph but which has not been approved as a nighttime sleep-aid monograph ingredient. Doxylamine succinate is the subject of an approved application for the nighttime sleep-aid indication.

3. Products containing ingredients for which an application for OTC use was approved before the ingredient was included in the OTC drug review. Examples include triprolidine hydrochloride (antihistamine) and dexbrompheniramine maleate (antihistamine). These applications remain in effect until a final monograph is issued and becomes effective.

4. Products containing ingredients that are not in the OTC drug review but which have indications for use approved in an application where the indications are similar to those in a proposed or final OTC drug monograph. Examples include loperamide hydrochloride (antidiarrheal), ibuprofen (analgesic/antipyretic), and tioconazole (topical antifungal).

5. Products containing ingredients that are not in the OTC drug review and

for which there currently are no similar OTC drug products. An example is clotrimazole for vaginal yeast infections.

The above examples are not intended to be all inclusive of the types of OTC drug products that are subject to an application.

II. OTC Application Labeling Policy

During the course of the OTC drug review, the agency has established labeling policy that is intended to promote uniformity and to help prevent consumer confusion in the marketplace. The agency's policy provides that OTC drug products containing an ingredient in any of the first four classes described above should be labeled in the same manner as a corresponding or similar OTC drug product labeled and marketed under a proposed or final OTC drug monograph. Where only an advance notice of proposed rulemaking (panel report) has been published, the agency has used it as a guide in approving labeling for OTC drug products marketed under an application. Where both a panel report and a tentative final monograph have been published, the agency has used the tentative final monograph as a guide, but has allowed OTC drug products approved under an application to follow either the panel report or the tentative final monograph. Where a final OTC drug monograph has been published, the agency has used the monograph as a guide in approving OTC labeling in an application. The agency intends to continue to follow this procedure during the completion of the OTC drug review in approving the labeling of OTC drug products subject to an application.

III. FDA Approved Language for New Drugs for OTC Use

In response to the proposal to establish alternate labeling for OTC drug products, one comment noted that section 301(l) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 331(l)) prohibits the use in labeling of any representation or suggestion that "approval of an application with respect to such drug * * * is in effect under section 505, 515, or 520(g) * * *." The comment argued that the use of the "FDA APPROVED" language is contrary to the intent and meaning of section 301(l) of the act. The comment stated that as a result, "non-NDA'd OTC drug products would be allowed to use such language, but that NDA'd OTC drug products would be prohibited from using it." The comment maintained that the issue of labeling of OTC drugs subject to an application as "FDA APPROVED" could only be resolved by amendment of the act. The comment cited the then pending "FDA Approval Labeling Act" (H.R. 2244) (Ref. 1) and mentioned that this act would have allowed the statement "FDA APPROVED," followed by the application number on prescription drugs. The comment suggested that FDA use a similar approach for the labeling of OTC drug products marketed under an application. (H.R. 2244 was passed by the House, but was never enacted.)

Another comment contended that section 301(l) of the act can be interpreted to apply only to statements connoting new drug approval pursuant to section 505 of the act (21 U.S.C. 355) and therefore terminology such as "APPROVED USES," when used with respect to a product's labeling, is not prohibited by the act.

This comment stated that equal treatment of OTC drug products marketed under an application and marketed under an OTC drug monograph would be consistent with FDA's policy of promoting uniformity in OTC drug labeling under applicable statutory standards. The comment maintained that uniformity would lessen consumer confusion about the label indications on OTC drugs, because there is no difference to the consumer between an OTC drug marketed pursuant to an application or one marketed under a monograph. The comments requested that the agency clarify that the "FDA APPROVED USES" language would also be permitted for OTC drugs marketed pursuant to an application, and that the agency declare that this language would not be in violation of section 301(l) of the act.

As discussed in the final rule (51 FR 16258), section 301(l) of the act, by its own terms, prohibits only representations or suggestions that an approval of an application under section 505 of the act is in effect for a drug product. It does not apply to requirements for labeling related to indications for use, such as those in the alternate labeling regulation in § 330.1(c). Similarly, the prohibition in section 301(l) of the act does not apply to the alternate labeling proposed in this notice.

Reference

(1) Comment No. C00072, Docket No. 82N–0154.

IV. Proposed Regulation

FDA is proposing to amend the labeling requirements in 21 CFR part 310 for new drugs approved for OTC use by adding new § 310.104. Because 21 CFR part 201 sets forth the general provisions for the labeling of drugs, new § 201.65 is being added as a cross-reference to new § 301.104 for the convenience of the reader. As proposed, the label and labeling of OTC drug products approved under an application would be permitted to contain in a prominent and conspicuous location either: (1) The designation "APPROVED USES," together with the specific wording on indications for use established under an approved application, all of which must appear within a boxed area, or (2) the designation "APPROVED INFORMATION," together with the specific wording on indications for use and other applicable labeling (e.g., statement of identity, warnings, and directions) established under an approved application, all of which must appear within a boxed area. The designation of the boxed area may be modified to read: "FDA APPROVED USES" or "FDA APPROVED INFORMATION," as appropriate, or "USES (or "INFORMATION") APPROVED BY THE FOOD AND DRUG ADMINISTRATION," or other similar wording.

Section 330.1(c) permits the label and labeling of OTC drug products that are marketed under an OTC drug monograph to use wording to describe indications for use other than that established in an OTC drug monograph. However, such alternative language must meet the statutory prohibitions against false or misleading labeling, and it may neither appear within a boxed area nor be designated as "APPROVED USES." Also, the regulations provide that such labeling may contain the approved monograph language on indications for use, within a boxed area designated "APPROVED USES," plus alternative language describing indications for use that is not false or misleading, which must appear elsewhere in the labeling (outside the box). In either case, manufacturers of OTC drugs covered by an OTC drug monograph may use these labeling alternatives without FDA preclearance of the labeling. However, all labeling for new drugs, including alternative language relating to indications for use, requires preclearance by FDA. FDA may approve alternate labeling language for describing indications for use during the process of approving applications for new OTC drugs. Therefore, since the proposal encompasses all labeling approved under an application, the present proposed regulation does not address, as a separate matter, possible labeling alternatives of the type allowed under a monograph.

The agency is also proposing to amend § 314.70(d) relating to changes to

an approved application. As proposed, if the "APPROVED USES"/"APPROVED INFORMATION"/boxed area concept is the only change being made in the application's approved labeling, manufacturers would not be required to submit a supplemental application but could inform the agency when this change occurred by including this information in the annual report for that application.

As discussed above, many classes of OTC drug products subject to an application are very closely related to OTC drug products included in the OTC drug review. In most instances, the labeling for OTC drug products is based on labeling developed during the course of the OTC drug review. Therefore, the labeling is virtually the same whether a product is marketed under an OTC drug monograph or an approved application. The agency has considered whether new drugs with applications approved for OTC use should be permitted to use the "APPROVED USES" or "APPROVED INFORMATION" language as part of their labeling, before an OTC drug monograph has become final for the corresponding class of OTC drugs. In the case of drugs marketed under a monograph, the "APPROVED USES" terminology described in § 330.1(c)(2) cannot be implemented until relevant OTC drug monographs are issued in final form. A product cannot bear an "APPROVED USES" designation until the use has, in fact, been approved by FDA, which will only occur when the final OTC drug monograph is issued. Moreover, for many years during the course of the OTC drug review, the agency has approved applications for new drugs for OTC use subject to the following conditions:

These (labeling) changes are requested to ensure parity of regulatory treatment among similar products marketed over-the-counter, whether or not they are the subject of an approved application. Please note that, should this ingredient be included in a final monograph concerning OTC (name of monograph) drug products, you will be expected to conform to the monograph requirements.

The use of "FDA APPROVED" language will be implemented on a drug category-by-category basis as final OTC drug monographs are issued. Because of the interrelationship of the labeling of drugs marketed under an OTC drug monograph and drugs approved under an application, the agency believes that new drugs for OTC use also should not use the "APPROVED USES" designation until the final OTC drug monograph for the corresponding class of OTC drugs has been issued. Thereafter, the "APPROVED USES"/boxed area concept would be implemented at the same time for all drug products in that category, whether marketed under an OTC drug monograph or an application. The agency believes that this approach would promote consistency in the labeling of OTC drugs and reduce consumer confusion. Unless labeling for both types of OTC drugs within the same drug category is implemented at the same time, consumers could be misled into believing that one of the two types of OTC drugs (whether subject to a monograph or to an application) has a special status.

V. Abbreviated Applications—"Same" Labeling Requirements

Section 505(j)(2)(A)(v) of the act requires that the labeling for a new drug approved via an abbreviated application be the same as the labeling approved for the listed drug except for changes required because of differences approved under a petition or because the new drug and the listed drug are produced or distributed by different manufacturers. If this "sameness" requirement were applied literally to this new alternate labeling proposal, it could be interpreted as meaning that a manufacturer of an OTC drug product approved via an abbreviated application could not use the "APPROVED USES" or "APPROVED INFORMATION" language in its product's labeling unless the manufacturer of the listed drug were to do so first. This could also mean that if the manufacturer of the listed drug chose not to use the "APPROVED USES" or "APPROVED INFORMATION" language in its product's labeling, then the manufacturers of other similar products approved via abbreviated applications could never use this language in their labeling. The agency does not find this to be an equitable situation.

The agency does not see any inequities if a new drug approved for marketing via an abbreviated application pursuant to section 505(j)(2) of the act (often referred to as a "generic drug") were to contain the "APPROVED USES" or "APPROVED INFORMATION" language and the listed drug did not contain this information in its labeling, or if the generic drug contained this information in its labeling before the listed drug did, or if the listed drug contained this information and some or all generic versions of the drug did not contain the information. Similarly, all manufacturers of OTC drug products marketed via monographs may not elect to use "APPROVED USES/APPROVED INFORMATION" labeling, nor will manufacturers implement such labeling at the same time. The agency does not believe that consumers would be misled by such a difference in product labeling, whether the product is marketed pursuant to an approved application or an OTC drug monograph. Accordingly, FDA proposes that manufacturers of new drugs approved via an abbreviated application pursuant to section 505(j)(2) of the act be allowed to use this limited alternative labeling provided for in proposed § 310.104. Unless otherwise required under § 314.70(b) or (c), manufacturers do not need to submit a supplement to make such changes, but shall describe the changes in the next annual report for the application in accord with the procedures proposed in § 314.70(d)(10). All conditions as to when such labeling could be implemented, as described above, would also apply to new drugs approved pursuant to section 505(j)(2) of the act.

The agency has examined the economic consequences of this proposed rulemaking and has determined that it does not require either a regulatory impact analysis, as specified in Executive Order 12866, or a regulatory flexibility analysis, as defined in the Regulatory Flexibility Act (Pub. L. 96–354). Manufacturers would normally have up to 12 months after each final OTC drug monograph is published in the **Federal Register** to revise their product labeling. In most cases, this would be routinely done at the next printing so that minimal costs should be incurred. Likewise, manufacturers of new drugs for OTC use are not expected to add the "FDA APPROVED" terminology to their product labeling until the next label printing. Because the labeling for these drug products will already have been approved by the agency, the agency is providing that manufacturers may include this change in the conditions in an approved application, as one of the changes described in the annual report for that application. (See § 314.70(d).) Thus, manufacturers will be able to incorporate alternate labeling, if any is selected, in the normal course of business. The impact of the proposed rule, if implemented, appears to be minimal. Therefore, the agency concludes that the proposed rule is not a major rule as defined in Executive Order 12866. Further, the agency certifies that the proposed rule, if implemented, will not have a significant economic impact on a substantial number of small entities as defined in the Regulatory Flexibility Act.

The agency invites public comment regarding any substantial or significant

economic impact that this rulemaking would have on manufacturers of new drug products for OTC use. Comments regarding the impact of this rulemaking on these manufacturers should be accompanied by documentation. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this rulemaking in the preamble to the final rule.The agency has determined under 21 CFR 25.24(c)(6) 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.

Interested persons may, on or before January 10, 1994, submit to the Dockets Management Branch (address above) written comments regarding this proposal. Three copies of all 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 and may be accompanied by a supporting memorandum or brief. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects

21 CFR Part 201

Drugs, Labeling, Reporting and recordkeeping requirements.

21 CFR Part 310

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

21 CFR Part 314

Administrative practice and procedure, Confidential business information, Drugs, Reporting and recordkeeping requirements.

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 201, 310, and 314 be amended as follows:

PART 201—LABELING

1. The authority citation for 21 CFR part 201 is revised to read as follows:

Authority: Secs. 201, 301, 501, 502, 503, 505, 506, 507, 508, 510, 512, 530–542, 701, 704, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 358, 360, 360b, 360gg–360ss, 371, 374, 379e); secs. 215, 301, 351, 354–360F, 361 of the Public Health Service Act (42 U.S.C. 216, 241, 262, 263b–263n, 264).

2. Section 201.65 is added to subpart C to read as follows:

§ 201.65 Labeling of new drug products for over-the-counter human use.

For labeling describing the "Indications" that have been established for a new drug product for over-the-counter human use, see § 310.104 of this chapter.

PART 310—NEW DRUGS

3. The authority citation for 21 CFR part 310 is revised to read as follows:

Authority: Secs. 201, 301, 501, 502, 503, 505, 506, 507, 512–516, 520, 601(a), 701, 704, 705, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 360b–360f, 360j, 361(a), 371, 374, 375, 379e); secs. 215, 301, 302(a), 351, 354–360F of the Public Health Service Act (42 U.S.C. 216, 241, 242(a), 262, 263b–263n).

4. Section 310.104 is added to subpart B to read as follows:

§ 310.104 Labeling of new drug products for over-the-counter human use.

(a)(1) The label and labeling of the product contain in a prominent and conspicuous location the labeling describing the "Indications" that have been established in an approved application or abbreviated application. Subject to the requirements of paragraph (c) of this section, at the discretion of the applicant, this portion of the labeling may be designated "APPROVED USES," or be given a similar designation as permitted by paragraph (a)(4) of this section, each time it appears in the labeling, e.g., on the outer carton, inner bottle label, and on any package insert or display material. If the "APPROVED USES" or a similar designation is used, the labeling involved shall appear within a boxed area.

(2) At the applicant's discretion, the "Indications" may be described in the boxed area together with other applicable labeling approved under the application or abbreviated application. If such other labeling is included, the boxed area shall be designated "APPROVED INFORMATION," not "APPROVED USES."

(3) The "Indications" information appearing in the boxed area shall be stated in the exact language approved in the application or abbreviated application. Other information, if included within the boxed area, also shall be stated in the exact language approved in the application or abbreviated application.

(4) At the applicant's discretion, the designation of the boxed area may read: "FDA APPROVED USES" or "FDA APPROVED INFORMATION," as appropriate, or "USES (or "INFORMATION") APPROVED BY THE FOOD AND DRUG ADMINISTRATION," or other similar wording.

(5) As provided in § 314.70 of this chapter, portions of the labeling described in this paragraph may be adopted without prior FDA approval.

(b) The term "prominent and conspicuous location" as used in paragraph (a) of this section means that the labeling within the boxed or nonboxed area shall be presented and displayed in such a manner as to render it likely to be read and understood by the ordinary individual under customary conditions at both time of purchase and use.

(c) The discretionary provisions of paragraph (a) of this section will be permitted only after a final OTC drug monograph for the corresponding class of OTC drugs has been established under part 330 of this chapter. If a relevant OTC drug monograph is pending at the time an application is approved, an applicant will be so informed. In such case, the applicant shall use only the wording approved in the application to label the product, until the pending OTC drug monograph becomes final. If there is no corresponding class of OTC drugs pending under part 330 of this chapter, then the provisions of paragraph (a) of this section can be implemented when an application is approved or at any time thereafter.

PART 314—APPLICATIONS FOR FDA APPROVAL TO MARKET A NEW DRUG OR AN ANTIBIOTIC DRUG

5. The authority citation for 21 CFR part 314 is revised to read as follows:

Authority: Secs. 201, 301, 501, 502, 503, 505, 506, 507, 701, 704, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 371, 374, 379e).

6. Section 314.70 is amended in by adding new paragraph (d)(10) to read as follows:

§ 314.70 Supplements and other changes to an approved application.

* * * * *

(d)* * *

(10) If the alternate labeling authorized by § 310.104 of this chapter is the only change being made in the approved labeling.

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Dated: November 2, 1993.

Michael R. Taylor,

Deputy Commissioner for Policy.

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21 CFR Part 330

[Docket No. 92N-0175]

RIN 0905-AA06

Labeling of Drug Products for Over-The-Counter Human Use; Technical Amendment

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to amend its alternative labeling policy for over-the-counter (OTC) drug products subject to an OTC drug monograph. This proposal involves nonsubstantive changes in wording and changes in the paragraph designations to make § 330.1(c) (21 CFR 330.1(c)) consistent with the alternative labeling policy for OTC drug products subject to an approved application or abbreviated application (hereinafter collectively called an application), proposed elsewhere in this issue of the **Federal Register**.

DATES: Written comments by January 10, 1994.

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, 301-594-5000.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of May 1, 1986 (51 FR 16258), FDA issued a final rule in § 330.1(c)(2) (21 CFR 330.1(c)(2)) establishing alternate labeling for OTC drug products marketed under an OTC drug monograph. The final rule established three alternatives for the "Indications" portion of OTC drug labeling. The label and labeling of OTC drug products marketed under an OTC drug monograph are required to contain, in a prominent and conspicuous location, the "Indications" that have been established in a final monograph. At the option of the manufacturer, this labeling may be designated "APPROVED USES," or given a similar permitted designation. If the "APPROVED USES" designation is used, the labeling must appear within a boxed area. Other labeling in the monograph may also be placed within the boxed area, in which case the labeling is designated "APPROVED INFORMATION," rather than "APPROVED USES." All information must be in the exact language established in the monograph. In addition, there must be a statement that the boxed information was published by FDA. In lieu of this latter statement, the designation of the boxed area may be modified to read "FDA APPROVED USES" or "FDA APPROVED INFORMATION," or similar wording.

As a second alternative, "Indications" labeling may contain other truthful and nonmisleading statements, describing only those indications for use that have been established in an applicable monograph. In this case, the "APPROVED USES" or "APPROVED INFORMATION" designation may not be used.

Under a third alternative, the labeling may meet the boxed area requirement, previously described, and in addition, use other truthful and nonmisleading substitute or alternate language describing indications for use. This additional language must appear elsewhere in the labeling (outside the boxed area).

In a proposed regulation published elsewhere in this issue of the **Federal Register**, the agency is proposing to extend this alternative labeling policy, in part, to OTC drug products subject to an application. That proposal would allow for the label and labeling of OTC drug products approved under an application to contain, in a prominent and conspicuous location, either: (1) The designation "APPROVED USES," together with the specific wording on indications for use established under an approved application, all of which must appear within a boxed area, or (2) the designation "APPROVED INFORMATION," together with the specific wording on indications for use and other applicable labeling (e.g., statement of identity, warnings, and directions) established under an approved application, all of which must appear within a boxed area.

In preparing the proposed regulation for OTC drug products subject to an application, the agency used the existing regulation in § 330.1(c) as a guide. The agency has made some revisions to the wording and paragraph designations in the proposal for alternative labeling for OTC drug products subject to an application so that the regulation would be clearer and easier to follow.

For clarity and consistency, the agency is also proposing to revise the regulation in § 330.1(c)(2)(i) to make it similar to the proposal in § 310.104 for OTC drugs subject to an application. These changes are nonsubstantive in nature.

The agency has examined the economic consequences of this proposed rulemaking and has determined that it does not require either a regulatory impact analysis, as specified in Executive Order 12866, or a regulatory flexibility analysis, as defined in the Regulatory Flexibility Act (Pub. L. 96-354). The impact of the proposed rule, if implemented, appears to be minimal. Therefore, the agency concludes that the proposed rule is not a major rule as defined in Executive Order 12866. Further, the agency certifies that the proposed rule, if implemented, will not have a significant economic impact on a substantial number of small entities as defined in the Regulatory Flexibility Act.

The agency invites public comment regarding any substantial or significant economic impact that this rulemaking would have on OTC drug products. Comments regarding the impact of this rulemaking on OTC drug products should be accompanied by documentation. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this rulemaking in the preamble to the final rule.

The agency has determined under 21 CFR 25.24(c)(6) 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.

Interested persons may, on or before January 10, 1994, submit to the Dockets Management Branch (address above) written comments regarding this proposal. Three copies of all 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.

List of Subjects in 21 CFR Part 330

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 part 330 be amended as follows:

PART 330—OVER-THE-COUNTER (OTC) HUMAN DRUGS WHICH ARE GENERALLY RECOGNIZED AS SAFE AND EFFECTIVE AND NOT MISBRANDED

1. The authority citation for 21 CFR part 330 continues to read as follows:

Authority: Secs. 201, 501, 502, 503, 505, 510, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 351, 352, 353, 355, 360, 371).

2. Section 330.1 is amended by revising paragraph (c)(2)(i) and by adding new paragraph (c)(2)(vii) as follows:

§ 330.1 General conditions for general recognition as safe, effective and not misbranded.

* * * * *

(c) * * *

(2)(i)(A) The label and labeling of the product contain in a prominent and conspicuous location the labeling describing the "Indications" that have been established in an applicable final monograph. At the discretion of the manufacturer, this portion of the labeling may be designated "APPROVED USES," or be given a similar designation as permitted by paragraph (c)(2)(i)(D) of this section, each time it appears in the labeling, e.g., on the outer carton, inner bottle label, and on any package insert or display material. If the "APPROVED USES" or a similar designation is used, the labeling involved shall appear within a boxed area.

(B) At the manufacturer's discretion, the "Indications" may be described in the boxed area together with other applicable labeling included in this subchapter and in subchapter C of this chapter. If such other labeling is included, the boxed area shall be designated "APPROVED INFORMATION," not "APPROVED USES."

(C) The "Indications" information appearing in the boxed area shall be stated in the exact language of the applicable monograph. Other information, if included within the boxed area, also shall be stated in the exact language where exact language had been established and identified by quotation marks in an applicable monograph or by regulation (e.g., § 201.63 of this chapter).

(D) At the manufacturer's discretion, the designation of the boxed area may read: "FDA APPROVED USES" or "FDA APPROVED INFORMATION," as appropriate, or "USES (or "INFORMATION") APPROVED BY THE FOOD AND DRUG ADMINISTRATION," or other similar wording.

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(vii) The labeling of a drug product in accordance with the provisions of this section will be permitted only after a final OTC drug monograph for the appropriate class of OTC drugs has been established under part 330.

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Dated: October 20, 1993.

Michael R. Taylor,

Deputy Commissioner for Policy.

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