manufacturers' discretion. One example is the word "consult" that appears in the directions for many OTC drug monograph ingredients. (See, for example, §§ 333.150(c)(1), 333.350(c)(2), and 340.50(c)(2); 21 CFR 333.150(c)(1), 333.350(c)(2), and 340.50(c)(2).) The agency believes the simpler term "ask" could be used in its place. "Ask" is shorter and may be better understood by consumers. Thus, the phrases "consult a physician," "consult a doctor," "ask a physician," and "ask a doctor" would be allowed interchangeably.

The agency believes that these terms, and possibly others, could be used interchangeably, and that a provision to this effect should also be included in § 330.1, rather than in each OTC drug monograph. Accordingly, the agency is proposing to amend § 330.1 to provide for the use of certain terms interchangeably in the labeling of OTC drug products. The agency is proposing to add paragraph (i) to § 330.1 as follows:

The following terms may be used interchangeably in any of the labeling established in parts 331 through 358 of this chapter:

(1) "Ask" or "consult".

(2) "Doctor" or "physician".

The agency is also aware that other terms included in various OTC drug monographs may be used interchangeably. The agency invites comments and suggestions as to such other terms. The terms selected should be general in nature and appear in more than one OTC drug monograph. After considering the comments and suggestions received, the agency will issue an appropriate proposal in a future issue of the **Federal Register**.

The agency has examined the economic consequences of this proposed rule and determined that it does not require either a regulatory impact analysis, as specified in Executive Order 12291, or a regulatory flexibility analysis, as defined in the Regulatory Flexibility Act (Pub. L. 96–354). If this proposed rule becomes a final rule, the labeling options could be implemented at very little cost by manufacturers at the next printing of labels, for those products for which the manufacturer chooses to make a change. Thus, the proposal would have no significant economic impact. The agency concludes that the proposed rule is not a major rule as defined in Executive Order 12291. 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 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 June 4, 1993, submit to the Dockets Management Branch (address above) written comments regarding this proposal. Written comments on the agency's economic impact determination may be submitted on or before June 4, 1993. 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 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 adding new paragraph (i) to read as follows:

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

* * * * *

(i) The following terms may be used interchangeably in any of the labeling established in parts 331 through 358 of this chapter:

(1) "Ask" or "consult".

(2) "Doctor" or "physician".

* * * * *

Dated: January 15, 1993.

Michael R. Taylor,

Deputy Commissioner for Policy.

[FR Doc. 93–7770 Filed 4–2–93; 8:45 am]

BILLING CODE 4160–01–F

21 CFR Part 358

[Docket No. 82N–0214]

RIN 0905–AA06

Dandruff, Seborrheic Dermatitis, and Psoriasis Drug Products for Over-the-Counter Human Use; Proposed Amendment to the Monograph

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking to amend the final monograph for over-the-counter (OTC) dandruff, seborrheic dermatitis, and psoriasis drug products to include 0.6 percent micronized selenium sulfide for the control of dandruff. This proposal is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments by June 4, 1993; written comments on the agency's economic impact determination by June 4, 1993. The agency is proposing that the final rule based on this proposal be effective 12 months after the date of its publication in the **Federal Register**.

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:

I. Background

In the **Federal Register** of December 4, 1991 (56 FR 63554), FDA issued a final monograph for OTC dandruff, seborrheic dermatitis, and psoriasis drug products in subpart H of part 358 (21 CFR part 358, subpart H). The monograph lists selenium sulfide 1 percent in § 358.710(a)(5) as an active ingredient that is used for the control of dandruff. The selenium sulfide included in the monograph is not micronized (reduced to a fine particle size).

In developing this monograph, the agency considered data from five studies conducted to demonstrate the safety and effectiveness of 0.6 percent micronized selenium sulfide in the control of dandruff and seborrheic dermatitis (56 FR 63554 at 63559). Only two of those studies (Protocols CP–CA83 and CP–CA70) can be regarded as well-designed controlled clinical trials.

Each study involved a double-blind comparison of the antidandruff efficacy of 0.6 percent micronized selenium sulfide, 1 percent nonmicronized selenium sulfide, and shampoo vehicle in treating dandruff symptoms. One study (Protocol CP–CA83) showed a statistically significant mean reduction of total dandruff scores from baseline that was greater in subjects using 0.6 percent micronized selenium sulfide and in subjects using 1 percent nonmicronized selenium sulfide than in subjects using the shampoo vehicle. The study also showed that 0.6 percent micronized selenium sulfide is as effective as 1 percent nonmicronized selenium sulfide. The other study (Protocol CP–CA70) showed that 0.6 percent micronized selenium sulfide was statistically equal in effectiveness in reducing dandruff to the 1 percent nonmicronized formulation, but failed to demonstrate that 0.6 percent micronized selenium sulfide was statistically more effective than the shampoo vehicle. The other three studies were not regarded as well-designed controlled clinical trials for several reasons. One study (Protocol 84–050) did not include a placebo, and the active control used did not provide very convincing results. One study (Protocol 82–028) was a dose-searching clinical trial that included neither a placebo nor an FDA-approved active control. The other study (Protocol 81–013) compared the antidandruff efficacy of a shampoo containing 0.2 percent micronized selenium sulfide with a shampoo containing 1 percent nonmicronized selenium sulfide. The agency found that study to be irrelevant because it did not involve the testing of 0.6 percent micronized selenium sulfide. The agency determined that the data submitted were insufficient to establish the effectiveness of 0.6 percent micronized selenium sulfide in the control of dandruff and seborrheic dermatitis. The agency stated that one additional well-controlled study of adequate sample size was needed to show that 0.6 percent micronized selenium sulfide is effective for the control of dandruff and that data from separate studies are needed to show its effectiveness for the control of seborrheic dermatitis (56 FR 63554 at 63561).

Subsequent to the closing of the administrative record for the submission of data to the notice of proposed rulemaking for OTC dandruff, seborrheic dermatitis, and psoriasis drug products, one additional study (Ref. 1) was submitted on April 30, 1991 to show the effectiveness of 0.6 percent micronized selenium sulfide in the control of dandruff symptoms. The agency has processed the submission as a request to amend the monograph.

Reference

(1) Comment No. RPT 3, Docket No. 82N–0214, Dockets Management Branch.

II. The Agency's Tentative Conclusions on the Submitted Data

1. One comment submitted data from a randomized, double-blind, parallel group, placebo-controlled clinical study (Ref. 1) to show the effectiveness of 0.6 percent micronized selenium sulfide as an OTC active ingredient for the control of dandruff. The study was conducted at a single study center for 8 weeks. The study was designed to compare the efficacy of an antidandruff shampoo containing 0.6 percent micronized selenium sulfide (described in Comment 2) to: (1) The shampoo vehicle without the antidandruff ingredient, and (2) an antidandruff shampoo containing 1 percent nonmicronized selenium sulfide (a monograph ingredient).

Two hundred and twenty potential participants were selected for the study. Participants were to be at least 18 years of age with a diagnosis of dandruff, but with no history of adverse reaction to antidandruff shampoo ingredients and with no other skin disease, open lesions, crusts, or excoriations (scratches or abrasions) on the scalp. Participants could not be pregnant, breast-feeding, or less than 4 weeks post partum. Participants using oral contraceptives had to be on the same product for at least 6 weeks. Participants agreed to use a nonantidandruff shampoo for the first 2 weeks of the study (to eliminate the effects of previously used antidandruff shampoos) and not to use any other hair grooming products except hair spray for the 6-week duration of the study. Swimming was not allowed, and only one member per household could participate in the study. After the 2-week wash-out period, potential participants were examined for both loose and adherent dandruff and were scored separately in each of five areas of the scalp using numeric scores ranging from 0 to 4, representing no readily apparent dandruff (0) to very severe dandruff (4). Thus, if a participant scored 4 on all five areas of the scalp for both loose and adherent dandruff, a total score of 40 was possible. A total dandruff (loose and adherent) score of 21 or more was required for enrollment in the study.

Of the potential participants, 169 met the enrollment criteria. The subjects ranged in age from 19 to 76 years old, with a mean of 43 years. Thirty four percent of the subjects were male and 66 percent were female; 93.5 percent were caucasian, 4.5 percent were black, and 2 percent were hispanic.

The subjects were assigned at random to one of the three shampoo preparations, which were similar in appearance. All subjects and the investigator were blinded to which shampoo the subjects received during the treatment period. Subjects used the assigned shampoo twice weekly (Wednesday and Saturday) for 6 weeks. Dandruff was assessed weekly by the investigator prior to that day's scheduled shampoo.

Dandruff scores were analyzed both for reduction in total dandruff and for rate of reduction in total dandruff. Half of the subjects missed either week 1 or week 2 evaluations because they fell on a religious holiday. Therefore, weeks 1 and 2 were not analyzed. Further, 13 subjects did not return after baseline assessment and were excluded from both analyses (reduction in total dandruff and the rate of reduction in total dandruff). Fifteen additional subjects missed at least one visit during the treatment phase and were excluded only from the rate of reduction analysis. Thus, data from 141 subjects were included in the rate of reduction analysis, and data from 156 subjects were included in the change in total mean dandruff analysis.

Subjects in the 0.6 percent micronized and 1.0 percent nonmicronized selenium sulfide groups exhibited a greater statistically significant reduction ($p = 0.05$) in the total dandruff scores and in the rate of reduction in total dandruff scores than the subjects in the vehicle group. There was no significant difference in either the reduction in total mean dandruff score or the rate of reduction scores observed between subjects in the 0.6 percent micronized and 1 percent nonmicronized selenium sulfide groups. There were no significant differences among the three treatment groups in age, baseline dandruff score, race, hair length, or scalp condition. The baseline difference among groups with respect to sex was significant. An exploratory analysis with terms for treatment, sex, and treatment-by-sex interaction revealed neither a significant main effect due to sex nor a significant interaction between treatment and sex. This was true for baseline dandruff scores as well as reduction in dandruff score from the baseline to weeks 3, 4, 5, and 6. At baseline there was no indication that any of the three groups differed with respect to total dandruff score. An exploratory analysis was done of the differences among treatments in

dandruff scores from baseline to week 6, using sex, race, hair length, and scalp condition as blocking factors and continuous variables age and total dandruff scores at week 0 as covariates. The sponsor found no indication that any of those factors affected the response. Although the difference due to sex was significant at baseline, further analysis showed no difference in the change of total dandruff score between sexes, nor was there an effect due to sex and treatment interaction.

Comparisons of the 0.6 percent micronized selenium sulfide and the 1 percent nonmicronized selenium sulfide with the shampoo vehicle showed that both active preparations were superior to the vehicle in reducing dandruff. The mean reduction from baseline in total dandruff scores at week 6 for the three groups were as follows: -48.3 percent for the 0.6 percent micronized selenium sulfide group, -47.4 percent for the 1 percent nonmicronized selenium sulfide group, and -23.8 percent for the placebo group. The p values for pairwise comparisons were as follows: $p = 0.049$ for 0.6 percent micronized selenium sulfide versus 1 percent nonmicronized selenium sulfide, $p = 0.001$ for 0.6 percent micronized selenium sulfide versus placebo, and $p = 0.001$ for 1 percent nonmicronized selenium sulfide versus placebo. The rate of reduction in total dandruff scores in log units per week were as follows: -0.056 for the 0.6 percent micronized selenium sulfide, -0.065 for the 1 percent nonmicronized selenium sulfide, and -0.023 for the placebo. The p values for pairwise comparisons of rate of reduction were as follows: $p = 0.062$ for the 0.6 percent micronized selenium sulfide versus 1 percent nonmicronized selenium sulfide, $p = 0.001$ for 0.6 percent micronized selenium sulfide versus placebo, and $p = 0.001$ for 1 percent nonmicronized selenium sulfide versus placebo. Statistically significant results were found at week 3, 4, and 5 between 0.6 percent micronized selenium sulfide and vehicle ($p = 0.005$, 0.0005, and 0.007, respectively) and between 1 percent nonmicronized selenium sulfide and vehicle ($p = 0.0001$, 0.0001, and 0.0001, respectively).

No serious adverse events were reported in the study. One adverse event, itching of the scalp and hair loss, was reported in the 0.6 percent micronized selenium sulfide group, but the investigator noticed no inflammation or hair loss. Several adverse events (e.g., itching, burning, rash) were reported in two subjects in the active control group and in two subjects in the placebo group. The number of adverse events reported in the 0.6 percent selenium sulfide group in this study (Ref. 1) and in the earlier studies (Ref. 2) were minimal. The agency concludes that the reported adverse events did not indicate any safety problems with this ingredient.

Thus, based on this additional study (Ref. 1) and on the studies previously submitted (Ref. 2), the agency tentatively concludes that 0.6 percent micronized selenium sulfide is safe and effective for OTC use in the control of dandruff.

References

(1) Comment No. RPT 3, Docket No. 82N–0214, Dockets Management Branch.

(2) Comment No. LET007, Docket No. 82N–0214, Dockets Management Branch.

2. The comment also described the micronized selenium sulfide used in the study as follows: "selenium sulfide which has been finely ground to have a median particle size of approximately 5 microns with not more than 0.1 percent greater than 15 microns and not more than 0.1 percent less than 0.5 microns."

The agency finds that this specification provides for a more uniform particle size than the example provided in the preamble to the final monograph for OTC dandruff, seborrheic dermatitis, and psoriasis drug products that stated: 90 percent of particles should be less than 10 microns; 99 percent should be less than 20 microns; and no particles should be greater than 20 microns (56 FR 63554 at 63561). The agency has reviewed the specification for micronized selenium sulfide described by the comment and tentatively concludes that it is adequate for this monograph. However, when describing the particle size, the term micron (μ) should be replaced by the term micrometer (μm) to conform to present-day nomenclature. Therefore, the agency is proposing to define selenium sulfide micronized according to the specification described by the comment (using up-to-date terminology) by adding new paragraph (e) in § 358.703, as follows: "Selenium sulfide that has been finely ground and that has a median particle size of approximately 5 micrometers (μm), with not more than 0.1 percent of the particles greater than 15 μm and not more than 0.1 percent of the particles less than 0.5 μm."

Based on this additional study, the previous studies submitted, and the comment's definition of micronized selenium sulfide, the agency tentatively concludes that 0.6 percent micronized selenium sulfide is safe and effective for OTC use in the control of dandruff. Accordingly the agency is proposing to amend the final monograph for OTC dandruff, seborrheic dermatitis, and psoriasis drug products to include 0.6 percent micronized selenium sulfide in § 358.710(a) as an active ingredi,ent for the control of dandruff. Products containing this active ingredient should bear the appropriate labeling found in § 358.750. The agency is also proposing to add a definition for selenium sulfide, micronized to § 358.703, based on the specifications described by the comment, as follows: "selenium sulfide which has been finely ground and that has a median particle size of approximately 5 micrometers (μm), with not more than 0.1 percent of the particles greater than 15 μm and not more than 0.1 percent of the particles less than 0.5 μm."

The agency advises that any final rule resulting from this proposed rule will be effective 12 months after its date of publication in the **Federal Register**. On or after that date, any OTC drug product that is not in compliance may not be initially introduced or initially delivered for introduction into interstate commerce unless it is the subject of an approved application or abbreviated application. Further, any OTC drug product subject to the rule that is repackaged or relabeled after the effective date of the rule must be in compliance with the rule regardless of the date that the product was initially introduced or initially delivered for introduction into interstate commerce Products containing 0.6 percent micronized selenium sulfide as an active ingredient used for the control of dandruff may not be marketed OTC until a final monograph amendment is issued, unless the product is the subject of an approved application or abbreviated application.

The agency has examined the economic consequences of this proposed rule in conjunction with other rules resulting from the OTC drug review. In a notice published in the **Federal Register** of February 8, 1983 (48 FR 5806), the agency announced the availability of an assessment of these economic impacts. The assessment determined that the combined impacts of all the rules resulting from the OTC drug review do not constitute a major rule according to the criteria established by Executive Order 12291. The agency therefore concludes that no one of these rules, including this proposed rule for OTC dandruff, seborrheic dermatitis, and psoriasis drug products, is a major rule.

The economic assessment also concluded that the overall OTC drug review was not likely to have a significant economic impact on a substantial number of small entities as defined in the Regulatory Flexibility Act

(Pub. L. 96–354). That assessment included a discretionary regulatory flexibility analysis in the event that an individual rule might impose an unusual or disproportionate impact on small entities. However, this particular rulemaking for OTC dandruff, seborrheic dermatitis, and psoriasis drug products is not expected to pose such an impact on small businesses. This proposed rule will not remove any existing products from the market or require any reformulation or relabeling of existing products. The proposed rule will increase the scope of active ingredients available to industry for this class of OTC drug products. This proposed rule would allow OTC drug products containing 0.6 percent micronized selenium sulfide and labeled for the control of dandruff to be marketed without having to obtain an approved application, as is currently required. This will be beneficial to small manufacturers. Therefore, the agency certifies that this final rule will not have a significant economic impact on a substantial number of small entities.

The agency invites public comment regarding any substantial or significant economic impact that this rulemaking would have on OTC dandruff, seborrheic dermatitis, and psoriasis drug products. Comments regarding the impact of this rulemaking on OTC dandruff, seborrheic dermatitis, and psoriasis drug products should be accompanied by appropriate documentation.

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 June 4, 1993, submit written comments on the proposed regulation to the Dockets Management Branch (address above). Written comments on the agency's economic impact determination may be submitted on or before June 4, 1993. 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 the heading of this document and may be accompanied by a supporting memorandum or brief. Comments received 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 358

Labeling, 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 358 be amended as follows:

PART 358—MISCELLANEOUS EXTERNAL DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

1. The authority citation for 21 CFR part 358 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 358.703 is amended by adding paragraph (e) to read as follows:

§ 358.703 Definitions.

* * * * *

(e) *Selenium sulfide, micronized.* Selenium sulfide that has been finely ground and that has a median particle size of approximately 5 micrometers (μm), with not more than 0.1 percent of the particles greater than 15 μm and not more than 0.1 percent of the particles less than 0.5 μm.

3. Section 358.710 is amended by redesignating paragraph (a)(6) as paragraph (a)(7) and by adding new paragraph (a)(6) to read as follows:

§ 358.710 Active ingredients for the control of dandruff, seborrheic dermatitis, or psoriasis.

* * * * *

(a) * * *

(6) Selenium sulfide, micronized, 0.6 percent.

* * * * *

Dated: January 15, 1993.

Michael R. Taylor,

Deputy Commissioner for Policy.

[FR Doc. 93–7771 Filed 4–2–93; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 1

[PS–100–88]

RIN 1545–AM81

Valuation Tables; Correction

AGENCY: Internal Revenue Service, Treasury.

ACTION: Correction to the correction of notice of proposed rulemaking.

SUMMARY: This document contains corrections to the correction of notice of proposed rulemaking (PS–100–88), which was published in the **Federal Register** for Wednesday, February 3, 1993 (58 FR 6922). The proposed regulations relate to the valuation of certain partial interests in property under section 7520 of the Internal Revenue Code of 1986, as added by section 5031 of the Technical and Miscellaneous Revenue Act of 1988.

FOR FURTHER INFORMATION CONTACT: William L. Blodgett, (202) 622–3090 (not a toll-free number).

SUPPLEMENTARY INFORMATION:

Background

The correction of the proposed regulations that is the subject of this document corrected amendments to regulations under 7520 of the Internal Revenue Code.

Need for Correction

As published, the document contains errors which may prove to be misleading and is in need of clarification.

Correction of Publication

Accordingly, the publication of the correction of proposed regulations (PS–100–88), which was the subject of FR Doc. 93–1630, is corrected as follows:

§ 1.170A–12 [Corrected]

1. On page 6923, column 1, under instructional paragraph 2a., § 1.170A–12(b)(2), second line under "Ix" in the explanation of the formula at the top of the page, the language "in Table LN of § 20.2031–7 of this" is corrected to read "in Table 80CNSMT of § 20.2031–7 of this".

2. On page 6923, column 2, under instructional paragraph 2a., § 1.170A–12(b)(3), under *Example*, first line in the column following the formula, the language "less its expected value at the end of 45 years)." is corrected to read "less its expected value at the end of 45 years ($20,000)).".

3. On page 6923, column 1, under instructional paragraph 2a., § 1.170A–12(e)(2), second line under "Ix and Iy" in the explanation of the formula in the middle of the page, the language "and y set forth in Table LN of § 20.2031–" is corrected to read "and y set forth in Table 80CNSMT of § 20.2031–".

Dale D. Goode,

Federal Register Liaison Officer, Assistant Chief Counsel (Corporate).

[FR Doc. 93–7764 Filed 4–2–93; 8:45 am]

BILLING CODE 4830–01–U