DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 357

[Docket No. 82N-0168]

Benigh Prostatic Hypertrophy Drug Products for Over-the-Counter Human Use; Proposed Rulemaking

AGENCY: Food and Drug Administration.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking in the form of a tentative final monograph that would establish conditions under which over-the-counter (OTC) benign prostatic hypertrophy drug products (drug products used to relieve the symptoms of enlarged prostate gland) are generally recognized as safe and effective and not misbranded. FDA is issuing this notice of proposed rulemaking after considering the report and recommendations of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products and public comments on an advance notice of proposed rulemaking that was based on those recommendations. This proposal is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments, objections, or requests for oral hearing on the proposed regulation before the Commissioner of Food and Drugs by April 21, 1987. New data by February 22, 1988. Comments on the new data by April 20, 1988. These dates are consistent with the time periods specified in the agency's revised procedural regulations for reviewing and classifying OTC drugs (21 CFR 330.10). Written comments on the agency's economic impact determination by June 22, 1987.

ADDRESS: Written comments, objections, new data, or requests for oral hearing to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drugs and Biologics (HFN-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-295-8000.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of October 1, 1982 (47 FR 43566), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking that would classify OTC drug products to treat the symptoms of benign prostatic hypertrophy as not generally recognized as safe and effective and as being misbranded and would declare these products to be new drugs within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)). The notice was based upon the recommendations of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products (Miscellaneous Internal Panel), which was the advisory review panel responsible for evaluating data on the active ingredients in this drug class. Interested persons were invited to submit comments by December 30, 1982. Reply comments in response to comments filed in the initial comment period could be submitted by January 31, 1983.

In accordance with § 330.10(a)(10), the data and information considered by the Panel were put on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration (address above), after deletion of a small amount of trade secret information.

In response to the advance notice of proposed rulemaking, 3 manufacturers, 16 congressmen, and 112 individuals submitted comments. In addition, hundreds of individuals sent form letters requesting that these drug products not be removed from the OTC market. Copies of the comments and letters received are on public display in the Dockets Management Branch.

In order to conform to terminology used in the OTC drug review regulations (21 CFR 330.10), the present document is designated as a "tentative final monograph." Its legal status, however, is that of a proposed rule. In this tentative final monograph (proposed rule) to establish Subpart L of Part 357 (21 CFR Part 357, FDA states for the first time its position on the establishment of a monograph for OTC benign prostatic hypertrophy drug products. Final agency action on this matter will occur with the publication at a future date of a final rule for OTC benign prostatic hypertrophy drug products.

This proposal constitutes FDA's tentative conclusions and recommendations on OTC benign prostatic hypertrophy drug products, based on the comments received and the agency's independent evaluation of the Panel's report.

The OTC procedural regulations (21 CFR 330.10) now provide that any testing necessary to resolve the safety or effectiveness issues that formerly resulted in a Category III classification, and submission to FDA of the results of that testing or any other data, must be done during the OTC drug rulemaking process before the establishment of a final monograph. Accordingly, FDA will no longer use the terms "Category I" (generally recognized as safe and effective and not misbranded), "Category II" (not generally recognized as safe and effective or misbranded), and "Category III" (available data are insufficient to classify as safe and effective, and further testing is required) at the final monograph stage, but will use instead the terms "nonmonograph conditions" (old Category I) and "monograph conditions" (old Categories II and III). This document retains the concepts of Categories I, II, and III at the tentative final monograph stage.

The agency advises that the conditions under which the drug products that are subject to this monograph would be generally recognized as safe and effective and not misbranded (monograph conditions) will be effective 12 months after the date of publication of the final monograph in the **Federal Register.** On or after that date, no OTC drug product that is subject to the monograph and that contains a nonmonograph condition, i.e., a condition that would cause the drug to be not generally recognized as safe and effective or to be misbranded, may be initially introduced or initially delivered for introduction into interstate commerce unless it is the subject of an approved application. Further, any OTC drug product subject to this monograph that is repackaged or relabeled after the effective date of the monograph must be in compliance with the monograph 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 monograph at the earliest possible date.

In the advance notice of proposed rulemaking, the agency stated that if it proposed to adopt the Panel's recommendations it would propose that benign prostatic hypertrophy drug products be eliminated from the OTC market effective 6 months after the date of publication of a final rule in the **Federal Register.** However, in this document the agency is proposing a monograph that would establish conditions under which OTC benign prostatic hypertrophy drug products would be generally recognized as safe and effective and not misbranded. Experience has shown that relabeling of products covered by the monograph is necessary in order for manufacturers to comply with the monograph. New labels containing the monograph labeling have to be written, ordered, received, and

incorporated into the manufacturing process. The agency has determined that it is impractical to expect new labeling to be in effect before 12 months after the date of publication of the final monograph. Experience has shown also that if the deadline for relabeling is too short, the agency is burdened with extension requests and related paperwork.

In addition, some products will have to be reformulated to comply with the monograph. Reformulation often involves the need to do stability testing on the new product. An accelerated aging process may be used to test a new formulation; however, if the stability testing is not successful, and if further reformulation is required, there could be a further delay in having a new product available for manufacture.

The agency wishes to establish a reasonable period of time for relabeling and reformulation in order to avoid an unnecessary disruption of the marketplace that could not only result in economic loss, but also interfere with consumers' access to safe and effective drug products. Therefore, the agency is proposing that the final monograph be effective 12 months after the date of its publication in the **Federal Register**. The agency believes that within 12 months after the date of publication most manufacturers can order new labeling and reformulate their products and have them in compliance in the marketplace.

If the agency determines that any labeling for a condition included in the final monograph should be implemented sooner than the 12-month effective date, a shorter deadline may be established. Similarly, if a safety problem is identified for a particular nonmonograph condition, a shorter deadline may be set for removal of that condition from OTC drug products.

I. The Agency's Tentative Conclusions on the Comments

1. One comment maintained that the review of benign prostatic hypertrophy drug products was improperly conducted because the firms marketing these products were not given adequate notification that the products were going to be reviewed. The comment stated that drug products to treat the symptoms of benign prostatic hypertrophy were not included in the call-for-data notices, which were published in the **Federal Register** on November 16, 1973 (38 FR 31696) and August 27, 1975 (40 FR 38179). Therefore, the comment argued that appropriate notification was not given to those concerned. The comment also contended that the evaluation of these products by the Miscellaneous Internal Panel was much too hasty and suggested that another panel be convened to conduct a proper review.

Although the comment is correct that the November 16, 1973 and August 27, 1975 call-for-data notices did not specifically mention benign prostatic hypertrophy drug products, those notices did advise that monographs resulting from the OTC drug review would be applicable to every OTC drug, regardless of whether a submission was made for a particular product. The purpose of the two notices was to invite submissions of data and information on any OTC drug product that was not previously part of the OTC drug review. In addition, a notice appearing in the **Federal Register** of July 21, 1981 (46 FR 37564) announced that the Miscellaneous Internal Panel invited comments on benign prostatic hypertrophy drug products, as well as other drug products, and stated that the agency would use these comments to develop proposed rulemakings for the drug categories listed. The notice also announced that the Panel might be discussing benign prostatic hypertrophy drug products, among others, at its meeting on August 21, 22, and 23, 1981. Time was provided at that meeting for interested persons to present data and information to the Panel on any of the drug categories listed in the notice.

Subsequent to publication of the advance notice of proposed rulemaking on benign prostatic hypertrophy drug products in the **Federal Register**, interested persons had an opportunity to submit comments on the Panel's recommendations. Additional opportunities continue to exist for interested persons to express their opinions and submit additional data. For example, time will be provided following publication of this proposed rule for submissions to comments, objections, new data, or requests for oral hearing.

No submissions on benign prostatic hypertrophy drug products were made to the agency in response to either of the call-for-data notices mentioned above, nor did anyone express interest in appearing before the Panel at its meeting on August 21, 22, and 23, 1981. Based on the limited amount of data available to the Panel, the agency does not believe the Panel's review was unduly hasty. FDA does not believe it is necessary to convene another panel to review these drug products because ample opportunity has existed and continues to exist for interested persons to express their views or submit data to the agency on benign prostatic hypertrophy drug products.

2. One comment objected to including benign prostatic hypertrophy drug products in the OTC drug review. The comment stated that a judicial proceeding, previously invoked by FDA, found that these products were safe and effective in providing relief of certain symptoms of prostate disorder. (See *United States* v. *Metobolic Products Corp. and Edward Y. Domina*, 1964 Food Drug Cosm. L. Rep. (CCH) ¶ 80,079, at 80,202 (D. Mass. Jan. 25, 1962).) The comment stated that expert witnesses for both the defendant and the government testified that patients with certain symptoms related to prostate disorders obtain relief from use of these products. Therefore, the comment contended that it was improper for the agency to invite a contrary finding in this rulemaking.

This court case was brought by the government to seek a permanent injunction against the introduction into interstate commerce of three particular benign prostatic hypertrophy drug products. The drug products were found to be in violation of the misbranding provisions of the 1938 act (section 502 (a) and (f)) because the labeling indicated these products to be a substitute for prostate surgery. The decision in the case was limited to granting a permanent injunction against the products as labeled.

The case was decided prior to the 1962 amendments to the act, which for the first time required drugs to be shown prior to marketing not only to be safe, but also to be effective for their intended uses. One of the purposes of the OTC drug review is to determine those ingredients that are generally recognized as both safe and effective for OTC use. Although the court found that many doctors had observed that the drug products provide relief from certain symptoms of prostate disorder, the court did not determine whether the drug products might be generally recognized as safe and effective if labeled differently. The requirements for establishing general recognition of safety and effectiveness are set forth in § 330.10(a)(4) of the OTC drug review procedural regulations.

Based on the discussion above, the agency concludes that the prior judicial proceeding does not preclude the inclusion in the OTC drug review of particular drug products that were the subject of the litigation. Nor does that litigation in any way preclude a rulemaking proceeding on OTC benign prostatic hypertrophy drug products.

3. Two comments objected to benign prostatic hypertrophy ingredients being placed in Category II based on the Panel's determination that the condition being treated is not self-diagnosable.

The comments stated that many OTC drug products treat symptoms of conditions that are not self-diagnosable. The comments pointed out that the labeling of the benign prostatic hypertrophy drug products reviewed by the Panel specifies that before using the product the user should confirm by medical diagnosis that his symptoms are due to benign prostatic hypertrophy. The comments contended that in view of this labeling the Panel's concern that a prostatic malignancy may go undiagnosed was irrelevant.

The agency recognizes that a number of OTC drug products are used to treat symptoms of conditions that are not self-diagnosable, e.g., bronchodilators for asthma and pancreatic enzymes for pancreatic enzyme deficiency. Although consumers must be able to recognize the symptoms they intend to relieve with an OTC drug product, self-diagnosis of the condition causing the symptoms is not a necessary prerequisite to the OTC availability of drug products. Under section 503(b)(1)(B) of the act (21 U.S.C. 353(b)(1)(B)), a drug may be dispensed only upon prescription when "because of its toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, [it] is not safe for use except under the supervision of a practitioner licensed by law to administer such drug."

As the Panel stated in its report, there is no evidence of any potential harm from ingestion of the combination of the three ingredients contained in benign prostatic hypertrophy drug products (glycine, alanine, and glutamic acid) (47 FR 43568). Benign prostatic hypertrophy is a fairly common condition, occurring in about 50 percent of all men over the age of 50. The agency believes that once the prostatic condition is diagnosed as benign, there is no reason why the symptoms of the condition, i.e., urinary urgency and frequency, excessive urinating at night, and delayed urination, could not be self-treated provided the products are effective. (See comment 4 below for effectiveness discussion.)

However, because the Panel's concern regarding the potential for a prostatic malignancy going undiagnosed is a valid one, the agency believes that the following warnings should appear in the labeling of OTC benign prostatic hypertrophy drug products: (1) "Do not take this product unless a diagnosis of benign prostatic hypertrophy (enlarged prostate) has been made by a doctor" and (2) "Because this drug relieves only the symptoms of enlarged prostate without affecting the disease itself, periodic reexamination by a doctor is strongly recommended."

4. Two comments submitted a total of nine published studies (Refs. 1 through 9) as evidence of the safety and effectiveness of benign prostatic hypertrophy drug products. The comments contended that these studies existed in the scientific literature during the Panel's deliberations and should have been considered by the Panel in its review of these products. The comments argued that these studies as well as the market experience with benign prostatic hypertrophy drug products and the thousands of testimonials received from satisfied consumers over the years provide sufficient evidence to generally recognize these drug products as safe and effective for OTC use. In addition, close to 1,000 comments and letters were submitted to the agency by concerned consumers in testimony that these drug products are safe and effective.

The agency has reviewed the submitted studies (not available to the Panel) and tentatively concludes that the evidence remains insufficient to support the general recognition of safety and effectiveness of amino acid therapy, specifically the combination of glycine, alanine, and glutamic acid, for OTC use in relieving the symptoms of benign prostatic hypertrophy.

Details about study design, conduct, and analysis of the studies are lacking and, therefore, the available data and information cannot be used to establish effectiveness. For example, the study by Feinblatt and Gant (Ref. 1) lacks information regarding evaluation of the effectiveness parameters so that the question of bias cannot be eliminated. In addition, the blindness of this study is compromised by assigning different treatment times for the drug group (3 months) and the placebo group (2 months). In the Damrau study (Ref. 2), no placebo group was employed; the results of this study were compared to the placebo results from the Feinblatt and Gant study. Valid conclusions cannot be drawn by comparing the results of the effectiveness parameters monitored with observations made by different investigators in different patient populations. The seven studies reported in the Japanese medical literature (Refs. 3 through 9), likewise, do not provide sufficient details to make a proper evaluation.

The Panel had stated that it was not aware of any definitive clinical trials with appropriate controls to support effectiveness (47 FR 43568). In view of the studies submitted, the agency has classified the mixture of amino acids in Category III. The agency has determined that additional data are necessary before the combination of glycine, alanine, and glutamic acid can be generally recognized as safe and effective for OTC use in relieving the symptoms of benign prostatic hypertrophy.

References

(1) Feinblatt, H.M., and J.C. Gant, "Palliative Treatment of Benign Prostatic Hypertrophy. Value of Glycine-Alanine-Glutamic Acid Combination," *The Journal of the Maine Medical Association,* 49:99–102, 1958.

(2) Damrau, F., "Benign Prostatic Hypertrophy: Amino Acid Therapy for Symptomatic Relief," *Journal of the American Geriatrics Society,* 10:426–430, 1962.

(3) Aito, K., and E. Iwatsubo, "The Conservative Treatment of Prostatic Hypertrophy with Paraprost," *Acta Urologica Japonica,* 18:41–44, 1972

(4) Shiga, K., E. Kumaki, and A. Imamura, "Amino Acids Therapy for Hypertrophy of the Prostate," *Acta Urologica Japonica,* 14:625–630, 1968.

(5) Shimaya, M., and H. Sugiura, "Double Blind Test of PPC for Prostatic Hyperplasia," *Acta Urologica Japonica,* 16:231–236, 1970.

(6) Ishigami, J., and K. Kuroda, "Clinical Effect of PPC for the Palliative Treatment of Benign Prostatic Hypertrophy," *Acta Urologica Japonica,* 15:68–75, 1969.

(7) Sugiura, H., and M. Shimaya, "Clinical Application of 'PPC' to Prostatic Hypertrophy and Others," *Acta Urologica Japonica,* 15:450–453, 1969.

(8) Nishimura, Y., "Clinical Application of PPC for Prostatic Hypertrophy and Female Cystopathy," *Acta Urologica Japonica,* 15:127–134, 1969.

(9) Yamauchi, S., M. Hirakida. and H. Tsuji, "Experimental Application of P.P.C. for Prostatic Disease," *Acta Urologica Japonica,* 14:633–637, 1968.

5. One comment argued that products containing the combination of the amino acids glycine, alanine, and glutamic acid should not be part of the OTC drug review because such products are grandfathered under provisions of the 1962 Kefauver-Harris amendments to the act. The firm submitting the comment stated that it had a letter from FDA in its files stating that the products in question are "not new drugs."

On May 28, 1968, FDA revoked all previous opinions stating that any product was "not a new drug" or "no longer a new drug" (33 FR 7756). This revocation of letters, such as the one referred to by the commenting firm, has been codified in 21 CFR 310.100. Consequently, the letter referred to by the comment has no legal significance.

Under the 1962 grandfather clause of the act, a drug product which on October 9, 1962, (1) was commercially used or sold in the United States, (2)

was not a "new drug" as defined in the 1938 act, and (3) was not covered by an approved new drug application (NDA) under the 1938 act, would not be subject to the added requirement of effectiveness "when intended solely for use under conditions prescribed, recommended, or suggested in the labeling with respect to such drugs." Pub. L. 87-781, section 701(c)(4), 76 Stat. 788, note following 21 U.S.C. 321.

The person seeking to show that a drug comes within a grandfather exemption must prove every essential fact necessary for invocation of the exemption . See *United States* v. *An Article of Drug . . . "Bentex Ulcerine,"* 469 F.2d 875, 878 (5th Cir. 1972), *cert. denied,* 412 U.S. 938 (1973). Furthermore, the grandfather clause will be strictly construed against one who invokes it. See id.; *United States* v. *Allan Drug Corp.,* 357 F.2d 713, 718 (10th Cir.), *cert. denied,* 385 U.S. 899 (1966).

A change in composition or labeling precludes the applicability of the grandfather exemption. (See *USV Pharmaceutical Corp.* v. *Weinberger,* 412 U.S. 655, 663 (1973).) Evidence was not provided by the firm to demonstrate that no changes had occurred in the composition or labeling of the products from October 9, 1962, until the present.

Furthermore, it should be noted also that the grandfather clause applies only to the new drug provisions of the act and not to the adulteration and misbranding provisions. The OTC drug review was designed to implement both the misbranding and the new drug provisions of the act. (See 21 CFR 330.10; 37 FR 9466 (May 11, 1972).) The grandfather clause does not preclude the agency from reviewing any currently marketed OTC drug, regardless of whether it has grandfather protection from the new drug provisions, in order to ensure that the drug is not misbranded. The agency concludes that the products referred to by the comment are subject to this proposed rulemaking.

II. The Agency's Tentative Conclusions on OTC Benign Prostatic Hypertrophy Drug Products

A. Summary of Ingredient Categories and Testing of Category II and Category III Conditions

1. Summary of ingredient categories

FDA has considered the comments and other relevant data and information available at this time and concludes that data are insufficient to determine that the combination of glycine, alanine, and glutamic acid can be generally recognized as safe and effective for OTC use to relieve the symptoms of benign prostatic hypertrophy.

2. Testing of Category II and Category III conditions

Interested persons may communicate with the agency about the submission of data and information to demonstrate the safety or effectiveness of any benign prostatic hypertrophy ingredient or condition included in the review by following the procedures outlined in the agency's policy statement published in the **Federal Register** of September 29, 1981 (46 FR 47740) and clarified April 1, 1983 (48 FR 14050). That policy statement included procedures for the submission and review of proposed protocols, agency meetings with industry or other interested persons, and agency communications on submitted test data and other information.

B. Summary of the Agency's Changes in the Panel's Recommendations

1. Based on new data previously unavailable to the Panel, the agency is classifying the combination of glycine, alanine, and glutamic acid in Category III. (See comment 4 above.)

2. The agency has proposed labeling in the tentative final monograph in the event that new data are submitted to establish "monograph conditions" for OTC benign prostatic hypertrophy drug products. (See comment 3 above.)

In the event that no new data are submitted to the agency during the allotted 12-month new data period or if submitted data are not sufficient to establish "monograph conditions" for OTC benign prostatic hypertrophy drug products, the final rule will declare these products to be new drugs under section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act), for which applications approved under section 505 of the act and 21 CFR Part 314 are required for marketing. Such rule will also declare that in the absence of an approved application, these products would be misbranded under section 502 of the act. The rule will then be incorporated into 21 CFR Part 310, Subpart E—Requirements for Specific New Drugs or Devices, instead of into an OTC drug monograph in Part 357.

In the **Federal Register** of May 1, 1986 (51 FR 16258), the agency published a final rule changing its labeling policy for stating the indications for use of OTC drug products. Under the final rule, the label and labeling of OTC drug products are required to contain in a prominent and conspicuous location, either (1) the specific wording on indications for use established under an OTC drug monograph, which may appear within a boxed area designated "APPROVED USES"; (2) other wording describing such indications for use that meets the statutory prohibitions against false or misleading labeling, which shall neither appear within a boxed area nor be designated "APPROVED USES"; or (3) the approved monograph language on indications, which may appear within a boxed area designated "APPROVED USES," plus alternative language describing indications for use that is not false or misleading, which shall appear elsewhere in the labeling. All required OTC drug labeling other than indications for use (e.g., statement of identity, warnings, and directions) must appear in the specific wording established under an OTC drug monograph. The proposed rule in this document is subject to the final rule revising the labeling policy.

The agency has examined the economic consequences of this proposed rulemaking 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 not one of these rules, including this proposed rule for OTC benign prostatic hypertrophy 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. The anslysis identified the possibilities of reducing burdens on small firms through the use of relaxed safety and efficacy standards or labels acknowledging unproven safety or efficacy. However, the analysis concluded that there is no legal basis for any preferential waiver, exemption, or tiering strategy for small firms compatible with the public health requirements of the Federal Food, Drug, and Cosmetic Act.

The agency invited public comment in the advance notice of proposed rulemaking regarding any substantial or significant economic impact that this rulemaking would have on OTC benign prostatic hypertrophy drug products. One comment stated that if these products were removed from the OTC

market, the result would be financial disaster to the firm. As stated above, there is no legal basis for any preferential waiver or exemption from the requirements of the act.

Any comments on the agency's initial determination of the economic consequences of this proposed rulemaking should be submitted by June 22, 1987. 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 that under 21 CFR 25.24(c)(6) (April 26, 1985; 50 FR 16636) that this action is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Interested persons may, on or before April 21, 1987, submit to the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857, written comments, objections, or requests for oral hearing before the Commissioner. A request for an oral hearing must specify points to be covered and time requested. Written comments on the agency's economic impact determination may be submitted on or before June 22, 1987. Three copies of all comments, objections, and requests are to be submitted, except that individuals may submit one copy. Comments, objections, and requests 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. Comments, objections, and requests may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. Any scheduled oral hearing will be announced in the **Federal Register.**

Interested persons, on or before February 22, 1988, may also submit in writing new data demonstrating the safety and effectiveness of those conditions not classified in Category I. Written comments on the new data may be submitted on or before April 20, 1988. These dates are consistent with the time periods specified in the agency's final rule revising the procedural regulations for reviewing and classifying OTC drugs, published in the **Federal Register** of September 29, 1981 (46 FR 47730). Three copies of all data and comments on the data are to be submitted, except that individuals may submit one copy, and all data and comments are to be identified with the docket number found in brackets in the heading of this document. Data and comments should be addressed to the Dockets Management Branch (HFA–305) (address above). Received data and comments may also be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

In establishing a final rule, the agency will ordinarily consider only data submitted prior to the closing of the administrative record on April 20, 1988. Data submitted after the closing of the administrative record will be reviewed by the agency only after a final rule is published in the **Federal Register** unless the Commissioner finds good cause has been shown that warrants earlier consideration.

List of Subjects in 21 CFR Part 357

Labeling, Over-the-counter drugs, Benign prostatic hypertrophy drug products.

Therefore, under the Federal Food, Drug, and Cosmetic Act and the Administrative Procedure Act, it is proposed that Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations be amended in Part 357 to read as follows:

1. The authority citation for Part 357 continues to read as follows:

Authority: Secs. 201(p), 502, 505, 701, 52 Stat. 1041–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Sat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 352, 355, 371); 5 U.S.C. 553; 21 CFR 5.10 and 5.11.

2. Subpart L is added to Part 357 to read as follows:

PART 357—MISCELLANEOUS INTERNAL DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

Subpart L—Benign Prostatic Hypertrophy Drug Products

Sec.

Subpart L—Benign Prostatic Hypertrophy Drug Products

§ 357.1001 Scope.

(a) An over-the-counter drug product to relieve the symptoms of benign prostatic hypertrophy in a form suitable for oral administration is generally recognized as safe and effective and is not misbranded if it meets each of the conditions in this subpart and each of the general conditions established in § 330.1.

(b) References in this subpart to regulatory sections of the Code of Federal Regulations are to Chapter I of Title 21 unless otherwise noted.

§ 357.1003 Definition.

As used in this subpart:

Benign prostatic hypertrophy. A benign (not malignant) enlargement of the prostate gland.

§ 357.1010 Benign prostatic hypertrophy active ingredients. [Reserved]

§ 357.1050 Labeling of benign prostatic hypertrophy drug products.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the product as an enlarged prostate symptom reliever."

(b) *Indications.* The labeling of the product states, under the heading "Indications," the following: "for relief of urinary urgency and frequency, excessive urinating at night, and delayed urination associated with benign prostatic hypertrophy (enlarged prostate)." Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in this paragraph (b), may also be used, as provided in § 330.1(c)(2), subject to the provisions of section 502 of the act relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act.

(c) *Warnings.* The labeling of the product contains the following warnings under the heading "Warnings":

(1) "Do not take this product unless a diagnosis of benign prostatic hypertrophy (enlarged prostate) has been made by a doctor."

(2) "Because this drug relieves only the symptoms of enlarged prostate without affecting the disease itself, periodic reexamination by a doctor is strongly recommended."

(d) *Directions.* [Reserved]

(e) The word "physician" may be substituted for the word "doctor" in any of the labeling statements in this section.

Dated: December 6, 1986.

Frank E. Young,

Commissioner of Food and Drugs.

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