DEPARTMENT OF HEALTH AND HUMAN SERVICES

21 CFR Part 310

[Docket No. 80N-0419]

RIN 0905-AA06

Aphrodisiac Drug Products for Over-the-Counter Human Use

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule establishing that any aphrodisiac drug product for over-the-counter (OTC) human use is not generally recognized as safe and effective and is misbranded. Aphrodisiac drug products claim to arouse or increase sexual desire (libido) or to improve sexual performance. FDA is issuing this final rule after considering public comments on the agency's proposed regulation, which was issued in the form of a tentative final rule, and all new data and information on aphrodisiac drug products that have come to the agency's attention. This final rule is part of the ongoing review of OTC drug products conducted by FDA.

EFFECTIVE DATE: January 8, 1990.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD-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 43572), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking that would classify OTC aphrodisiac drug products 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 on 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 display in the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, after deletion of a small amount of trade secret information.

The agency's proposed regulation, in the form of a tentative final rule, for OTC aphrodisiac drug products was published in the **Federal Register** of January 15, 1985 (50 FR 2168). Interested persons were invited to file by May 15, 1985, written comments, objections, or requests for oral hearing before the Commissioner of Food and Drugs regarding the proposal. Interested persons were invited to file comments on the agency's economic impact determination by May 15, 1985. New data could have been submitted until January 15, 1986, and comments on the new data until March 17, 1986. Final agency action occurs with the publication of this final rule on OTC aphrodisiac drug products.

As discussed in the proposed regulation for OTC aphrodisiac drug products (50 FR 2168), the agency advised that the drug products covered by this regulation would be subject to the regulation effective 6 months after the date of publication of the final rule in the **Federal Register**. On or after January 8, 1990, no OTC drug products that are subject to this final rule may be initially introduced or initially delivered for introduction into interstate commerce unless they are the subject of an approved new drug application (NDA). If, in the future, any ingredient is determined to be generally recognized as safe and effective for use in an OTC aphrodisiac drug product, the agency will promulgate an appropriate regulation at that time.

In response to the proposed rule on OTC aphrodisiac drug products, 35 consumers and 2 health care groups submitted comments. Requests for oral hearing before the Commissioner were also received on seven different issues. Copies of the comments and the hearing requests received are on public display in the Dockets Management Branch. Additional information that has come to the agency's attention since publication of the proposed rule is also on public display in the Dockets Management Branch.

In proceeding with this final rule, the agency has considered all objections, requests for oral hearings, and the changes in the procedural regulations.

I. The Agency's Conclusions on the Comments

1. Numerous comments requested that the notice of proposed rulemaking for aphrodisiac drug products for OTC use be withdrawn or, as an alternative, that a new Panel be convened with "appropriate," qualified experts including nutritionists, herbalists, sexologists, or physicians with expertise in sex therapy. The comments contended that the Miscellaneous Internal Panel lacked expertise in the fields relevant to the use of aphrodisiacs, and because the Panel did not consult a "biochemist, physician, psychologist, or other scientist with successful clinical experience using nutritional aphrodisiacs," it was in violation of FDA's own regulations under 21 CFR 330.10(a) which require that the Commissioner appoint "qualified experts" to the panel. The comments contended that the food supplement industry, food manufacturers, and the public have been denied the benefits of a full scientific discourse on aphrodisiac products by qualified experts in the field. The comments also requested a hearing on these issues before the Commissioner.

The comments further stated that the Miscellaneous Internal Panel, which was mandated to cover a wide variety of drugs, ranging from weight reduction ingredients to smoking deterrents, was a biased panel that regarded aphrodisiacs as a "throw away" as shown by the fact that only two studies on aphrodisiacs were reviewed, when additional data were available. Stating that the agency "does not like" aphrodisiac products, the comments claimed that the rather short "shrift" given these products by the Panel, along with the fact that none of the Panel members were experts in this field, suggests that the agency may have prejudged the entire issue of the safety and effectiveness of OTC aphrodisiacs.

The agency has determined that the Miscellaneous Internal Panel was qualified to review OTC aphrodisiac drug products and that such a panel was not in violation of FDA regulations. The Panel was composed of pharmacists and physicians. Although the Panel reviewed a wide variety of drugs, and Panel members were not specialists in aphrodisiac drug products, the agency believes that the scientific background and knowledge of the Panel were sufficient to provide an impartial and scientific review of the various classes of drug products that were evaluated. Further, representatives of consumer and industry interests served as nonvoting members of the Panel, and the Panel utilized consultants in pharmacognosy and statistics. In summary, the Panel was chosen carefully to insure representation from a variety of groups, and the Panel called

upon individuals with expertise in other fields as necessary.

All interested parties had the opportunity to appear before the Panel, but none made such a request. Further, no submissions of data were made to the Panel. The Panel on its own initiative found seven references concerning aphrodisiacs (47 FR 43572 at 43575). The agency reviewed two additional references that were submitted in response to the Panel's report (50 FR 2168 at 2169). Furthermore, as part of its review for this final rule, the agency has evaluated additional materials in this document. (See comment 8 below.)

The comments' contention that the entire issue of the safety and efficacy of OTC aphrodisiacs may have been prejudged by the agency is not supported by any factual basis. The agency concludes that this drug category has been reviewed in accordance with the administrative procedures set forth in 21 CFR 330.10 in the same manner as all other OTC drug categories included in the agency's OTC drug review program. Thus, the agency has not treated aphrodisiacs differently from any other class of drugs in the OTC drug review.

The agency also concludes that a hearing on this issue is not warranted. The comment related only to procedural matters and did not identify any factual issues relating to the safety or effectiveness of OTC aphrodisiac drug products.

2. One comment objected to the inclusion of topical aphrodisiacs in the proposed rulemaking for OTC aphrodisiac drug products (50 FR 2168 at 2169) on the grounds that neither the Panel nor the agency suggested inclusion of topical aphrodisiacs in the advance notice of proposed rulemaking for OTC aphrodisiac drug products (47 FR 43572). The comment stated that the Panel repeatedly indicated throughout its deliberations that only systemic aphrodisiacs would be considered, and that the advance notice of proposed rulemaking indicated that the rulemaking was restricted to products taken internally [or for oral use] (47 FR 43572). The comment contended that expanding the scope of the proposed regulation at the notice of proposed rulemaking stage to include topical aphrodisiacs as well as those taken internally violates standard administrative law principles of notice, is inconsistent with the requirement that the agency follow its own rules, and is not supported by adequate evidence or by the record. The comment requested a hearing on this matter before the Commissioner.

The agency disagrees with the comment. At the same time that the agency published its first call-for-data notice in the **Federal Register** requesting data on aphrodisiacs for internal use (38 FR 31696), the agency also requested data on all external OTC drug products "not previously the subject of a request for data and information for this OTC Review" (38 FR 31697). Any views regarding topical aphrodisiacs could have been presented at that time. A second opportunity for presenting data and information occurred when the agency made a second request for supplemental and original data and information (40 FR 38179), which covered both OTC miscellaneous external and internal drug products.

Further, there is no violation of administrative law principles resulting from the inclusion of OTC topical aphrodisiac drug products for the first time at the notice of proposed rulemaking stage because that document provided adequate notice and an opportunity for views on this subject to be considered before the rule is finalized. The notice of proposed rulemaking on OTC aphrodisiac drug products was published in the **Federal Register** of January 15, 1985 (50 FR 2168). As stated above, the agency provided adequate notice (12 months for new data, and an additional 2 months for comments on the new data) for interested persons to submit comments, objections, new data, or requests for oral hearing on both OTC internal and external aphrodisiac drug products. The comment is incorrect in suggesting that the agency cannot include material in a notice of proposed rulemaking that was not contained in an advance notice of proposed rulemaking.

The agency also concludes that a hearing on this issue is not warranted. The comment related only to legal interpretations and procedural matters and did not identify any factual issues related to the safety or effectiveness of OTC aphrodisiac drug products.

3. Numerous comments contended that herbs, vitamins, minerals, amino acids, and other foods truthfully labeled with non-misleading aphrodisiac claims should not be regulated as prescription drugs. The comments requested that FDA hold a full public oral hearing and then withdraw or amend its proposed rulemaking on aphrodisiacs before issuing a final rule.

One comment claimed that aphrodisiacs are not drugs under section 201(g)(1)(B) of the act (21 U.S.C. 321(g)(1)(B)) because they are not necessarily used to cure, mitigate, treat, or prevent a disease. The comment also argued that many products with aphrodisiac claims, e.g., zinc, licorice, mandrake, fennel, and anise, are clearly foods and are expressly excluded by the parenthetical phrase (other than food) from the definition of drug under section 201(g)(1)(C) of the act (21 U.S.C. 321(g)(1)(C)). The comment concluded that claims such as "arouses or increases sexual desire * * *" or "improves performance * * *," which were listed as Category II in the notice of proposed rulemaking (50 FR 2170), are not drug claims because a person who takes what is otherwise a food for these purposes is not thereby taking a drug for a disease.

The act defines a drug as "(A) articles recognized in the official United States Pharmacopeia, official Homeopathic Pharmacopeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any articles specified in clause (A), (B), or (C); but does not include devices or their components, parts, or accessories" (21 U.S.C. 321(g)(1)). The act defines a food as "(1) articles used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any such article" (21 U.S.C. 321(f)).

It is well established that the definitions of "food" and "drug" in 21 U.S.C. 321 (f) and (g)(1) are not mutually exclusive. An article of "food" that is intended for use in the treatment of disease may also be a "drug" under 21 U.S.C. 321(g)(1)(B) of the act. See *Nutrilab, Inc.* v. *Schweiker*, 713 F.2d 335, 336 (7th Cir. 1983) and cases cited therein. Accordingly, when articles of food are marketed as aphrodisiacs for use in the cure, mitigation, or treatment of sexual dysfunction, or related disease conditions, they are drugs under 21 U.S.C. 321(g)(1)(B).

The comment's assertion that the "other than food" exception in 21 U.S.C. 321(g)(1)(C) applies to aphrodisiac products is also without merit. The Court in the *Nutrilab* case, *supra*, noted that double use of the word "food" in 21 U.S.C. 321(f) requires careful analysis of the parenthetical "other than food" exclusion in the drug definition in 21 U.S.C. 321(g)(1)(C). The Court stated that in the exclusion Congress obviously meant a drug to be something "other than food," but it is not clear whether Congress was referring to "food" as a term of art in the statutory sense or to

food in its ordinary meaning. The Court stated that because all foods are "intended to affect the structure or any function of the body of man or other animals" and would thus come within the Part C drug definition exclusion, presumably Congress meant to exclude only common-sense foods. The Court concluded that when the act defines "food" as "articles used for food," it means that the statutory definition of "food" includes articles used by people in the ordinary way most people use food—primarily for taste, aroma, or nutritive value.

Articles containing ingredients that have food uses but that are marketed with claims for their aphrodisiac effects do not meet the exception for food in 21 U.S.C. 321(g)(1)(C). The claims made for these products make clear that their primary intended use is to improve sexual performance or to increase sexual desire, both of which are functions of the body within the meaning of 21 U.S.C. 321(g)(1)(C). These products are not intended to be used as a food—that is, they are not intended to be consumed for their taste, aroma, or nutritive value.

Thus, in determining whether a product is a food or a drug, the agency considers the purpose for which a particular ingredient or product is intended. For example, starch blockers, which are prepared from raw beans, and spirulina, which is derived from algae, have both been declared by the agency to be drugs because of the claimed effects of the products on the function of the body. In both instances, the manufacturers were promoting products containing these ingredients for nonfood purposes, even though both are derived from plant sources. The starch blockers were claimed to block or interfere with digestion of starch (Ref. 1), and spirulina was claimed to act on the brain's appetite center (Ref. 2). The Court in the *Nutrilab* case, *supra,* stated that starch blockers were drugs under 21 U.S.C. 321(g)(1)(C). The Court found that they indisputably satisfy the requirement of "intended to affect the structure or any function of the body of man or other animals" because they are intended to affect digestion in the people who take them.

Similarly, aphrodisiacs are drugs because they are offered for a non-food purpose (i.e., other than for their taste, aroma, or nutritive value) and purport to affect the function of the body. The Panel defined an aphrodisiac as "any drug which is claimed to arouse or increase sexual desire or improve sexual performance," (47 FR 43572 at 43573). Dorland's (Ref. 3) defines an aphrodisiac as exciting the libido or any drug that arouses the sexual instinct. Food, in contrast, when used in the ordinary way is not intended for these purposes. Accordingly, products containing ingredients that are intended to be used as aphrodisiacs, whether or not these ingredients have food uses, and making aphrodisiac claims are clearly drugs within the definition of 21 U.S.C. 321(g)(1)(C).

The agency also notes that some aphrodisiacs have been traditionally sold as drugs (Ref. 4). Yohimbine, for example, has been marketed as a prescription drug (5 milligram (mg) tablet) with indications such as used "experimentally for the treatment and the diagnostic classification of certain types of male erectile impotence" and "may have activity as an aphrodisiac," (Ref. 4). (Additional discussion of prescription versus OTC status is contained in comment 6 below.)

In conclusion, ingredients that are derived from normal food items but that are sold for their aphrodisiac effects are drugs and not foods because they are intended to treat a disease condition or because they are intended to affect the function of the body. The Commissioner also concludes that a hearing on this issue is not warranted. The issue relates solely to the legal question of whether aphrodisiacs are drugs and does not raise factual matters relating to the safety or effectiveness of OTC aphrodisiac drug products.

References

(1) HHS News, FDA, News Release, Subject: Starch Blockers, July 1, 1982.

(2) Talk Paper, FDA, "Spirulina," June 23, 1981.

(3) "Dorland's Illustrated Medical Dictionary," 27th Ed., W.B. Saunders Co., Philadelphia, 1988, s.v. "aphrodisiac."

(4) Huff, B.B., editor, "Physicians' Desk Reference," 42d Ed., Medical Economics Publishing Co., Oradell, NJ, pp. 1111–1112, 1521, 2076, 1988.

4. One comment stated that it is well-established in botanical application in the healing arts of India, known as "Ayurveda" and "Kayakalpa," that a variety of herbs and food sources, such as asparagus and mineral pitch, serve to "revitalize and rejuvenate the human organism" leading to "increased sexual stamina and improved performance." The comment cited two references and requested a hearing on this subject before the Commissioner, adding that further references and expert testimony will be presented at the hearing (Ref. 1).

The agency emphasizes that the purpose of the OTC drug review is to determine whether there is general recognition of the safety and efficacy of particular classes of drugs used for self-medication. Therapeutic practices and procedures such as the "healing arts of India" and their relation to certain food sources are outside the scope of the OTC drug review. The agency also concludes that a hearing on this issue is not warranted because no genuine issues of material facts were raised relating to the safety and effectiveness of particular ingredients used in OTC aphrodisiac drug products.

Reference

(1) Comment No. HER002, Docket No. 80N–0419, Dockets Management Branch.

5. One comment stated that even if aphrodisiacs are found to be drugs, they are not new drugs. The comment explained that since these drugs have been used in this manner for centuries, as noted by FDA at 47 FR 43572 to 43574, they are exempt from the NDA requirement of section 505 of the act (21 U.S.C. 355) because they are "grandfathered." The comment further cited examples of use of these drugs dating back to biblical times. The comment requested a hearing on this issue before the Commissioner.

To qualify for exemption from the "new drug" definition under the 1938 grandfather clause of the act, the drug product must have been subject to the Food and Drug Act of 1906, prior to June 25, 1938, and at such time its labeling must have contained the same representations concerning the conditions of its use (21 U.S.C. 321(p)(1)). 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 effective 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 labeling with respect to such drug on that day." Pub. L. 87–781, section 107(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).

No evidence was submitted to the agency to show that the labeling and composition of aphrodisiac drug products have remained unchanged since either 1938 or 1962. Without such evidence, the products cannot qualify for either grandfather exemption. The burden of proof with respect to the grandfather exemption is not on FDA, but on the person seeking the exemption. See *An Article of Drug * * * "Bentex Ulcerine," supra.*

In any event, the 1938 and 1962 grandfather clauses apply 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 clauses do 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 a hearing on this issue is not warranted; the question of whether a drug is a "new drug" is a matter of law and not a material and substantial issue of fact that could be resolved at a hearing.

6. One comment contended that the agency's conclusions regarding self-medication with aphrodisiacs are inconsistent with the law and public policy. The comment stated that the agency had erroneously based its "conclusion that OTC distribution of these substances is inappropriate on the nature of the condition, not on the risks of the product." The comment argued that none of the criteria for restricting a drug to prescription status as set forth in section 503(b)(1) of the act (21 U.S.C. 353(b)(1)) apply to aphrodisiac drug products, i.e., (1) there is no evidence that yohimbine or other herbs are habit-forming drugs to which section 502(d) of the act (21 U.S.C. 352(d)) applies; (2) there is no indication of toxicity or other potentially harmful effect, method of use, or collateral measures necessary to use that make these products not safe except for use under the supervision of a doctor; or (3) the product is not limited by an approved application under section 505 of the act (21 U.S.C. 355) to use under professional supervision. In addition, the comment asserted that a disorder such as impotence is ppropriate for self-medication because n the majority of cases it is not a serious medical disorder and cited an article by Slag et al. (Ref. 1) in support of this position. The comment requested a hearing on this issue before the Commissioner.

The agency disagrees with the comment. The OTC drug review is determining whether aphrodisiac drug products intended for OTC use are generally recognized as safe and effective for OTC use. There is no evidence to establish that such drug products are generally recognized as safe and effective. Therefore, an approved NDA is required to permit marketing of such products. The prescription or OTC status for aphrodisiac drug products will be determined in conjunction with the evaluation of safety and effectiveness data submitted, if any, in support of an NDA. The agency emphasizes that this rulemaking does not, in itself, restrict all aphrodisiac drug products to prescription status. If the data submitted as part of an NDA support OTC marketing for a particular aphrodisiac drug product, then such a product could be marketed OTC under the NDA.

However, as previously stated in both the Panel's report (47 FR 43572 at 43575) and the tentative final monograph (50 FR 2168 at 2169), the agency believes that, based on the data available to date, individuals suffering from decreased libido and impaired sexual performance should seek treatment under professional supervision. Moreover, the agency believes that the study on impotence cited by the comment (Ref. 1), rather than illustrating the suitability of aphrodisiacs for OTC use, gives support to the position that these types of products should be restricted to use under a physician's supervision. Impotence is defined by Dorland (Ref. 2) as the lack of power, chiefly of copulative power in the male due to failure to initiate an erection or to maintain an erection until ejaculation. It may be atonic, due to paralysis of the motor nerves without evidence of lesion of the central nervous system; paretic, due to lesion in the central nervous system, particularly in the spinal cord; psychic, dependent on mental complex; or symptomatic, due to some other disorder, such as injury to nerves in the perineal region, by virtue of which the sensory portion of the erection reflex arc is interrupted. The article (Ref. 1) identifies a number of reasons for impotence, including medication effect, psychogenic causes, neurological and cardiovascular complications, diabetes, and hormonal imbalances. The agency believes that this information strongly suggests that a physician's diagnostic expertise is warranted before a sexual dysfunction condition is treated and a physician's supervision is required during treatment in order to monitor its progress.

The agency disagrees with the comment that the criteria for restricting a drug to prescription status (as set forth in section 503(b)(1) of the act) may not be applicable to some or all aphrodisiac drug products. The statutory criteria in section 503(b)(1)(B) of the act could be applicable to all or some aphrodisiac drugs. The collateral measures necessary to use, e.g., the need for a physician to diagnose the condition, determine its cause, and determine whether drug treatment is the appropriate therapy, are important factors in determining whether aphrodisiac drug products should be marketed OTC or on a prescription basis. The Panel stated that sexual drive (libido) and sexual performance are governed by multiple factors, the most common of which are psychological, and that impotence and frigidity have often been successfully treated by psychotherapy (47 FR 43572 at 43574). If the psychotherapy included drug treatment, it would have to be under a physician's supervision. The Panel further noted that hormonal factors also affected libido (47 FR 43572 at 43574). Any hormonal imbalance would also have to be treated by a physician.

In addition, the agency is concerned that the OTC use of some aphrodisiac drugs could present a safety concern, thus falling within the "toxicity or other potentiality for harmful effect" provision of section 503(b)(1)(B) of the act. The agency is aware that several manufacturers currently market products containing yohimbine hydrochloride as a prescription drug indicated as a sympathicolytic and mydriatic, with possible activity as an aphrodisiac (Ref. 3). The package inserts for these products state that the action of yohimbine on peripheral blood vessels is similar to that of reserpine (which is a prescription drug). It is also stated that yohimbine exerts a stimulating action on mood and can increase anxiety, but that these actions have not been adequately studied or related to dosage. The only contraindications provided are sensitivity to the drug and renal diseases. However, the statement is made that "no additional contraindications can be offered due to the limited and inadequate information available." A warning is provided that the drug is not for use in cardio-renal patients with gastric or duodenal history or in geriatric patients. It is also stated that the drug should not be used in

conjunction with mood modifying agents such as antidepressants, nor in psychiatric patients. In addition, a number of adverse reactions are listed, e.g., antidiuresis, central excitation, elevation of blood pressure and heart rate, tremor, and increased motor activity.

The agency also has some concerns about yohimbine being available as an OTC drug because of reports of its stimulant and hallucinogenic properties (Refs. 4 and 5). In addition, the agency is aware of at least two reports of adverse reactions involving overdoses of yohimbine (Refs. 5 and 6). A 2½-year-old boy died due to direct toxic effects on the capillaries after ingesting 300 to 400 mg of yohimbine hydrochloride, and a 16-year-old girl suffered from headache, hallucinations, dizziness, chest pains, and partial hearing loss after ingesting 250 mg of yohimbine. Although the reported dosage was high, the reports indicate potential problems in having a safe OTC dose for this ingredient. For the above reasons, the agency is of the opinion that the "toxicity and other potentiality for harmful effect" provision of section 503(b)(1)(B) of the act applies to drug products containing yohimbine or any of its derivatives. However, it is possible that other aphrodisiac ingredients may be safe for OTC use if efficacy is eventually established under appropriate NDA approval procedures.

The agency also concludes that a hearing on this issue is not warranted because issues of material and substantial facts were not raised relating to the safety or effectiveness of ingredients used in OTC aphrodisiac drug products.

References

(1) Slag, M.F., et al., "Impotence in Medical Clinic Outpatients," *The Journal of the American Medical Association,* 249:1736–1740, 1983.

(2) "Dorland's Illustrated Medical Dictionary," 26th Ed., W.B. Saunders Company, Philadelphia, 1981, s.v. "yohimbine."

(3) Huff, B.B., editor, "Physicians' Desk Reference," 42d Ed., Medical Economics Publishing Co., Oradell, NJ, pp. 1111–1112, 1521, 2076, 1988.

(4) Spoerke, D.G., "Topic: Plants—Yohimbine," contained in computerized list: Poisindex® Substance Identification, Vol. 57, Micromedex, Inc., August 1988.

(5) Linden, C.H., et al., "Yohimbine: A New Street Drug," *Annals of Emergency Medicine,* 14:1002–1004, 1985.

(6) Patscheider, H., and R. Dirnhofer, "Fatal Poisoning of a Small Child by Yohimbine," *Beitrage Zur Gerichtlichen Medizin,* 30:336–344, 1973.

7. One comment contended that the agency's determination that aphrodisiac products are to be available only on a prescription basis, or not at all, will have a severe economic impact that the agency has not considered. The comment stated that this decision will increase costs by requiring people who want to use these products for "enhancement of sexual pleasure" to do so under the supervision of a physician and to incur the costs of visits to physicians, which is a "hardly cost-effective" means of dealing with these people's desires. The comment also cited several examples of the agency's and Congress' traditionally favorable view of the concept of self-medication.

The comment submitted no documentation in support of its contention that a severe economic impact will occur, and the agency points out that it has not made a decision that all aphrodisiac drugs products are to be sold only by prescription. (See comment 6 above.) The agency has concluded at this time that the traditionally-used aphrodisiac ingredients have not been shown to be generally recognized as safe and effective for OTC use based on currently-available data and, therefore, these products will require an approved NDA for marketing. In addition, the agency has 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. (See Part II. below—The Agency's Final Conclusions on OTC Aphrodisiac Drug Products.)

The agency therefore concludes that not one of these rules, including this final rule for OTC aphrodisiac drug products, is a major rule. Accordingly, the agency finds that issuance of this final rule will not have an adverse economic impact on consumers.

8. Many comments contended that yohimbine is an effective aphrodisiac. Citing a number of supporting references (Refs. 1 through 8), one comment maintained that sufficient data exist to demonstrate the effectiveness of "yohimbe" and other herbs for aphrodisiac use. (The comment stated that it used the term "yohimbe" to include the ingredient's derivatives such as yohimbine, yohimbinum, and yohimbine hydrochloride. The agency is using the term yohimbine in this document to refer collectively to all of these ingredients.) The comment stated that the Panel rejected the study by Bruhl and Leslie (Ref. 1) because (1) the drugs were coded A and B and the code could be deciphered, and (2) the low placebo success rate was questionable because "psychological factors are so important" (47 FR 43572 at 43574). However, the comment contended that there is no evidence that the code was broken, and that more recent data have suggested that the emphasis on psychological factors may have been misplaced (Ref. 9). The comment also noted that the Queen's University study (Ref. 2) concluded that yohimbine is effective; however, the agency found fault with the study because "the number of satisfactory results is lower than the number given in previous reports" (50 FR 2168 at 2169). The comment stated that it was unaware of any requirement under the law that the "number of satisfactory results" be equal to or higher than a "number given in previous reports."

The comments concluded that the available data support the effectiveness of yohimbine and other herbs and substances for aphrodisiac use, and requested a hearing on this issue before the Commissioner.

The agency has reviewed the references (Refs. 1 through 9) cited by one comment and noted the comment's criticism of the Panel's rejection of the Bruhl and Leslie study (Ref. 1). The agency finds that, regardless of the study defects mentioned by the Panel (i.e., inadequate blinding, low placebo response rate, and failure to define the study measurements of effectiveness (47 FR 43572 at 43574)), this study does not support the effectiveness of yohimbine because the product contained other ingredients in addition to yohimbine. The product contained 5 mg each of methyltestosterone, nux vomica, and yohimbine. Thus, any favorable results could not be attributed solely to yohimbine, because there were no studies to demonstrate the effectiveness of that ingredient alone. Furthermore, in four additional studies cited by the comment as supportive of the effectiveness of yohimbine (Refs. 3 through 6), the product used also contained a combination of methyltestosterone, nux vomica, and yohimbine. Therefore, these studies cannot be considered supportive of the effectiveness of yohimbine alone.

The study by Albert-Puleo (Ref. 7) regarding herbs (fennel and anise) as estrogenic agents narrates the history of use of these herbs, but does not provide any data relating to safety or efficacy. Clark et al. (Ref. 8) found that yohimbine increased sexual motivation in genital anesthetized rats. Although such data are encouraging, this preliminary animal study cannot be used to demonstrate the effectiveness of yohimbine in humans.

Slag et al. (Ref 9) studied the causes of impotence in 1,180 middle-aged men and

concluded that although erectile dysfunction has long been considered to be primarily a psychogenic disorder, underlying organic disease is often responsible for the impotence. They found that in 25 percent of the patients, the effect of medication was the likely cause of the impotence, 14 percent had psychogenic causes, 7 percent were of neurological origin (e.g., cerebrovascular accident), 44 percent were due to organic disease (e.g., urologic problems, diabetes, hypo/hyperthyroidism), 7 percent were due to unknown causes, and 4 percent were of miscellaneous origin. The agency concludes that this study has no relevance to the efficacy of yohimbine, but it does point out the need for patients to undergo a thorough medical evaluation to determine the cause of impotence.

The study from Queen's University by Reid et al. (Ref. 2) is a 10-week, placebo-controlled, double-blind, partial crossover study involving the use of capsules containing yohimbine (6 mg) and riboflavin (2 mg) versus placebo capsules containing only riboflavin. The capsules were taken three times a day. The study was designed to determine yohimbine's effect in restoring erectile function. Forty-eight subjects meeting strict diagnostic criteria for psychogenic impotence were included in the study. Impotence was defined as "failure to obtain an erection sufficient for intromission for at least 3 months." In phase I of the study, 29 subjects received yohimbine and 19 received placebo. Patients and their partners made independent ratings of treatment response according to the following scale of 0 through 2:

2=complete; return to satisfactory sexual functioning with erections sufficient for penetration.

1=partial; some improvement in the quality, frequency, or rigidity of erections, but not sufficient to restore satisfactory sexual functioning.

0=none; no change in sexual functioning from pretreatment levels.

At the end of phase I, 9 yohimbine patients reported "complete improvement," 9 reported "partial improvement," and 11 reported "no improvement." Of the patients, receiving the placebo, 1 reported "complete improvement," 2 reported "partial improvement," and 16 reported "no improvement."

At the end of the first 10 weeks, the 19 patients who had received the placebo were crossed over to yohimbine (phase II of the study). However, a complete crossover was not used because the investigators felt it would be disruptive to marital relationships to switch those patients who had taken the yohimbine to a placebo. Patients who crossed over from placebo to yohimbine did not show a significant change in sexual functioning from pretreatment levels. Three patients reported "complete improvement," 1 reported "partial improvement," and 15 reported "no improvement." No serious undesirable effects were reported.

The agency concludes that the study (Ref. 2) provides some suggestive evidence that yohimbine may be useful in treating male impotence. In phase I of the study, 31 percent of the yohimbine patients reported complete improvement versus 5 percent of the placebo patients. However, in phase II, only 16 percent reported complete improvement. The investigators speculated that this lower response of patients who received yohimbine after receiving placebo may have been due to a negative expectancy effect. The agency concludes that this small scale study is not sufficient to establish the general recognition of yohimbine or any of its derivatives as safe and effective for treating male impotence. Further studies using adequate numbers of patients are needed to determine yohimbine's effectiveness in treating male impotence. In addition, the agency has safety concerns regarding OTC use of yohimbine. (See comment 6 above.) The agency encourages further study of yohimbine or any of its derivatives to establish their safety and usefulness in relieving male impotence. Such data may be submitted as the subject of an NDA. (See 21 CFR Part 314.) As an alternative, where there are adequate data establishing general recognition of safety and effectiveness, such data may be submitted in an appropriate citizen petition to establish a monograph. (See 21 CFR 10.30.)

The agency has carefully considered the data in the administrative record and the arguments included in the comments. The agency has determined that at present there is insufficient evidence to establish that any ingredient, including yohimbine, used in OTC aphrodisiac drug products is generally recognized as safe and effective. Because these matters have been fully considered and because the agency concludes that a hearing on this issue is not likely to provide any additional useful information or insights, the agency concludes that a hearing is not warranted.

References

(1) Bruhl, D. E., and C. H. Leslie, "Afrodex: Double-Blind Test in Impotence," *Medical Record and Annals,* 56:22–23, 1963.

(2) Reid, et al., "Double-Blind Trial of Yohimbine in Treatment of Psychogenic Impotence," *The Lancet,* 2:421–423, 1987.

(3) Miller, W. W., "Afrodex in the Treatment of Male Impotence: A Double-Blind Cross-Over Study," *Current Therapeutic Research,* 10:354–359, 1968.

(4) Margolis, R., et al., "Statistical Summary of 10,000 Male Cases Using Afrodex in the Treatment of Impotence," *Current Therapeutic Research,* 13:616–622, 1971.

(5) Sobotka, J. J., "An Evaluation of Afrodex in the Management of Male Impotency: A Double-Blind Crossover Study," *Current Therapeutic Research,* 11:87–94, 1969.

(6) Margolis, R., et al., "Review of Studies on a Mixture of Nux Vomica, Yohimbine, and Methyl Testosterone in the Treatment of Impotence," *Current Therapeutic Research,* 8:280–283, 1966.

(7) Albert-Puleo, M., "Fennel and Anise as Estrogenic Agents," *Journal of Ethnopharmacology,* 2:337–344, 1980.

(8) Clark, J. T., E. R. Smith, and J. M. Davidson, "Enhancement of Sexual Motivation in Male Rats by Yohimbine," *Science,* 225:847–849, 1984.

(9) Slag, M. F., et al., "Impotence in Medical Clinic Outpatients," *The Journal of the American Medical Association,* 249:1736–1740, 1983.

9. One comment requested that publication of the final monograph be delayed until data from studies, reportedly ongoing, on yohimbine can be appropriately considered.

The comment was submitted in May 1985. The agency has received no additional information on these or any other studies. The agency cannot further delay publication of this final rule to await results of any reportedly ongoing studies. Such a delay would allow products that have not been shown to be safe and effective to remain in the marketplace for a prolonged period of time and is not in the public interest. Further, manufacturers have been alerted about the proposed nonmonograph status of aphrodisiacs since the Panel's report was published in the **Federal Register** on October 1, 1982 (47 FR 43572). The agency reiterated the proposed nonmonograph status of aphrodisiacs in the notice of proposed rulemaking over 3 years ago in the **Federal Register** of January 15, 1985 (50 FR 2168). Thus, manufacturers have had ample opportunity to conduct clinical trials and to submit the results to the agency.

The agency points out that publication of a final rule does not preclude a manufacturer's testing an ingredient. New, relevant data can be submitted to

the agency at a later date as the subject of an NDA that may provide for prescription or OTC marketing status. (See 21 CFR Part 314.) As an alternative, where there are adequate data establishing general recognition of safety and effectiveness, such data may be submitted in an appropriate citizen petition to establish a monograph. (See 21 CFR 10.30.)

For the above reasons, the agency will not delay the final rule until publication of these studies.

II. The Agency's Final Conclusions on OTC Aphrodisiac Drug Products

The agency has determined that all products that bear labeling claiming that they will arouse or increase sexual desire, or that they will improve sexual performance, are aphrodisiac drug products. Moreover, the agency has determined that no aphrodisiac drug product has been found to be generally recognized as safe and effective and not misbranded for use in treating sexual dysfunction. Therefore, all aphrodisiac drug products, including those containing such ingredients as anise, cantharides, don qual, estrogens, fennel, ginseng, golden seal, gotu kola, Korean ginseng, licorice, mandrake, methyltestosterone, minerals, nux vomica, Pega Palo, sarsaparilla, strychnine, testosterone, vitamins, yohimbine, yohimbine hydrochloride, and yohimbinum, are considered nonmonograph ingredients and misbranded under section 502 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352) and are new drugs under section 201(p) of the act (21 U.S.C. 321(p)) for which an approved NDA under section 505 of the act (21 U.S.C. 355) and Part 314 of the regulations (21 CFR Part 314) is required for marketing. In appropriate circumstances, a citizen petition to establish a monograph may be submitted under 21 CFR 10.30 in lieu of an NDA. Any such OTC drug product initially introduced or initially delivered for introduction into interstate commerce after the effective date of this final rule that is not in compliance with the regulation is subject to regulatory action.

In response to the agency's request for specific comment on the economic impact of this rulemaking (50 FR 2168), one comment was received. (See comment 7 above.) The agency has examined the economic consequences of this final 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 final rule for OTC aphrodisiac 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 aphrodisiac drug products is not expected to pose such an impact on small businesses. Therefore, the agency certifies that this final rule will not have a significant economic impact on a substantial number of small entities.

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.

List of Subjects in 21 CFR Part 310

Administrative practice and procedure, Drugs, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and the Administrative Procedure Act, Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations is amended in Part 310 to read as follows:

PART 310—NEW DRUGS

1. The authority citation for 21 CFR Part 310 continues to read as follows:

Authority: Secs. 501, 502, 503, 505, 701, 704, 705, 52 Stat. 1049–1053 as amended, 52 Stat. 1055–1056 as amended, 67 Stat. 477 as amended, 52 Stat. 1057–1058 (21 U.S.C. 351, 352, 353, 355, 371, 374, 375); 5 U.S.C. 553; 21 CFR 5.10 and 5.11.

2. New § 310.528 is added to Subpart E to read as follows:

§ 310.528 Drug products containing active ingredients offered over-the-counter (OTC) for use as an aphrodisiac.

(a) Any product that bears labeling claims that it will arouse or increase sexual desire, or that it will improve sexual performance, is an aphrodisiac drug product. Anise, cantharides, don qual, estrogens, fennel, ginseng, golden seal, gotu kola, Korean ginseng, licorice, mandrake, methyltestosterone, minerals, nux vomica, Pega Palo, sarsaparilla, strychnine, testosterone, vitamins, yohimbine, yohimbine hydrochloride, and yohimbinum have been present as ingredients in such drug products. Androgens (e.g., testosterone and methyltestosterone) and estrogens are powerful hormones when administered internally and are not safe for use except under the supervision of a physician. There is a lack of adequate data to establish general recognition of the safety and effectiveness of any of these ingredients, or any other ingredient, for OTC use as an aphrodisiac. Labeling claims for aphrodisiacs for OTC use are either false, misleading, or unsupported by scientific data. The following claims are examples of some that have been made for aphrodisiac drug products for OTC use: "acts as an aphrodisiac;" "arouses or increases sexual desire and improves sexual performance;" "helps restore sexual vigor, potency, and performance;" "improves performance, staying power, and sexual potency;" and "builds virility and sexual potency." Based on evidence currently available, any OTC drug product containing ingredients for use as an aphrodisiac cannot be generally recognized as safe and effective.

(b) Any OTC drug product that is labeled, represented, or prompted for use as an aphrodisiac is regarded as a new drug within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act, (the act), for which an approved new drug application under section 505 of the act and Part 314 of this chapter is required for marketing. In the absence of an approved new drug application, such product is also misbranded under section 502 of the act.

(c) Clinical investigations designed to obtain evidence that any drug product labeled, represented, or promoted for OTC use as an aphrodisiac is safe and effective for the purpose intended must comply with the requirements and procedures governing the use of investigational new drugs set forth in Part 312 of this chapter.

(d) After January 6, 1990, any such OTC drug product initially introduced or initially delivered for introduction into interstate commerce that is not in compliance with this section is subject to regulatory action.

Dated: March 20, 1989.

Frank E. Young,

Commissioner of Food and Drugs.

[FR Doc. 89-15954 Filed 7-6-89; 8:45 am]

BILLING CODE 4160-01-M

Date: July 6, 1989.

Steven Newburg-Rinn,

Acting Director, Information Management Division, Office of Toxic Substances.

[FR Doc. 89-16543 Filed 7-13-89; 8:45 am]

BILLING CODE 6560-50-M

[OPTS-59272; RRL-3616-3]

Toxic and Hazardous Substances; Test Market Exemption Applications

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: EPA may upon application exempt any person from the premanufacturing notification requirements of section 5(a) or (b) of the Toxic Substance Control Act (TSCA) to permit the person to manufacture or process a chemical for test marketing purposes under section 5(h)(1) of TSCA. Requirements for test marketing exemption (TME) applications, which must either be approved or denied within 45 days of receipt are discussed in EPA's final rule published in the **Federal Register** of May 13, 1983 (48 FR 21722). This notice, issued under section 5(h)(6) of TSCA, announces receipt of 2 application(s) for exemption, provides a summary, and requests comments on the appropriateness of granting this exemption.

DATES: Written comments by:

T 89-17, July 22, 1989.

T 89-18, July 27, 1989.

ADDRESS: Written comments, identified by the document control number "[OPTS-59272]" and the specific TME number should be sent to: Document Processing Center (TS-790), Office of Toxic Substances, Environmental Protection Agency, 401 M Street SW., Room L-100, Washington, DC 20460 (202) 382-3532.

FOR FURTHER INFORMATION CONTACT: Michael M. Stahl, Director, TSCA Assistance Office (TS-799), Office of Toxic Substances, Environmental Protection Agency, Room EB-44, 401 M Street SW., Washington, DC 20460, (202) 554-1404, TDD (202) 554-0551.

SUPPLEMENTARY INFORMATION: The following notice contains information extracted from the nonconfidential version of the submission provided by the manufacturer of the TME received by EPA. The complete nonconfidential document is available in the Public Reading Room NE-G004 at the above address between 8:00 a.m. and 4:00 p.m., Monday through Friday, excluding legal holidays.

T 89-17

Close of Review Period. August 5, 1989.

Manufacturer. Confidential.

Chemical. (G) Crosslinked starch hydrolized acrylonitrile copolymer.

Use/Import. (G) Oil fracturing fluid thickening agent. Prod. range: 250,000 kg/yr.

T 89-18

Close of Review Period. August 10, 1989.

Manufacturer. Confidential.

Chemical. (G) Rosin, polymer with substituted phenols, formaldehyde, pentaerythritol and metal hydroxide.

Use/Import. (G) Ink resin. Prod. range: Confidential. Prod. range: 250,000 kg/yr.

Date: July 6, 1989.

Steven Newburg-Rinn,

Acting Director, Information Management Division, Office of Toxic Substances.

[FR Doc. 89-16542 Filed 7-13-89; 8:45 am]

BILLING CODE 6560-50-M

[FRL-615-8]

Sole Source Aquifer Designation for the Vinalhaven Island Aquifer System, Maine

AGENCY: U.S. Environmental Protection Agency.

ACTION: Notice.

SUMMARY: In response to a petition from the State of Maine, notice is hereby given that the Regional Administrator, Region I, of the U.S. Environmental Protection Agency (EPA) has determined that the Vinalhaven Island Aquifer System satisfies all determination criteria for designation as a sole source aquifer, pursuant to section 1424(e) of the Safe Drinking Water Act. The following findings were made in accordance with the designation criteria: Vinalhaven Island Aquifer System is the principal source of drinking water for the residents of Vinalhaven Island; there are no viable alternative sources of sufficient supply; the boundaries of the designated area and project review area have been reviewed and approved by EPA; and, if contamination were to occur, it would pose a significant public health hazard and a serious financial burden to the State of Maine. As a result of this action, all federal financially assisted projects proposed for construction or modification to take place on Vinalhaven Island will be subject to EPA review to minimize the risk of ground water contamination from these projects.

DATES: This determination shall be promulgated for purposes of judicial review at 1:00 p.m. Eastern time two weeks after the date of publication in the **Federal Register.**

ADDRESSES: The data upon which these findings are based are available to the public and may be inspected during normal business hours at the U.S. Environmental Protection Agency, Region I, JFK Federal Building, Water Management Division, WGP 2113, Boston, MA 02203. The designation petition submitted may also be inspected at the Maine State Planning Office in Augusta, Maine.

FOR FURTHER INFORMATION CONTACT: Robert E. Mendoza, Chief of the Ground Water Management Section, EPA Region I, JFK Federal Building, WGP-2113, Boston, MA 02203, 617-565-3600.

SUPPLEMENTARY INFORMATION:

I. Background

Section 1424(e) of the Safe Drinking Water Act (42 U.S.C.) 300f, 300h-3(e), Pub. L. 93-523) states:

> If the Administrator determines, on his own initiative or upon petition, that an area has an aquifer which is the sole or principal drinking water source for the area and which, if contaminated, would create a significant hazard to public health, he shall publish notice of that determination in the **Federal Register.** After the publication of any such notice, no commitment for federal financial assistance (through a grant, contract, loan guarantee, or otherwise) may be entered into for any project which the Administrator determines may contaminate such aquifer through a recharge zone so as to create a significant hazard to public health, but a commitment for Federal financial assistance may, if authorized under another provision of law, be entered into to plan or design the project to assure that it will not so contaminate the aquifer.

On June 3, 1988, EPA received a petition from the State of Maine requesting the designation of the Vinalhaven Island Aquifer System as a sole source aquifer. EPA determined that the petition fully satisfied the Completeness Determination Checklist. A public meeting was then scheduled and held on March 6, 1989 on Vinalhaven Island, Maine, in accordance with all applicable notification and procedural requirements. A one month comment period followed the meeting.

II. Basis for Determination

Among the factors considered by the Regional Administrator as part of the detailed review and technical verification process for designating an area under section 1424(e) were:

1. The Vinalhaven Aquifer System is a interconnected bedrock aquifer which the population draws for their fresh water needs. It serves as the principal source of drinking water to all residents within the service area.

2. There exists no reasonable alternative drinking water source or combination of sources of sufficient quantity to supply the designated service area.

3. EPA has found that the State of Maine has appropriately delineated the boundaries of the aquifer recharge area, project designation area and project review area.

4. Although the quality of the Island's ground water is considered adequate, it is vulnerable to contamination due to the Island's geological characteristics and possible land use activities. Because of this, contaminants can be rapidly introduced into the aquifer system from many sources with minimal assimilation. Since the aquifer serves as the principal source of drinking water for the residents, a serious contamination incident could pose a significant public health hazard.

III. Description of the Vinalhaven Island Aquifer System Designated Area and Project Review Area

The Vinalhaven Island is a 20 square miles ocean island located in the mid-coastal region of Maine, approximately 10 miles east of Rockport, the nearest mainland town. The aquifer system is comprised of a interconnected bedrock aquifer. The island's bedrock consists predominately of granite, gabbro, diorite and pelite of Devonian age. The Island has relief of 216 feet, with a irregular topographic profile.

The designated area is defined as the surface area above the aquifer system and its recharge area. For the Vinalhaven Island Aquifer System the boundary of the designated area coincides with the boundary of the watershed basin. The watershed boundary is the surface water divide based on topography, which corresponds to the ground water divide. The designated area, project review area and service area are conterminous, encompassing all of the Island.

IV. Information Utilized in Determination

The information utilized in this determination includes: the petition submitted to EPA Region I by the State of Maine and letters of support received. This information is available to the public and may be inspected at the address listed above.

V. Project Review

EPA Region I is working with the federal agencies most likely to provide financial assistance to projects in the project review area. Interagency procedures and Memoranda of Understanding have been developed through which EPA will be notified of proposed commitments by federal agencies to projects which could contaminate the Vinalhaven Island Aquifer System. EPA will evaluate such projects and, where necessary, conduct an in-depth review, including soliciting public comments when appropriate. Should the Regional Administrator determine that a project may contaminate the aquifer through its recharge zone so as to create a significant hazard to public health, no commitment for federal financial assistance may be entered into. However, a commitment for federal financial assistance may, if authorized under another provision of law, be entered into to plan or design the project to ensure that it will not contaminate the aquifer. Included in the review of any federal financially assisted project will be the coordination with state and local agencies and the project's developers. Their comments will be given full consideration and EPA's reviw will attempt to complement and support state and local ground water protection measures. Although the project review process cannot be delegated, EPA will rely to the maximum extent possible on any existing or future state and/or local control measures to protect the quality of ground water in the Vinalhaven Island Aquifer System.

VI. Summary and Discussion of Public Comments

During the public meeting, a request for an extension of the public comment period was made. It was extended an additional two weeks and expired on April 6, 1989. One comment raised the concern that the State of Maine, serving as the petitioner should have contacted the Island's municipal officials earlier in the process. This concern was conveyed to the appropriate state agency. Letters in support of designation were submitted to EPA.

Paul Keough,

Regional Administrator.

Date: May 31, 1989.

[FR Doc. 89-16544 Filed 7-13-89; 8:45 am]

BILLING CODE 6560-50-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

Advisory Committee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration (FDA). This notice also summarizes the procedures for the meetings and methods by which interested persons may participate in open public hearings before FDA's advisory committees.

Meeting: The following advisory committee meeting is announced:

Pulmonary-Allergy Drugs Advisory Committee

Date, time, and place. July 31 and August 1, 1989, 8:30 a.m., Wilson Hall Auditorium, National Institutes of Health, Bldg. 1, 9000 Rockville Pike, Bethesda, MD.

Type of meeting and contact person. Open public hearing, July 31, 1989, 8:30 a.m. to 9:30 a.m., unless public participation does not last that long; open committee discussion, 9:30 a.m. to 5 p.m.; open public hearing, August 1, 1989, 8:30 a.m. to 9:30 a.m., unless public participation does not last that long; open committee discussion, 9:30 a.m. to 5 p.m.; Isaac F. Roubein, Center for Drug Evaluation and Research (HFD-9), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4695.

General function of the committee. The committee reviews and evaluates available data on the safety and effectiveness of marketed and investigational human drugs for use in the treatment of pulmonary disease and diseases with allergenic and/or immunologic mechanisms.

Agenda—Open public hearing. Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Those desiring to make formal presentations should notify the contact person before July 15, 1989, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time required to make their comments.

Open committee discussion. On July 31, 1989, the committee will discuss promethazine. On August 1, 1989, the

committee will discuss a status report on surfactant replacement therapy and the guidelines for the evaluation of bronchodilator drugs.

The agency issued a proposal in the **Federal Register** to allow over-the-counter (OTC) marketing of promethazine in cough-cold products. Comments have been received on this proposal concerning the advisability of switching the marketing of such products containing promethazine from a prescription basis to an OTC basis. The agency wishes to discuss this issue in an open public meeting of the advisory committee.

The committee's discussion and conclusions regarding promethazine hydrochloride will be considered by the agency both in: (1) Reviewing the current marketing status and labeling of cough-cold drug products containing promethazine hydrochloride and (2) preparing a final monograph on OTC cold, cough, allergy, bronchodilator, and antiasthmatic combination drug products. Such a monograph is being developed as part of the OTC drug review. The tentative final monograph (proposed rule) for these products was published in the **Federal Register** of August 12, 1988 (53 FR 30522). The agency is not aware of any OTC marketing of any combination product containing promethazine hydrochloride. Manufacturers of prescription promethazine products have voluntarily agreed to withhold OTC marketing at this time.

FDA public advisory committee meetings may have as many as four separable portions: (1) An open public hearing, (2) an open committee discussion, (3) a closed presentation of data, and (4) a closed committee deliberation. Every advisory committee meeting shall have an open public hearing portion. Whether or not it also includes any of the other three portions will depend upon the specific meeting involved. There are no closed portions for the meetings announced in this notice. The dates and times reserved for the open portions of each committee meeting are listed above.

The open public hearing portion of each meeting shall be at least 1 hour long unless public participation does not last that long. It is emphasized, however, that the 1 hour time limit for an open public hearing represents a minimum rather than a maximum time for public participation, and an open public hearing may last for whatever longer period the committee chairperson determines will facilitate the committee's work.

Public hearings are subject to FDA's guideline (Subpart C of 21 CFR Part 10) concerning the policy and procedures for electronic media coverage of FDA's public administrative proceedings, including hearings before public advisory committees under 21 CFR Part 14. Under 21 CFR 10.205, representatives of the electronic media may be permitted, subject to certain limitations, to videotape, film, or otherwise record FDA's public administrative proceedings, including presentations by participants.

Meetings of advisory committees shall be conducted, insofar as is practical, in accordance with the agenda published in this **Federal Register** notice. Changes in the agenda will be announced at the beginning of the open portion of a meeting.

Any interested person who wishes to be assured of the right to make an oral presentation at the open public hearing portion of a meeting shall inform the contact person listed above, either orally or in writing, prior to the meeting. Any person attending the hearing who does not in advance of the meeting request an opportunity to speak will be allowed to make an oral presentation at the hearing's conclusion, if time permits, at the chairperson's discretion.

Persons interested in specific agenda items to be discussed in open session may ascertain from the contact person the approximate time of discussion.

Details on the agenda, questions to be addressed by the committee, and a current list of committee members are available from the contact person before and after the meeting. Transcripts of the open portion of the meeting will be available from the Freedom of Information Office (HFI-35), Food and Drug Administration, Rm. 12A-16, 5600 Fishers Lane, Rockville, MD 20857, approximately 15 working days after the meeting, at a cost of 10 cents per page. The transcript may be viewed at the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, approximately 15 working days after the meeting, between the hours of 9 a.m. and 4 p.m., Monday through Friday. Summary minutes of the open portion of the meeting will be available from the Freedom of Information Office (address above) beginning approximately 90 days after the meeting.

This notice is issued under section 10(a)(1) and (2) of the Federal Advisory Committee Act (Pub. L. 92-643, 86 Stat. 770-776 (5 U.S.C. App. I)), and FDA's regulations (21 CFR Part 14) on advisory committees.

Dated: July 10, 1989.

Alan L. Hoeting,

Acting Associate Commissioner for Regulatory Affairs.

[FR Doc. 89-16702 Filed 7-12-89; 2:14 pm]

BILLING CODE 4160-01-M

Public Health Service

Health Resources and Services Administration; Native Hawaiian Health Care Act of 1988; Delegation of Authority

Notice is hereby given that in furtherance of the delegation of authority of June 14, 1989, from the Assistant Secretary for Health to the Administrator, Health Resources and Services Administration, the Administrator has redelegated all of the authorities delegated to him under the Native Hawaiian Health Care Act of 1988, as amended hereafter, to the Director, Bureau of Health Care Delivery and Assistance. Excluded was the authority to issue regulations and to submit reports to the Congress.

Redelegation

These authorities may be redelegated.

Effective Date

This delegation became effective on July 6, 1989.

John H. Kelso,

Acting Administrator

Date: July 6, 1989.

[FR Doc. 89-16515 Filed 7-13-89; 8:45 am]

BILLING CODE 4160-15-M

Social Security Administration

Agency Forms Submitted to the Office of Management and Budget for Clearance

Each Friday the Social Security Administration publishes a list of information collection packages that have been submitted to the Office of Management and Budget (OMB) for clearance in compliance with Pub. L. 96-511, The Paperwork Reduction Act. The following clearance packages have been submitted to OMB since the last list was published in the **Federal Register** on June 30, 1989.

(Call Reports Clearance Officer on (301) 965-4149 for copies of package)

1. Pain Instrument Development Studies—New—The information collected by these forms will be used by the Social Security Administration to develop and refine final information collection forms which will be used