DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 358

[Docket No. 81N-0201]

Pediculicide Drug Products for Over-the-Counter Human Use; Tentative Final Monograph

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) pediculicide drug products (products used for the treatment of head, pubic (crab), and body lice) 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 External 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 June 2, 1989. New data by April 3, 1990. Comments on the new data by June 4, 1990. Written comments on the agency's economic impact determination by August 1, 1989.

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 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 June 29, 1982 (47 FR 28312), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC pediculicide drug products, together with the recommendations of the Advisory Review Panel on OTC Miscellaneous External Drug Products, which was the advisory review panel responsible for evaluating data on the active ingredients in this drug case. Interested persons were invited to submit comments by September 27, 1982. Reply comments in response to comments filed in the initial comment period could be submitted by October 27, 1982.

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 (address above), after deletion of a small amount of trade secret information. In response to the advance notice of proposed rulemaking, four manufacturers submitted comments and one manufacturer submitted a reply comment. Copies of the comments received are on public display in the Dockets Management Branch (address above).

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 G of Part 358 (21 CFR Part 358; proposed in the **Federal Register** of September 3, 1982; 47 FR 39108) FDA states for the first time its position on the establishment of a monograph for OTC pediculicide drug products. Final agency action on this matter will occur with the publication at a future date of a final monograph, which will be a final rule establishing a monograph for OTC pediculicide drug products.

This proposal constitutes FDA's tentative adoption of the Panel's conclusions and recommendations on OTC pediculicide drug products as modified on the basis of the comments received and the agency's independent evaluation of the Panel's report. Modifications have been made for clarity and regulatory accuracy and to reflect new information. Such new information has been placed on file in the Dockets Management Branch (address above). These modifications are reflected in the following summary of the comments and FDA's responses to them.

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 date are insufficient to classify as safe and effective, and further testing is required) at the final monograph stage, but will use instead the terms "monograph conditions" (old Category I) and "nonmonograph 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 products 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 for OTC pediculicide drug products (published in the **Federal Register** of June 29, 1982, 47 FR 28312), the agency suggested that the conditions included in the monograph (Category I) be effective 6 months after the date of publication of the final monograph in the **Federal Register**. 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 6 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.

All "OTC Volumes" cited throughout this document refer to the submissions made by interested persons pursuant to the call-for-data notice published in the **Federal Register** of November 16, 1973 (38 FR 31697) and August 27, 1975 (40 FR 38179) or to additional information that has come to the agency's attention since publication of the advance notice of proposed rulemaking. The volumes are on public display in the Dockets Management Branch (address above).

I. The Agency's Tentative Conclusions on the Comments

1. One comment submitted a copy of a label of an OTC aerosol pediculicide drug product, Personal Insecticide, bearing an Environmental Protection Agency registration number and which to the best of the comment's knowledge was being marketed for use on humans, and requested information regarding the procedure for registering this type of product with FDA.

In the **Federal Register** of November 5, 1979 (44 FR 63749), the United States Environmental Protection Agency (EPA) issued a final regulation to clarify its policy regarding the registration of pesticide products (which included pediculicide products) that are not new drugs or new animal drugs. Basically, EPA has jurisdiction over pesticide products marketed OTC and used as pediculicides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and regulations in 40 CFR Part 162, whereas FDA has jurisdiction over pediculicide drug products under the Federal Food, Drug, and Cosmetic Act (the act) and regulations in 21 CFR Parts 314 and 330. Section 162.5(d)(1) of EPA's regulations (40 CFR 162.5(d)(1)) provides that a pesticide, such as pyrethrins, is exempt from the requirements of FIFRA if the product is offered solely for human use and is a new drug within the meaning of section 201(p) of the act (21 U.S.C. 321) or has been determined not to be a new drug by the Secretary of Health and Human Services by a regulation establishing conditions for use of the product. At the present time, FDA has not declared pediculicide products containing pyrethrins to be new drugs nor established conditions for use of these products in a regulation. Therefore, EPA currently has jurisdiction over such products. However, as the EPA final rule explains (see 44 FR 63749), when FDA develops a monograph, products meeting its conditions will be exempt from FIFRA registration. Therefore, the tentative final monograph in this document, when finalized, would be an FDA regulation that establishes conditions for use of these products and, thus, would exempt pediculicide drug products containing pyrethrins from the requirements of FIFRA. Accordingly, once the final monograph becomes effective, a pesticide product containing pyrethrins labeled for use as an OTC pediculicide drug product for human use would no longer be under EPA's jurisdiction, but would have to conform to the labeling requirements of the final monograph. In the meantime, a pediculicide drug product may receive either FDA approval for marketing via a new drug application (NDA) under section 505 of the act (21 U.S.C. 355) and 21 CFR Part 314 or EPA approval for marketing under 40 CFR Part 162.

2. Two comments contended that aerosol forms of pediculicide drug products containing "OTC concentrations" of pyrethrins and piperonyl butoxide can be safely marketed as OTC drugs (Refs. 1 and 2). One of the comments stated that pulmonary absorption of any significant percentage of aerosolized pyrethrins and other potentially harmful product constituents can be minimized by utilizing an applicator and a method of application which restrict delivery of the aerosol "solely" to the infested area, and, additionally, by minimizing the number of aerosol particles below about 15 microns in diameter (Ref. 1). The comment referred to a specific aerosolized pediculicide drug product with an applicator which facilitates application in close proximity to skin and scalp to ensure essentially complete dermal impaction of the drug. The applicator generates an aerosol particle size distribution such that less than 2 percent of the delivered aerosol (by weight) is comprised of particles smaller than 16 microns in diameter and presents no inhalation toxicity problem. The comment stated that if all the aerosolized particles under 16 microns in size that are present in one average effective treatment using this product were absorbed systemically, they would represent approximately 0.15 milligram (mg) pyrethrins or less than 1/1,000,000 of the estimated LD_{50} in humans. The comment added that untoward chance contact of the product with mucous membrane can be minimized by delivery of the aerosol via use of a special applicator, limiting small, inhalable particle distribution, and by closing the mouth and eyes and covering the facial area with a damp cloth during spraying. The comment stated that an average patient treatment of head lice infestation requires five 1-second atomizations which approximate 2.25 grams (g) of the product, representing 7.5 mg pyrethrin extract and 62 mg piperonyl butoxide. The comment referred to the toxicity data (oral toxicity studies in mice and inhalation studies in rats and guinea pigs) previously submitted (Ref. 3) and stated that these data support the safety of the aerosol product. The comments concluded that broad international experience with this product has confirmed its safety as an OTC drug product.

The agency has reviewed the data previously submitted (Ref. 3), the Panel's statements, and the additional data and information submitted by the comments (Refs. 1 and 2) and has determined that the data are sufficient to establish the safety of aerosolized OTC pediculicide drug products as an alternative suitable dosage form provided that (1) an appropriate applicator is used which facilitates application of the product in close proximity to the affected area, (2) less than 2 percent of the delivered aerosol (by weight) is comprised of particles smaller that 16 microns in diameter, (3) the labeling states that the mouth and eyes are closed during application and the facial area is appropriately covered (e.g., with a damp cloth during spraying), (4) the labeling based upon adequate data, states an appropriate time period during which

the product can be safely and effectively used before washing off the affected area, and (5) the directions provide for an initial treatment followed by a second treatment in 7 to 10 days to kill any nits that may have hatched. Although the proposed labeling submitted to the Panel (Ref. 3) contained directions for treatment and preventative treatment, the agency has determined that the data do not support the use of aerosolized pediculicides every third day for prevention of lice infestation. Additional safety data for such use in aerosol and nonaerosol dosage forms would be needed to establish a preventative treatment claim.

The agency's evaluation of the data follows:

Using an aerosol product containing 0.33 percent pyrethrins and 2.67 percent piperonyl butoxide in petroleum oil, Mercier (Ref. 1) conducted four trials:

(1) *Acute toxicity after oral administration to albino mice.* This test was intended to determine toxicity in case of accidental ingestion or the vaporization of massive doses of the product on foodstuffs.

The LD_{50} was determined to be 8.77 grams/kilogram (g/kg). On histological examination only half of the controls, which had been given only 0.2 milliliter (mL)/20 g of olive oil, showed moderate steatosis of the liver while the treated animals all showed an excess of hepatic lipids. The excess was not always in proportion to the dose given. Nevertheless, vacuolation of the cytoplasm accompanied the excess lipids but no other inflammatory or sclerotic deterioration of the liver was found.

(2) *Trial to determine any possible toxic effect after inhalation of massive doses.* This test was conducted to demonstrate the bronchopulmonary or general toxicity by atomizing the product in a 4,700 liter semi-closed chamber containing guinea pigs and albino Wistar rats. The animals breathed the aerosol for 15 minutes during atomization and were kept in the chamber for 15 minutes after atomization. The animals were then observed for 1 week. This experiment showed that inhalation of large doses causes bronchopulmonary, bucconasal, and ocular irritation in test animals. The irritant effects were reversible within a few hours and did not lead to any lethal effect.

(3) *Trial to determine any toxic effect after inhalation of low dosages and the ingestion of food on which the vaporized material has fallen.* This experiment was conducted to determine whether the atomization of large quantities of the product into a room or the use of the aerosol, without precaution, could have a toxic effect.

Six female albino Wistar rats and 12 female albino Swiss mice, in ordinary cages, were placed in a room with a volume of 43 cubic meters. Over a 15-minute period, the contents of four 90 g containers were atomized near the animals. The animals were monitored every 15 minutes for 1 hour, then every 30 minutes for 3 hours for 4 days, in the same room where atomization occurred. This experiment showed that low doses of aerosol do cause moderate eye irritation and bucconasal irritation. Neither congestion of the eyes nor nasal or salivary hypersecretion was found. Also, there was no sign of bronchopulmonary irritation resulting in cough or dyspnea. No lethal effect due to inhalation of the product or to the ingestion of food on which it had fallen was observed.

(4) *Local tolerance of the finished product in macaca monkeys.* Each day except Sunday, three females and one male were given an atomization of the product using the nozzle intended for treatment of the occipital region. Each spray lasted 10 seconds, and a total of 18 atomizations were given.

Daily spraying for 3 weeks did not cause lesions in the treated area. The skin did not show any inflammatory reaction and no desquamation. No anomaly was found in the pilary system. The aerosol product did not appear to cause irritation to mucous membranes; there were no bouts of sneezing, watering eyes, or rhinorrhea. The 10-second spraying did not appear to cause reactions which could correspond with a painful or disagreeable sensation.

After reviewing the submitted data, the agency finds that the animal studies submitted support the safety of an aerosolized dosage form for human treatment use. Based on the above discussion, at this time, the agency is classifying aerosolized pediculicides for treatment use in Category I for safety. Preventative treatment use is being classified in Category III for safety. The effectiveness of these products (Category III) is discussed in comment 3 below. Should aerosolized pediculicides be included in the monograph, the agency will propose appropriate standards at that time.

References

(1) Comment No. C00002, Docket No. 81N-201, Dockets Management Branch.

(2) Comment No. C00004, Docket No. 81N-0201, Dockets Management Branch.

(3) OTC Volume 160403.

3. One comment stated that FDA should only consider an aerosol as a method of administration of a pediculicide on the basis of a full NDA in which clinical studies of the effectiveness of the aerosol are compared with that of currently approved methods of treatment. The comment argued that spraying the hair with an aerosol would require a probe to get the spray to the scalp area, that using this technique would be extremely difficult to cover adequately all areas of the scalp, and that delivery of the medication onto the lice and nits could not be assured. The comment contended that adequate coverage of a topically applied medication requires the use of a liquid which will bring the active ingredient to the entire scalp and hair. The comment added that inadequate treatment, such as might be provided via the use of an aerosol, could result in the exposure of lice to sublethal levels of the drug and that, over a period of many generations, adaptive mechanisms could enable the lice to withstand what originally had been a lethal concentration of drug.

A reply comment stated that its aerosol pediculicide product with a unique applicator has been used extensively and effectively outside the United States. The reply comment argued that the adequacy of distribution of aerosolized particles over the infested ("scalp") area, and the completeness of effective contact of the drug with infesting parasites, is supported not only by efficacy as an OTC pediculicide, but also by laboratory studies and human clinical evaluation (Refs. 1, 2, and 3). The reply comment added that two Canadian researchers compared the ovicidal activity of its aerosol product with other pediculicides marketed in Canada and showed a 100-percent ovicidal activity of the product (Ref. 4).

Based on the submitted data, the reply comment concluded that its aerosol pediculicide with unique applicator appears to be at least as effective as nonaerosol pediculicide products marketed in the United States. Accordingly, the reply comment stated that the comment's suggestion that an aerosol pyrethrin pediculicide (with suitable applicator) would provide inferior therapy for head lice infestations, and hence increase the potential for development of pyrethrin-resistant strains of lice, is not valid. The reply comment indicated that it was unaware of any reported development of significant resistance to pyrethrin-piperonyl butoxide formulations, that its experimental evidence indicates greater effectiveness for aerosol-administered pyrethrins, and that aerosol administration might reduce the change

of ineffective treatment and development of parasite resistance.

The agency has evaluated the studies submitted by the reply comment. In one study, Timon-David (Ref. 1) investigated the activity of an aerosol formulation containing 0.33 percent pyrethrins and 2.67 percent piperonyl butoxide in vitro against head, body, and public lice using three techniques of exposure: (1) Immersion of the lice in the spray premix (total formulation less propellant), (2) placement of the lice in a Petri dish containing a cotton disk impregnated with spray premix, and (3) spraying of the lice with a "microfog" generated by an aerosol container.

Using the immersion technique, 10 body lice (then 10 head lice, then 5 pubic lice) were placed into each of 10 dishes containing 5 mL of pyrethrins and piperonyl butoxide with petroleum oil. The closed dishes were incubated at 28°C at 60 percent humidity in the dark, as were the dishes containing untreated controls. The male and female lice of the three species died in under 5 minutes (100 percent killed), while the control lice survived for longer than 72 hours.

Using a 5.5-centimeters (cm) disc of cotton impregnated with the same pyrethrin mixture, the disc in five dishes were impregnated with 0.1 mL of the mixture while the discs in another five dishes were impregnated with 0.2 mL of the mixture. A group of 10 head lice (then 10 body lice, then 5 pubic lice) were placed into each dish with no distinction between males and females. The dishes were closed and placed in the dark and incubated at 28°C and 60 percent humidity. The survival of the lice was monitored with a low-power binocular microscope every 5 minutes. The untreated lice survived for over 72 hours while the lice treated with the 0.2 mL solution were 100 percent killed in under 10 minutes. The head and body lice were more sensitive and were 100 percent killed in under 5 minutes. In the 0.1 mL solution treated dishes, head and body lice were 100 percent killed in under 30 minutes while the pubic lice were 100 percent killed in under 45 minutes.

The technique using the "microfog" generated from the aerosol container most nearly approaches the conditions of use in vivo. Each species of louse (head, body, and pubic) was divided into three lots. The first lot was given a 2-second atomization, 25 cm from the lice-containing dishes. The second lot was given a 5-second atomization at 25 cm, while the third lot was given a 15-second atomization at 25 cm. Using the applicator nozzle, 100 percent kill was achieved in under 15 minutes. The 5- and 15-second atomizations were too long a period on the small surface area of the petrie dish and resulted in the lice lying paralyzed and drowned in the test solution comparable to the conditions in the immersion technique. However, the 15-second atomization corresponds with the time necessary to carry out the complete spraying of the average scalp. Timon-David concluded that the comparative effect (of equal quantities of drug) was much more rapid via aerosol application. He attributed this observation to the "immediate contact" of the micromist with the whole of the cerolipid cuticle of the insect and the micromist's rapid penetration of the respiratory system leading to more rapid paralysis and death. Timon-David also demonstrated that eggs of the respective parasite species were killed in under three to five hours when treated with a 2-second spray of the aerosol, larvae which had reached the hatching stage were killed on hatching, and larvae treated at an earlier stage of development were killed in situ without development to the hatching stage.

In a second controlled study, Coz (Ref. 2) studied the activity of the aerosol against a strain of body louse adapted to the rabbit, including lice of different ages (nymphs and adults) and eggs. The age of treated lice varied between 4 and 48 days with adults considered as being over 14 days of age. Each lot of lice, placed on a fabric support, was treated with a 2-second spray containing 0.33 percent pyrethrins and 2.67 percent piperonyl butoxide. The lice were left in contact with the product for periods varying between 2 to 5 minutes. When the time of contact had elapsed, the lice were washed with water to simulate usual conditions of use of the material. Lots of control lice, similar in age to the treated lice, were kept under conditions similar to those of the lots treated by spraying with the aerosol. The controls were also given a water wash. The number of dead lice on rabbits was recorded after 24 hours. During the period of observation the lice were kept on fabric, incubated at 28°C with 70 to 80 percent humidity. In the control lice, 12.4 percent dead insects occurred from natural causes while the aerosol treated lice reflected a death rate of 100 percent independent of age and of time of contact between the parasite and the mixture of active ingredients. The efficacy of the aerosol is complete even for periods of less than 2 minutes.

Eggs of body lice were treated on a fabric support with a 2-second spray of the aerosol and left in contact with the material for 2, 5, or 10 minutes. After the contact period, the lice eggs were washed with water to simulate usual conditions of use. Each treated lot was paired with a control lot. The eggs were incubated at 28 °C with 70 to 80 percent humidity. Every day except Sunday, the cloths supporting the eggs were placed on the shaved stomach of a rabbit. Hatching occurred over several days. The day on which the maximum number of hatched lice were seen was chosen for the determination of the percentage hatch. Analysis of the results showed that with a 2-minute contact time a hatch of 0 percent of the eggs was obtained from 328 eggs treated with the aerosol whereas, for the control lots, the mean level of 44.4 percent hatchings from 408 eggs occurred. With a 5-minute contact time, 0 percent eggs hatched from 391 treated eggs compared to a mean level of 55.7 percent hatches from 406 control eggs. With a 10-minute contact time, 0 percent eggs hatched from 353 treated eggs while the mean level of hatching for the control was 62.81 percent from 449 eggs.

In the third study, Privat (Ref. 3) treated 118 patients having pediculosis (90 with head lice, 26 with public lice, and 2 with body lice) with the aerosol product containing 0.33 percent pyrethrins and 2.6 percent piperonyl butoxide. Treatment consisted of a series of 1-second atomizations in such a way as to cover the whole of the hair or the hair-covered areas. After a 24-hour contact period, the hair or hair covered areas were washed two to three times followed by rinsing. A single treatment was considered sufficient provided the individual was not re-exposed to infestation and provided there was regular clinical supervision for the four weeks following treatment to reveal any possible failure in the therapy. Of the 113 patients available for followup evaluation, 109 showed complete eradication of parasitosis. In only four cases (two head lice and two public lice) was there a reappearance of infestation; however, the investigator was unable to determine whether these recurrences were treatment failures or reinfestations following effective treatment.

Although the reply comment referred to a personal communication with two Canadian researchers, no details of the communication were provided (Ref. 4). Because no data were provided to confirm the claimed 100 percent ovicidal activity of the aerosol under experimental conditions, the agency cannot determine the validity of this claim and any reference to these researchers' findings cannot be used to support the effectiveness of the aerosol product.

The agency has also considered the comment's arguments that an aerosol

would not provide adequate treatment, that an aerosol would not bring the active ingredient to the entire scalp and hair, and that an aerosol would cause formation of sublethal levels of drug which would cause a tolerance to be developed over generations; however, because the comment did not document its arguments, the agency cannot fully address them. Instead, the agency welcomes the submission of data and comments addressing these arguments. Any comments submitted will be addressed in the final monograph. The agency believes that most of these questions would be answered by additional clinical studies.

The agency finds that the two laboratory studies (Refs. 1 and 2) are supportive of the effectiveness of the aerosolized pediculicide; however, they are not adequate to establish general recognition of effectiveness. Although the clinical study (Ref. 3) did demonstrate the effectiveness of an aerosol form of pyrethrins/piperonyl butoxide after 24 hours, the study was not comparable to the directions contained in the labeling proposed for the aerosol product i.e., that the treated area should be shampooed 30 minutes after application of the product. In addition, because the aerosolized pediculicide product was allowed to act for 24 hours, there are no data demonstrating at which point in time the product was effective. Data are needed to demonstrate an appropriate time period for which an aerosolized pediculicide drug product must remain on the affected area in order to be effective before it is then washed off. It should be further noted that, based upon the safety data, the Panel recommended that products containing pyrethrins/piperonyl butoxide be limited to topical use for 10 minutes but no longer (47 FR 28315–28319). If new data demonstrating effectiveness indicate that a longer period of exposure is necessary for effective treatment, additional safety data may be necessary. Any new data submitted should include information as to any observed adverse effects. Therefore, at this time the agency is proposing a Category III classification for effectiveness for treatment use of aerosolized pediculicide products containing pyrethrins and piperonyl butoxide.

References

(1) Timon-David, P., "Report on Parasitological Trial," Centre De Recherche D'Applications Pharmaceutiques, Laboratoires Applipharm, *Marseille*, March, 1979, in Reply Comment coded RC0001, Docket No. 81N–0201, Dockets Management Branch.

(2) Coz, J., "Report on a Supplementary Parasitological Experimental Trial," Centre De Recherche D'Applications Pharmaceutiques, Laboratoires Applipharm, Marseille, February, 1979, in Reply Comment coded RC0001, Docket No. 81N–0201, Dockets Management Branch.

(3) Privat, Y., "Clinical Trial of the Activity and Tolerance of the Para 2 Aerosol," Centre De Recherche D'Applications Pharmaceutiques, Laboratoires Applipharm, Marseille, October, 1979, in Reply Comment coded RC0001, Docket No. 81N–0201, Dockets Management Branch.

(4) Reply Comment coded RC0001, Docket No. 81N–0201, Dockets Management Branch.

(5) OTC Volume 160403.

4. One comment contended that using the term "pediculicide" may be meaningless to many persons and suggested that the phrase "for lice control" would be a better statement of identity.

The agency agrees with the comment that the term "pediculicide" may not be well understood by many consumers. If manufacturers wish to use the technical term as the statement of identity, the agency believes it should be used with a nontechnical term that would be understood by consumers. Alternatively, the nontechnical term used alone would be an adequate statement of identity.

The agency has determined that "lice treatment" would be a more appropriate nontechnical term than the phrase "for lice control" because "treatment" language is more consistent with the indications for use of these products and is similar to other statements of identity which the agency has proposed in other OTC drug rulemakings, e.g., "nocturnal leg muscle cramps treatment" or "pinworm treatment." (See the **Federal Registers** of November 8, 1985 (50 FR 46582) and August 1, 1986 (51 FR 27756).) Accordingly, the following statements of identity are being proposed in § 358.650(b) of this tentative final monograph: "pediculicide (lice treatment)" or "lice treatment."

The agency has no objection to terms such as "for lice control" appearing elsewhere in the labeling provided they do not appear in any portion of the labeling required by the monograph and do not detract from the required information. The agency believes that this approach will minimize the likelihood of confusion.

5. Referring to the Panel's recommended indication in § 358.650(b), one comment stated that the term "body lice" is a misnomer because "body lice do not live on the body but rather in the clothing, going to the body only for feeding." The comment contended that *body lice are almost* exclusively confined to persons who do not regularly change their clothing and, accordingly, it would not be necessary to treat the body with a pediculicide but would only be necessary to launder the clothing in hot water (135 °F) for 10 minutes or more. Therefore, the comment recommended that the agency not include the indication for body lice in the tentative final monograph.

The agency disagrees with the comment's contention that the term "body lice" is a misnomer. "Body lice" is an appropriate and commonly accepted name for blood-sucking lice particularly affecting the skin on the waist and armpits where there is close contact between garment and wearer (47 FR 28314 to 28315). At any given time, some lice will be in the clothing, but others, during feeding time, will be on the body. Even though body lice can be removed by changing clothing and laundering the infested clothes in hot water, as suggested by the comment, any lice that were feeding on the body would remain to reinfest other clothing. Accordingly, the agency believes that it would be inadequate treatment to only launder clothes in hot water without treating the body at the same time with a pediculicide. Therefore, the agency is including the Panel's recommended indication "for * * * body lice" in the tentative final monograph.

6. Stating that "it is important that the entire scalp and hair are covered with the product," one comment suggested that the first sentence of the directions recommended by the Panel in § 358.650(d) be revised as follows: "Apply to the hair and scalp until all the hair is thoroughly wet with the product."

The agency agrees in substance with the comment's suggested revision, i.e., that the affected area, whether scalp, body, or pubic area, should be covered with the pediculicide drug product until all the hair is thoroughly wet. However, the comment's suggested revision to include the term "scalp" would refer only to treatment of head lice, whereas the intent of the directions in § 358.650(d) is to provide a general direction that is applicable for the treatment of all lice that affect humans, i.e., head lice, body lice, and pubic lice. Therefore, in this tentative final monograph, the first sentence of the directions in § 358.650(d) is not being modified as suggested by the comment.

7. Contending that pyrethrins with piperonyl butoxide need not necessarily be limited to formulation as a lotion, one comment suggested that the directions recommended by the Panel in § 358.650(d), which in part read "Wash area thoroughly with warm water and soap or shampoo," be revised to provide for products which are formulated in a

shampoo base. The comment pointed out the marketing of an EPA-approved product formulated with pyrethrins and piperonyl butoxide in a shampoo base and contended that it would be unnecessary to add soap or shampoo, but merely water. The comment therefore suggested that for products formulated in a shampoo base the directions for use should provide for alternate wording, such as, "Add sufficient warm water to form a lather and shampoo as usual."

The agency agrees with the comment that specific directions should be included in the tentative final monograph for pediculicide shampoo products. Therefore, the agency is revising the directions in § 358.650(d) as suggested by the comment. Regarding the comment's reference to an EPA approved product, the agency notes that EPA has the authority to regulate these products pending the promulgation of a final FDA monograph on OTC pediculicide drug products. (See comment 1 above.)

8. Referring to that part of the Panel's recommended labeling in § 358.650(e)(1) that states "Personal articles of clothing or bedding that cannot be washed may be dry-cleaned or sealed in a plastic bag for a period of about two weeks," one comment pointed out the marketing of several EPA-approved aerosol sprays containing either pyrethrins with piperonyl butoxide or one of several pyrethroids intended to kill lice on personal articles. The comment contended that the use of these products would eliminate the need to quarantine bedding or objects that can be neither washed nor dry-cleaned. The comment suggested that § 358.650(e)(1) be revised to provide for the use of these products by adding the following sentence: "In lieu of this, such articles can be treated with an aerosol product specifically designed for this purpose."

The agency agrees with the comment's suggestion; however, because not all of the products used as sprays to treat inanimate objects are aerosols, i.e., some are pump sprays, the agency is revising the sentence suggested by the comment for clarity and is including it in § 358.650(e)(1) of the tentative final monograph. Section 358.650(e)(1) will now read as follows: "Personal articles of clothing or bedding that cannot be washed may be dry-cleaned, sealed in a plastic bag for a period of about 2 weeks, or sprayed with a product specifically designed for this purpose."

II. The Agency's Tentative Adoption of the Panel's Report

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

1. Summary of ingredient categories

The agency has reviewed all claimed active ingredients submitted to the Panel, as well as other data and information available at this time, and has made no changes in the categorization of pediculicide active ingredients recommended by the Panel. As a convenience to the reader, the following list is included as a summary of the categorization of pediculicide active ingredients recommended by the Panel and the proposed categorization by the agency.

Pediculicide active ingredients	Panel	Agency
alkaloids of sabadilla	II	II
aqueous coconut oil soap	II	II
benzocaine	II	II
benzyl alcohol	II	II
benzyl benzoate	II	II
copper oleate	II	II
dichlorodiphenyl trichloroethane (DDT).	II	II
dioctyl sodium sulfosuccinate	II	II
isobornyl thiocyanoacetate	II	II
picrotoxin	II	II
propylene glycol	II	II
pyrethrins with piperonyl butoxide (aerosol).	N/A	III [1]
pyrethrins with piperonyl butoxide (nonaerosol).	I	I
sublimed sulfur	II	II
thiocyanoacetate	II	II

[1] Safe (Category I) for treatment use.

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 pediculicide ingredient or condition (including aerosol dosage forms) 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 includes 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

FDA has considered the comments and other relevant information and concludes that it will tentatively adopt the Panel's report and recommended monograph with the changes described in FDA's responses to the comments above and with other changes described in the summary below. A summary of the changes made by the agency follows.

1. The agency has determined that effectiveness of aerosolized products containing pyrethrins and piperonyl butoxide has not been established at this time. Such products are classified in Category III in this rulemaking. The treatment use of aerosolized pediculicides is Category I for safety. Preventative treatment use is being classified in Category III for safety. (See comments 2 and 3 above.)

2. In the Panel's discussion of pyrethrins with piperonyl butoxide (47 FR 28315 to 28319), the Panel noted that pyrethrins are brown, viscous, liquid oleoresins that must be extracted and then refined. Pyrethrins are obtained from the flowers of *Chrysanthemum cinerariaefolium* and that extraction produces two pyrethrin fractions—pyrethrins I which contains the esters of chrysanthemic acid (pyrethrin I, cinerin I, and jasmolin I) and pyrethrins II which contains the esters of pyrethric acid (pyrethrin II, cinerin II, and jasmolin II). The pyrethrin content ranges from 0.7 percent to as high as 3 percent with the active constituents reaching their highest concentration in mature flower heads. There are two methods of extracting the crude oleoresin with the pyrethrum concentration varying from 25 to 35 percent. The reduction and refinement of the crude oleoresin containing the pyrethrins produces a light-colored relatively nonstaining extract. The Panel described two methods of refinement which use a low temperature process to decrease the possibility that the molecular structure of the pyrethrins will change. These processes have a high recovery of pyrethrins (about 95 percent); however, there are other methods in which the percent of pyrethrins recovered is not as great.

The active insecticidal constituents of pyrethrum flowers have been identified as four compounds: cinerin I, cinerin II, pyrethrin I, and pyrethrin II (Ref. 1). The first and third of these compounds are esters of chrysanthemum monocarboxylic acid with the alcohols cinerolone and pyrethrolone; the second and fourth are esters of the same alcohols with chrysanthemum dicarboxylic acid. The monocarboxylic acid esters are claimed to be more effective (Ref. 1). In discussing the results of a study submitted to the Panel (Ref. 2), an investigator noted that one factor to be considered in interpreting

results is the fact that pyrethrins are natural products consisting of 6 esters with potency ("activity") variability. In this study, the investigator also noted that "although each pyrethrum-containing product was tested at least three times, different lot-numbered products were used for each separate test. Thus, activity varied within products. However, the findings of this study are consistent across separate experiments."

Nevertheless, the agency is concerned that before general recognition of the safety and effectiveness of these pyrethrins can be established, the composition of the pyrethrins must be more clearly defined. The agency's concerns, as discussed above, were communicated in a letter to each interested party who had previously submitted data on the composition of pyrethrins (Refs. 3 through 8). Subsequently, data were submitted by a manufacturers' association (Ref. 9). Those data have been reviewed and the agency has determined that, while the data provide a broader understanding of the composition of the pyrethrin fractions and suggest that there is little disconformity in potency, variation is possible. It is because of the possibility of potency variations that the agency believes that extracts derived from different purification processes should be compared with caution in terms of pyrethrins recovery and chemical composition and should be compared in terms of biological activity (Ref. 10). Further, the agency is concerned that these compounds are heat and light sensitive, prone to oxidation, and tend to become increasingly unstable with increasing concentration and purity (Ref. 10). The agency believes that it would be appropriate for interested parties to develop with the United States Pharmacopeial Convention (USPC) suitable standards for the quality and purity of pyrethrins. Accordingly, the agency has referred the data to the USPC for consideration (Ref. 11). In this tentative final monograph, pyrethrins are proposed in Category I. However, should interested parties fail to provide necessary information so that an appropriate standard may be established, pyrethrins will not be included in a final monograph.

In order for pyrethrins to be generally recognized as safe and effective as a pediculicide, the agency must have sufficient data on the composition and concentration of the different pyrethrin constituents and the quantity (range) of each that is contained in marketed products. For an ingredient or mixture to be included in an OTC drug final monograph, it is necessary to have publicly available chemical information that can be used by all manufacturers to determine that the ingredient is appropriate for use in their products.

References

(1) Melnikov, N.N., "Chemistry of Pesticides," Edited by Gunther, F. and J.D. Gunther, Springer-Verlag, New York, pp. 130–132, 1971.

(2) Gerberg, E., "Comparative in-vitro Activity of Commercial Pediculicidal Products," Report Number Rx–18–80, OTC Volume 160400.

(3) Letter from W.E. Gilbertson, FDA, to Norcliff Thayer, Inc., coded LET00003, Docket No. 81N–0201, Dockets Management Branch.

(4) Letter from W.E. Gilbertson, FDA, to Fairfield American Corporation, coded LET00004, Docket No. 81N–0201, Dockets Management Branch.

(5) Letter from W.E. Gilbertson, FDA, to AMLAB, Inc., coded LET00005, Docket No. 81N–0201, Dockets Management Branch.

(6) Letter from W.E. Gilbertson, FDA, to Pfizer Pharmaceuticals, coded LET00006, Docket No. 81N–0201, Dockets Management Branch.

(7) Letter from W.E. Gilbertson, FDA, to Block Drug Company, Inc., coded LET00007, Docket No. 81N–0201, Dockets Management Branch.

(8) Letter from W.E. Gilbertson, FDA, to Laboratories Applipharm, coded LET00008, Docket No. 81N–0201, Dockets Management Branch.

(9) Comment No. LET00009, Docket No. 81N–201, Dockets Management Branch.

(10) Hopkins, L.O., "Processes for Preparing Refined Pyrethrum Extract. A Review," *Pyrethrum Post*, 7:34–44 and 48, 1964.

(11) Letter from J. Davis, FDA, to J.G. Valentino, United States Pharmacopeial Convention, Inc., dated June 17, 1988 in OTC Volume 16KTFM.

3. The agency is expanding the statement of identity so that these products can now be identified as a "pediculicide (lice treatment)" or "lice treatment." (See comment 4 above.)

4. The agency is adding directions in the tentative final monograph for the use of pediculicide products formulated as shampoos. (See comment 7 above.)

5. The agency is revising the Panel's recommended "Other required statements" in § 358.650(e)(1) by adding the phrase * * * or sprayed with a product specifically designed for this purpose * * *" in order to provide for the use of EPA approved spray products that eliminate the need to quarantine bedding or objects that can be neither washed nor dry-cleaned. (See comment 8 above.)

6. In an effort to simplify OTC drug labeling, the agency proposed in a number of tentative final monographs to substitute the word "doctor" for "physician" in OTC drug monographs on the basis that the word "doctor" is more commonly used and better understood by consumers. Based on comments received to these proposals, the agency has determined that final monographs and any applicable OTC drug regulation will give manufacturers the option of using either the word "physician" or the word "doctor." This tentative final monograph proposes that option.

7. In the warnings section, the agency is adding the statement "For external use only." Use of this statement is consistent with a number of other OTC drug monographs for topical drug products. (See, for example, the tentative final monograph for OTC external analgesic drug products (February 8, 1983; 48 FR 5852); the tentative final monograph for OTC skin protectant drug products (February 15, 1983; 48 FR 6820); and the final monograph for OTC topical otic drug products (August 8, 1986; 51 FR 28656).) Based on the warning against use of a pediculicide near the eyes, the agency is also proposing the statement, "Consult a doctor if infestation of eyebrows or eyelashes occurs," to provide additional information for consumers. Accordingly, the warning in § 358.650(c)(2) will now read as follows: "For external use only. Do not use near the eyes or permit contact with mucous membranes. If product gets into the eyes, immediately flush with water. Consult a doctor if infestation of eyebrows or eyelashes occurs."

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 pediculicide 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 pediculicide drug

products is not expected to pose such an impact on small businesses. Therefore, the agency certifies that this proposed rule, if implemented, will not have a significant economic impact on a substantial number of small entities.

The agency invited public comment in the advance notice of proposed rulemaking regarding any impact that this rulemaking would have on OTC pediculicide drug products. No comments on economic impacts were received. Any comments on the agency's initial determination of the economic consequences of this proposed rulemaking should be submitted by August 1, 1989. 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) 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.

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 21 CFR 330.1(c)(2), 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 other OTC drug labeling required by a monograph or other regulation (e.g., statement of identity, warnings, and directions) must appear in the specific wording established under the OTC drug monograph or other regulation where exact language has been established and identified by quotation marks, e.g., 21 CFR 201.63 or 330.1(g). The proposed rule in this document is subject to the labeling provisions in § 330.1(c)(2).

Interested persons may, on or before June 2, 1989, submit to the Dockets Management Branch (address above) written comments, objections, or requests for oral hearing before the Commissioner on the proposed regulation. 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 Agusut 1, 1989. 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 April 3, 1990, 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 June 4, 1990. 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. 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 monograph, the agency will ordinarily consider only data submitted prior to the closing of the administrative record on June 4, 1990. Data submitted after the closing of the administrative record will be reviewed by the agency only after a final monograph 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 358

Labeling, Over-the counter drugs, Pediculicide 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 358 (proposed in the **Federal Register** of September 3, 1982; 47 FR 39108), by adding new Subpart G, to read as follows:

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

1. The authority citation for 21 CFR Part 358 is revised 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 Stat. 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. Part 358 is amended by adding new Subpart G to read as follows:

Subpart G—Pediculicide Drug Products

Sec.

Subpart G—Pediculicide Drug Products

§ 358.601 Scope.

(a) An over-the-counter pediculicide drug product in a form suitable for topical application is generally recognized as safe and effective and is not misbranded if it meets each condition in this subpart and each general condition established in § 330.1 of this chapter.

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

§ 358.603 Definition.

As used in this subpart:

Pediculicide drug product. A drug product for the treatment of head, pubic (crab), and body lice.

§ 358.610 Pediculicide active ingredients.

The active ingredients of the product consist of the combination of pyrethrins (0.17 to 0.33 percent) with piperonyl butoxide (2 to 4 percent) in a nonaerosol dosage formulation.

§ 358.650 Labeling of pediculicide 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 a "pediculicide (lice treatment)" or "lice treatment."

(b) *Indications.* The labeling of the product states, under the heading "Indications," the following: "For the treatment of head, pubic (crab), and body lice." 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) of this chapter, 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 or 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) "Use with caution on persons allergic to ragweed."

(2) "For external use only. Do not use near the eyes or permit contact with mucous membranes. If product gets into the eyes, immediately flush with water. Consult a doctor if infestation of eyebrows or eyelashes occurs."

(3) "If skin irritation or infection is present or develops, discontinue use and consult a doctor."

(4) The word "physician" may be substituted for the word "doctor" in any of the warning statements in this paragraph.

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions":

(1) *For nonshampoo products.* "Apply to affected area until all the hair is thoroughly wet with product. Allow product to remain on area for 10 minutes but no longer. Wash area thoroughly with warm water and soap or shampoo. A fine-toothed comb may be used to help remove dead lice or their eggs (nits) from hair. A second treatment must be made in 7 to 10 days to kill any newly hatched lice."

(2) *For products formulated for use as a shampoo.* "Apply to affected area until all the hair is thoroughly wet with product. Allow product to remain on area for 10 minutes but no longer. Add sufficient warm water to form a lather and shampoo as usual. Rinse thoroughly. A fine-toothed comb may be used to help remove dead lice or their eggs (nits) from hair. A second treatment must be made in 7 to 10 days to kill any newly hatched lice."

(e) *Other required statements.* (1) "*Head Lice:* Head lice live on the scalp and lay small white eggs (nits) on the hair shaft close to the scalp. The nits are most easily found on the nape of the neck or behind the ears. All personal headgear, scarfs, coats, and bed linen should be disinfected by machine washing in hot water and drying, using the hot cycle of a dryer for at least 20 minutes. Personal articles of clothing or bedding that cannot be washed may be dry-cleaned, sealed in a plastic bag for a period of about 2 weeks, or sprayed with a product specifically designed for this purpose. Personal combs and brushes may be disinfected by soaking in hot water (above 130 °F) for 5 to 10 minutes. Thorough vacuuming of rooms inhabited by infected patients is recommended."

(2) "*Pubic (Crab) Lice:* Pubic lice may be transmitted by sexual contact, therefore, sexual partners should be treated simultaneously to avoid reinfestation. The lice are very small and look almost like brown or grey dots on the skin. Pubic lice usually cause intense itching and lay small white eggs (nits) on the hair shaft generally close to the skin surface. In hairy individuals, pubic lice may be present on the short hairs of the thighs and trunk, underarms, and occasionally on the beard and mustache. Underwear should be disinfected by machine washing in hot water; then drying, using the hot cycle for at least 20 minutes."

(3) "*Body Lice:* Body lice and their eggs are generally found in the seams of clothing, particularly in the wasteline and armpit area. They move to the skin to feed, then return to the seams of the clothing where they lay their eggs. Clothing worn and not laundered before treatment should be disinfected by the same procedure as described for head lice, except that sealing clothing in a plastic bag is not recommended for body lice because their nits (eggs) from these lice can remain dormant for a period of up to 30 days."

Dated: February 27, 1989.

Frank E. Young,

Commissioner of Food and Drugs.

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