

reinfestation. In the last few years, pediculosis fact sheets have recommended longer sealing times. One sheet (Ref. 1) instructs to "pack the items in a sealed plastic bag for a minimum of two weeks." Another sheet (Ref. 2) instructs to "pack non-washable items in a sealed plastic bag for 21 days to eliminate the risk from dormant nits." Based on these recent recommendations, the agency has determined that a 4-week time period will give greater assurance of preventing head lice reinfestation.

(Comment 5) One comment stated that the amended final monograph should allow for special instructions specific to particular products to enhance product-specific directions. The comment gave examples of "shake the product well before use," "apply to dry hair," or conditions for storage. The comment requested that the monograph state that "a reasonable degree of flexibility will be given to companies choosing to amplify the directions appropriately."

The agency disagrees with the need to include the comment's suggested statements in the FM for OTC pediculicide drug products. That monograph does not prohibit manufacturers from including statements such as "shake well before using" or information about conditions for storage in the product's labeling. The direction under the heading "Treat" for shampoo and nonshampoo products in § 358.650(d)(4)(i) and (d)(4)(ii) imply that the hair is dry before the product is first applied. FDA is amending these sections to give the option of adding the word "dry" before "hair".

C. Will Labeling for New Drug Application (NDA) Products be Revised at the Same Time as the Monograph Products?

(Comment 6) One comment asked FDA to coordinate the revised NDA labeling for OTC pediculicide drug products marketed under NDAs and under the OTC drug monograph. The comment stated that the implementation for all products should occur at the same time.

FDA strives for consistency in labeling of similar products that are marketed OTC under an OTC drug monograph or an NDA. The effective date for the amended labeling in this final rule is 18 months after the date of publication in the **Federal Register**. The agency intends to notify NDA holders to make changes in labeling consistent with this final rule and believes these changes can be completed by the effective date.

III. The Agency's Final Conclusions

A. Summary of Major Labeling Changes

Based on the available evidence, FDA is issuing a final rule amending the FM for OTC pediculicide drug products to make the following changes:

- *Statement of Identity.* We revised the "Statement of identity" to read "lice treatment" and eliminated the term "pediculicide."
- *Warnings.*

(1) We shortened some warnings and stated all warnings in the new format in § 201.66 using the subheadings "Do not use", "Ask a doctor before use if you are", "When using this product", and "Stop use and ask a doctor if".

(2) We revised one warning for greater clarity by adding a few words after the statement "See a doctor" to read "Do not use • near eyes • inside nose, mouth, or vagina • on lice in eyebrows or eyelashes. See a doctor if lice are present in these areas."

- *Directions.* We added the following:

(1) Two introductory statements entitled "Important: Read warnings before use" [statement shall appear first and in bold type] and "adults and children 2 years and over" [in bold type];

(2) Headings entitled "Inspect", "Treat", and "Remove lice and their eggs (nits)";

(3) "Dry" as an optional word before "hair" in the first sentence in the heading for "Treat" for shampoo and nonshampoo products.

- *Other information.*

(1) We allow information to appear in a package insert.

(2) We expanded the time for sealing items in a plastic bag from 2 to 4 weeks.

(3) We added the statement "• vacuum all carpets, mattresses, upholstered furniture, and car seats that may have been used by affected people".

B. Statement About Warnings

Mandating warnings in an OTC drug monograph does not require a finding that any or all of the OTC drug products covered by the monograph actually caused an adverse event, and FDA does not so find. Nor does FDA's requirement of warnings repudiate the prior OTC drug monographs and monograph rulemakings under which the affected drug products have been lawfully marketed. Rather, as a consumer protection agency, FDA has determined that warnings are necessary to ensure that these OTC drug products continue to be safe and effective for their labeled indications under ordinary conditions of use as those terms are defined in the Federal Food, Drug, and Cosmetic Act.

This judgment balances the benefits of these drug products against their potential risks (see 21 CFR 330.10(a)).

FDA's decision to act in this instance need not meet the standard of proof required to prevail in a private tort action (*Glatetter v. Novartis Pharmaceuticals Corp.*, 252 F.3d 986, 991 (8th Cir. 2001)). To mandate warnings, or take similar regulatory action, FDA need not show, nor do we allege, actual causation. For an expanded discussion of case law supporting FDA's authority to require such warnings, see Labeling of Diphenhydramine-Containing Drug Products for Over-the-Counter Human Use final rule (67 FR 72555, December 6, 2002).

C. Marketing Conditions

No OTC pediculicide drug product that is marketed under part 358, subpart G, and that contains a nonmonograph condition may be initially introduced or initially delivered for introduction into interstate commerce unless it is the subject of an approved NDA:

- 24 months after the date of publication of this final rule in the **Federal Register** for products with sales less than \$25,000;

- 18 months after the date of publication in the **Federal Register** for all other such drug products.

Further, any OTC drug product subject to this final rule that is repackaged or relabeled after the compliance dates in the final rule must be in compliance with part 358, subpart G regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufacturers are encouraged to comply voluntarily as soon as possible.

IV. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (2 U.S.C. 1501 *et seq.*). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Under the Regulatory Flexibility Act, if a rule has a significant impact on a substantial number of small entities, an agency must analyze regulatory options that would minimize any significant impact of the rule on small entities. Section