

detailed comments and evaluation of the above data are on file in the Dockets Management Branch (Ref. 2).

The agency considers this product to be a drug. (See discussion in section I.B., comment 5.) The agency has been informed that the comment plans to conduct another study to establish the effectiveness of this product for the drying of water-clogged ears (Refs. 3 and 4). When the study is completed, the comment should submit the data in the form of a petition to establish a monograph for this type of OTC drug product.

References

(1) Brookler, K. H., "Evaluation of Auro-Dri in the Relief for Water-Clogged Ears," Comment No. C2, Docket No. 77N-334S, Dockets Management Branch.

(2) Letter from W. E. Gilbertson, FDA, to H. W. Gordon, Del Laboratories, coded LET5, Docket No. 77N-334S, Dockets Management Branch.

(3) Comment No. C5, Docket No. 77N-334S, Dockets Management Branch.

(4) Memorandum of meeting between representatives of Del Laboratories, Inc., and FDA, coded MM1, Docket No. 77N-334S.

5. One comment discussed the status of glycerin in a product containing 5 percent anhydrous glycerin in 95 percent isopropyl alcohol. The comment contended that glycerin was not an active ingredient, but that glycerin was the vehicle. The comment stated that the product did not make any claims for glycerin as an active ingredient and thus no further testing for the glycerin in this product was necessary. The comment stated that glycerin was miscible with both water and alcohol (Ref. 1) and, thus, glycerin was particularly appropriate for use as a vehicle in this product.

The comment pointed out that the agency had previously stated (Ref. 2):

In order to meet the requirements for a combination product, each ingredient must be tested alone and also in combination to show effectiveness for the proposed claims. However, if glycerin functions only as a vehicle (and the need for it as a vehicle is shown) and no claims are made for it as an active ingredient, additional testing would not be required for this ingredient.

The comment added that the Panel stated in its report on OTC topical otic drug products (42 FR 63556 at 63562) that "glycerin is used in topical otic products * * * as a vehicle because of its solvent properties. * * * Its viscosity makes it useful as an ingredient in both liquid and ointment forms of medication. * * * Glycerin is widely accepted as a vehicle of choice in otic products."

The agency does not have sufficient information demonstrating that

anhydrous glycerin functions only as a vehicle in this product. The anhydrous glycerin could have an active role in the product. One text states that anhydrous glycerin alone, or mixed with vinegar, will help to remove water from the ear (Ref. 3). The comment did not provide any data to show that at the 5 percent concentration present the anhydrous glycerin does not contribute to the effect of the product. In order to show that glycerin does not have an active role in the product, it needs to be shown that the product with the glycerin is not superior to 95 percent isopropyl alcohol used alone. If the combination is superior, this would show that the anhydrous glycerin contributes to the product's effectiveness. The agency believes that a four-arm study (combination, 95 percent isopropyl alcohol, anhydrous glycerin alone, and placebo, which would be no treatment) should be conducted to clarify the role of the glycerin in the product.

In addition, if the glycerin were found to act only as a vehicle, then the product would have to be labeled accordingly. The product could not continue to be labeled as 5 percent anhydrous glycerin in 95 percent isopropyl alcohol.

References

(1) "The Pharmacological Basis of Therapeutics," 6th ed., edited by L. S. Goodman, and A. G. Gilman, The McMillan Co., New York, p. 951, 1980.

(2) Letter from W. E. Gilbertson, FDA, to H. W. Gordon, Commerce Drug Co., Inc., coded LET10, Docket No. 77N-0334, Dockets Management Branch.

(3) "Handbook of Nonprescription Drugs," 10th ed., American Pharmaceutical Association, Washington, p. 400, 1993.

C. Comments on the Isopropyl Alcohol and Acetic Acid

6. One comment requested that a combination product containing 95 percent isopropyl alcohol and 3 percent acetic acid be included in the final monograph with a claim for the prevention of swimmer's ear. The comment urged the agency to consider this combination because isopropyl alcohol with anhydrous glycerin was proposed as category III for drying of water in the ears (51 FR 27366 at 27370) and 2 percent acetic acid in distilled water was category III for prevention of swimmer's ear (51 FR 27367). The comment stated that preliminary data from a study suggested that this product may be statistically significant in diminishing the frequency of otitis externa in children during the summer months. The comment concluded that a product containing 95 percent isopropyl alcohol and 3 percent acetic acid was effective in drying of excess moisture in

the ears as well as re-establishing the acid mantle in the ear canals.

As the comment noted, in the tentative final monograph, the agency placed several products in category III: (1) 2 percent acetic acid in distilled water or propylene glycol and the combination of 5 percent anhydrous glycerin and 95 percent isopropyl alcohol for the prevention of swimmer's ear, and (2) the combination of 5 percent anhydrous glycerin and 95 percent isopropyl alcohol for the drying of water in the ears or for the relief of the discomfort of water-clogged ears by drying excess water.

The comment did not submit any data on this combination, nor was this combination considered by the Panel in its report or the agency in the tentative final monograph. More data were needed on all of these products. Likewise, adequate data to demonstrate the safety and effectiveness of the comment's product are needed. Because no data were submitted to establish safety and effectiveness, the combination of 95 percent isopropyl alcohol and 3 percent acetic acid for the prevention of swimmer's ear is not being included in a monograph.

II. The Agency's Final Conclusions on OTC Topical Otic Drug Products for the Prevention of Swimmer's Ear and for the Drying of Water-Clogged Ears

At this time, there is a lack of data from adequate and well-controlled studies to establish that acetic acid, isopropyl alcohol, anhydrous glycerin, or any other ingredients are safe and effective for use as a topical otic drug product for the prevention of swimmer's ear or for the drying of water-clogged ears.

Therefore, any ingredient that is labeled, represented, or promoted for OTC use as a topical otic drug product for the prevention of swimmer's ear or for the drying of water-clogged ears is considered nonmonograph and misbranded under section 502 of the act and is a new drug under section 201(p) of the act for which an approved application under section 505 of the act 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 application. 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 the **Federal Register** of November 7, 1990 (55 FR 46914), the agency published a final rule in 21 CFR part