

excess water in the ear could impair hearing. Therefore, the drying of water-clogged ears may affect the function of the ear by reducing a loss of hearing in some individuals. Accordingly, the agency concludes that products that dry water in the ears are drugs under section 201(g) of the act.

References

(1) Letter from W. E. Gilbertson, FDA, to H. W. Gordon, Commerce Drug Co., Inc., coded LET006, Docket No. 77N-0334, Dockets Management Branch.

(2) Letter from W. E. Gilbertson, FDA, to H. W. Gordon, Commerce Drug Co., Inc., coded LET010, Docket No. 77N-0334, Dockets Management Branch.

2. One comment requested that products for drying water-clogged ears be allowed to make the claim "helps relieve swimmer's ear." The comment stated that the agency's proposed definition of "swimmer's ear" in § 344.3(e) (51 FR 27366 at 27373) was too restrictive because it included a demonstration of effectiveness against external otitis in a susceptible target population. The comment mentioned that consumers have long used the term "swimmer's ear" to refer to the retention of excess water in the ears after swimming, showering, or bathing. The comment argued that a demonstration of efficacy against external otitis should not be a prerequisite for a claim relating to "swimmer's ear."

The agency disagrees with the comment. The Panel (42 FR 63556 at 63565) defined swimmer's ear as a "diffuse external otitis," an infection of the skin lining the external auditory canal. Likewise, other medical experts (Ref. 1) define swimmer's ear as external otitis associate with swimming. Clinical symptoms include an itchy or painful, discharging ear, and a tender edematous canal filled with debris. *Pseudomonas aeruginosa* is the predominant bacterial pathogen in cases of external otitis. Successful treatment of the infection can require a combination of topical therapies, including antibiotics, steroids, drying agents, and acetic acid. If not successfully treated, swimmer's ear may lead to malignant external otitis and mastoiditis. For these reasons, the agency considers diagnosis and treatment of this infection by a physician to be necessary.

The comment did not submit any data to demonstrate that ear water-drying aid products alone "help relieve swimmer's ear." Data showing effectiveness of an ear water-drying aid product as a single agent against external otitis would be a prerequisite for a claim relating to "swimmer's ear." The agency concludes that the existing data are inadequate to

support a relief of swimmer's ear claim for any ear water-drying aid drug product.

Reference

(1) Mandell, G. L., G. Douglas, and J. E. Bennett, "Principles and Practice of Infectious Diseases," 3d ed., Churchill Livingstone, New York, pp. 1680-1681, 1990.

3. One comment requested that the proposed indications in § 344.52(b) for products for drying water-clogged ears be expanded to permit mention of the source of the water in the ears causing the problem. The comment suggested adding the following words to the indications: ("caused by" or "resulting from") "swimming, showering, or bathing."

The agency would have no problems in allowing the indications to mention the source of the water. However, this would not be required information because the proposed indications adequately describe the use of the product. The agency would allow the source of the water to appear as optional additional information that could appear at the manufacturer's choice. At this time, indications for these products will not appear in the final rule because no active ingredients are included in a monograph for this class of OTC drug products. Should a monograph be proposed in the future, the optional expanded indications will be considered.

B. Comments on Isopropyl Alcohol and Anhydrous Glycerin

4. One comment submitted a study (Ref. 1) to support the effectiveness of 5 percent anhydrous glycerin in 95 percent isopropyl alcohol for the drying of water-clogged ears. The comment stated that if FDA determines that this product is a drug, it should be classified as Category I.

The agency has reviewed the study and determined that the data are insufficient to demonstrate the effectiveness of 5 percent anhydrous glycerin in 95 percent isopropyl alcohol for the drying of water-clogged ears. This study involved 27 male or female volunteers, between 18 and 65 years of age, with a history of water-clogged ears. The subjects were in generally good health with ears free of obstructions and tympanic membranes free of any perforations. The objective of the study was to determine the effectiveness of 5 percent anhydrous glycerin in 95 percent isopropyl alcohol placed in the external auditory canal to speed up the evaporation of water. Each subject was placed in the supine position, and the ear was inspected with an operating microscope. The ear to be tested was

then filled with lukewarm water. Each subject was permitted to tilt his/her head to allow the water to run freely out of the ear onto absorbent cotton. Only those subjects with water remaining in their ears were selected. The presence of water was recorded on tape by means of an operating microscope and its television camera. Five drops of product or water, as a placebo, were then randomly instilled into the ear. The samples were coded to maintain a double-blind so that both the investigator and subjects were unaware of the material instilled. After 5 minutes, the ear was inspected under the operating microscope and the presence or absence of water was determined. The quantity of water present after treatment was recorded as "more," "same," "less," or "none." The findings were recorded on tape and the subject record form.

Because participants were selected based on a history of some problem with retaining water in the ears after exposure, it is the agency's view that it is inappropriate to use a water-only placebo in a study of the indication for relief of "water-clogged ears." In such situations, the water-only group would be expected to do worse than a group left untreated after water exposure. The agency is also concerned that the method used in the study did not specify how the head was tilted nor did it specify the time allowed for the water to run freely out of the ear onto the absorbent cotton. The position of the head and the length of time allowed for the water removal from the ear should have been specified.

The agency does not consider a study population of 27 subjects adequate to demonstrate that the results are statistically significant. Based on its statistical evaluation of the results, the comment reported that the product was effective in 22 out of 25 subjects' ears (88 percent) and that the placebo was effective in 3 out of 24 subjects' ears (12 percent), a highly significant result (Chi Square \leq 99.9 percent). However, the agency finds that a Yates correction of Chi Square should have been used for this small cell size study. A reanalysis using this correction was never provided.

While the study provides some supportive information on the product's drying effect, at least one additional well-designed confirmatory study with an adequate number of subjects is needed. Because the submitted data are inadequate to establish effectiveness for the drying of symptoms of water-clogged ears, neither anhydrous glycerin nor isopropyl alcohol is included in a monograph for this use. The agency's