**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

**21 CFR Part 344**

**[Docket No. 77N-0334]**

# Topical Otic Drug Products for Over-the-Counter Human Use; Final Monograph

**AGENCY:** Food and Drug Administration.

**ACTION:** Final rule.

**SUMMARY:** The Food and Drug Administration (FDA) is issuing a final rule in the form of a final monograph establishing conditions under which over-the-counter (OTC) topical otic drug products (drug products for the ear) are generally recognized as safe and effective and not misbranded. 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 monograph, and all new data and information on topical otic drug products that have come to the agency's attention. This final monograph is part of the ongoing review of OTC drug products conducted by FDA.

**EFFECTIVE DATE:** August 10, 1987.

**FOR FURTHER INFORMATION CONTACT:** William E. Gilbertson, Center for Drugs and Biologics (HFN-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-295-8000.

**SUPPLEMENTARY INFORMATION:** In the **Federal Register** of December 16, 1977 (42 FR 63556), 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 topical otic drug products, together with the recommendations of the Advisory Review Panel on OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Prevention Treatment Drug Products, 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 March 16, 1978. Reply comments in response to comments filed in the initial comment period could be submitted by April 14, 1978.

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 monograph, for topical otic drug products was published in the **Federal Register** of July 9, 1982 (47 FR 30012). Interested persons were invited to file by September 7, 1982, 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 November 9, 1982. New data could have been submitted until September 11, 1983. Final agency action occurs with the publication of this final monograph, which is a final rule establishing a monograph for OTC topical otic drug products.

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 is no longer using 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 data are insufficient to classify as safe and effective, and further testing is required) at the final monograph state, but is using instead the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Categories II and III).

As discussed in the proposed regulaton for OTC topical otic drug products (47 FR 30013), the agency advises that the conditions under which the drug products that are subject to this monograph will be generally recognized as safe and effective and not misbranded (monograph conditions) will be effective 12 months after the date of publication in the **Federal Register**. Therefore, on or after August 10, 1987 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 product 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 response to the proposed rule on OTC topical otic drug products, five drug manufacturers, one association for drug manufacturers, and one college of pharmacy submitted comments. Copies of comments received are on public display in the Dockets Management Branch. Any 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 monograph, the agency has considered all comments and the changes in the procedural regulations.

This final monograph applies only to earwax removal aids. Active ingredients for claims for the prevention of swimmer's ear and treatment of water-clogged ears were submitted in comments to the tentative final monograph. They were not included in the Panel's report, nor considered by the agency in the tentative final monograph on topical otic drug products. Therefore, in order to obtain public comment on these active ingredients and claims, the agency published a proposed rule to amend the tentative final monograph for OTC topical otic drug products to include drugs used for the prevention of swimmer's ear and the treatment of water-clogged ears in the **Federal Register** of July 30, 1986 (51 FR 27366).

## I. The Agency's Conclusions on the Comments

### *A. General Comments on Topical Otic Drug Products*

1. One comment contended that OTC drug monographs are interpretive, as opposed to substantive, regulations. The comment referred to statements on this issue submitted earlier to other OTC drug rulemaking proceedings.

The agency addressed this issue in paragraphs 85 through 91 of the preamble to the procedures for classification of OTC drug products, published in the **Federal Register** of May 11, 1972 (37 FR 9464) and in paragraph 3 of the preamble to the tentative final monograph for antacid drug products, published in the **Federal Register** of November 12, 1973 (38 FR 31260). FDA reaffirms the conclusions stated there. Subsequent court decisions have confirmed the agency's authority to issue substantive regulations by rulemaking. See, e.g., *National Nutritional Foods Association* v.

*Weinberger,* 512 F.2d 688, 696–98 (2d Cir. 1975) and *National Association of Pharmacetical Manufacturers* v. *FDA,* 487 F. Supp. 412 (S.D.N.Y. 1980), *Aff'd,* 637 F.2d 887 (2d Cir. 1981).

2. One comment contended that FDA does not have the authority to legislate the exact wording of OTC labeling claims to the exclusion of what the comment described as other truthful, accurate, not misleading, and intelligible labeling for the products.

During the course of the OTC drug review, the agency has maintained that the terms that may be used in an OTC drug product's labeling are limited to those terms included in a final OTC drug monograph. (This policy has become known as the "exclusivity policy.") The agency's position has been that it is necessary to limit the acceptable labeling language to that developed and approved through the OTC drug review process in order to ensure the proper and safe use of OTC drugs. The agency has never contended, however, that any list of terms developed during the course of the review exhausts all the possibilities of terms that appropriately can be used in OTC drug labeling. Suggestions for additional terms or for other labeling changes may be submitted as comments to proposed or tentative final monographs within the specified time periods or through petitions to amend monographs under § 330.10(a)(12). For example, the labeling n this final monograph has been expanded and revised in response to comments received.

During the course of the review, FDA's position on the "exclusivity policy" has been questioned many times in comments and objections filed in response to particular proceedings and in correspondence with the agency. The agency has also been asked by The Proprietary Association to reconsider its position. In a notice published in the **Federal Register** of July 2, 1982 (47 FR 29002), FDA announced that a hearing would be held to assist the agency in resolving this issue. On September 29, 1982, FDA conducted an open public forum at which interested parties presented their views. The forum was a legislative type administrative hearing under 21 CFR Part 15 that was held in response to a request for a hearing on the tentative final monographs for nighttime sleep-aides and stimulants (published in the **Federal Register** of June 13, 1978; 43 FR 25544).

After considering the testimony presented at the hearing and the written comments submitted to the record, in the **Federal Register** of April 22, 1985 (50 FR 15810), FDA proposed to change its exclusivity policy for the labeling of OTC drug products. In the **Federal Register** of May 1, 1986 (51 FR 16258), the agency published a final rule changing the exclusivity policy and establishing three alternatives for stating the indications for use in OTC drug labeling. Under the final rule, 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 required OTC drug labeling other than indications for use (e.g., statement of identity, warnings, and directions) must appear in the specific wording established under an OTC drug monograph.

In the tentative final monograph (47 FR 30020), supplemental language relating to indications had been proposed and captioned as *Other Allowable Statements.* Under FDA's revised exclusivity policy (51 FR 16258), such statements are included at the tentative final stage as examples of other truthful and nonmisleading language that would be allowed elsewhere in the labeling without prior FDA review. In accordance with the revised exclusivity policy, such statements would not be included in a final monograph. However, the agency has decided that, because these additional terms have been reviewed by FDA, they should be incorporated, wherever possible, in final OTC drug monographs under the heading "Indications" as part of the indications developed under that monograph.

3. One comment from a small manufacturer stated that the 12-month period of time provided for manufacturers to comply with the final monograph is too restrictive. The company requested that this time period be expanded to 18 months or at least long enough to use existing supplies of cartons and labels. The company explained that to keep costs as low as possible, labels are ordered in large quantities that will provide an 18-month supply. Consequently, meeting the present 12-month requirement could result in the manufacturer having a surplus of unusable labels. The company argued that the cost of unusable labels could increase company costs, thus increasing the cost of the product to the consumer and possibly adversely affecting sales of the product.

In some advance notices of proposed rulemaking previously published in the OTC drug review, the agency suggested a 6-month effective date for monograph conditions. However, as explained in the tentative final monograph (proposed rule) for OTC topical otic drug products (47 FR 30012), the agency concluded that, generally, it is more reasonable to have a final monograph be effective 12 months after the date of its publication in the **Federal Register.** The agency believes that this period of time should enable most manufacturers to reformulate, relabel, or take other steps necessary to comply with a new monograph with a minimum disruption of the marketplace, thereby reducing economic loss and ensuring that consumers have continued access to safe and effective OTC drug products. However, in an assessment of the economic impacts of the OTC drug review, the agency concluded that although the OTC drug review was not a major rule as defined in Executive Order 12291, significantly large impacts might be experienced by some small firms in some years (Ref. 1).

Nevertheless, FDA has a statutory mandate to assure that OTC drug products are safe and effective for their intended use and are properly labeled. The statute does not allow FDA to waive these important public health considerations even though additional costs may be incurred by a manufacturer in order to achieve compliance with a monograph.

Reference

(1) "Assessment of the Economic Impacts of the OTC Drug Review Process," Docket No. 82N–0143, Dockets Management Branch.

4. One comment questioned the meaning of the word "effective." The comment asked FDA to consider whether consumer acceptance and usage of a product, without the use of coercive advertising, indicates some effectiveness of the product. The comment stated that some drugs are more effective than others and questioned whether this means that the less effective drugs are considered as being not effective at all.

As defined in § 330.10(a)(4)(ii), effectiveness means a reasonable expectation that, in a significant proportion of the target population, the pharmacological effect of the drug, when

used under adequate directions for use and warnings against unsafe use, will provide clinically significant relief of the type claimed. The regulation provides that reports of significant human experience during marketing may be used to corroborate controlled clinical investigations and other studies, in order to establish general recognition of the effectiveness of a drug. However, isolated case reports, random experience, and reports lacking the details that permit scientific evaluation are not considered. Without more substantive data, mere consumer acceptance and usage of a product is not enough to constitute proof of effectiveness.

With regard to the comment's inquiry concerning "less effective drugs," the agency does not consider the comparative efficacy of a drug in determining general recognition of effectiveness; it only considers that the drug has been shown to be effective based on the standards discussed above.

*B. Comments on Topical Otic Drug Ingredients*

5. One manufacturer expressed concern about the agency's decision to reclassify glycerin as an earwax removal aid from Category I to Category III "so that studies may be performed to establish effectiveness." The manufacturer stated that in response to the advance notice of proposed rulemaking on OTC topical otic drugs, it reformulated its earwax product to contain only glycerin as an active ingredient. The propylene gylcol in the product was removed. However, the comment asserted that because of the reclassification of glycerin to Category III, the expensive process of reformulation and relabeling will have to be repeated. The comment maintained that it is unfair and costly for the agency to urge manufacturers to comply with advance proposals and then change the Panel's recommendation.

Since the beginning of the OTC drug review, the agency has stated that a panel's findings are prepared independently of FDA and do not necessarily reflect the agency's position. Although the agency encourages manufacturers to comply voluntarily with a panel's recommendations in formulating and labeling their products prior to the effective date of a final monograph, manufacturers are at risk because a panel's recommendation may be accepted, rejected, or modified by the agency in the tentative final and final monographs. This concept was discussed in the preamble to each Panel's report including the report on OTC otic drug products. (See, e.g., 42 FR 63556.) The agency does not modify a panel's recommendations arbitrarily. Before making any change, the agency carefully considers all relevant data and information.

The agency reclassified glycerin as an earwax removal aid from Category I to Category III in the tentative final monograph because there were no well-controlled studies that demonstrated effectiveness. The only published effectiveness study cited by the Panel (42 FR 63562) was an in vitro study that showed that glycerin had no effect on earwax after 60 minutes and caused only surface softening of earwax after 24 hours (47 FR 30014). Therefore, there was no basis for the agency to accept the Panel's Category I classification of glycerin as an earwax removal aid. In addition, because no data were submitted after publication of the tentative final monograph to establish the effectiveness of glycerin as an earwax removal aid, it is not being included in this final monograph.

This final monograph is effective 12 months after the date of publication in the **Federal Register**. Thus, manufacturers will have a reasonable period of time to reformulate and relabel currently marketed products to comply with the monograph.

*C. Comments on Labeling of Topical Otic Drug Products*

6. Two comments disagreed with the agency's proposed substitution of the word "doctor" for "physician" in OTC drug labeling. One comment stated that because "physician" is a term that is recognized by people of all ages and social and economic levels, there is no need for the change, which would be costly and provide no benefit. The comment further contended that physician is a more accurate term, whereas "doctor" is a broad term that could confuse and mislead the lay person into taking advice on medication from persons other than medical doctors, such as optometrists, podiatrists, and chiropractors. The other comment favored the use of easily understood language in labeling, but noted that both "doctor" and "physician" are accurate and meaningful and argued that the use of either term should be allowed.

The agency recognizes that the term "doctor" is not a precise synonym for the word "physician," but believes that the terms are frequently used interchangeably by consumers and that the word "doctor" is likely to be more commonly used and better understood by consumers. 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." Based on comments submitted following publication of these tentative final monographs, the agency has determined that final monographs will give manufacturers the option of using either the word "physician" or the word "doctor." This final monograph includes that option.

7. One comment suggested that, in the interest of consumer education, the warning, "Never use instruments such as cotton swabs, toothpicks, or hairpins to remove wax from ear canal" be required. To preclude the use of unsafe instruments to remove the earwax softened by carbamide peroxide, the comment also suggested that the phrase "the only medically approved way for safely removing earwax" be permitted in the labeling of carbamide peroxide that is packaged with a rubber bulb ear syringe for the purpose of flushing the ear.

The comment submitted no data in support of its request. Based on data and information that are available, the agency concludes that the warnings proposed in the tentative final monograph adequately inform consumers how to use these products safely and that it is unnecessary to require the comment's suggested warning in the labeling of topical otic drug products. However, as long as the required warning appears on the product's label, the agency has no objection to the information described in the comment also appearing in some other portion of the label. Such information may not appear in any portion of the labeling that is required by the monograph.

The phrase "the only medically approved way for safely removing earwax" is not being included in the monograph for use in labeling unit packages containing carbamide peroxide and a rubber bulb ear syringe. By appearing on such packages, the phrase would imply that a rubber bulb ear syringe used in conjunction with carbamide peroxide constitutes the only medically approved way of safely removing earwax. In fact, carbamide peroxide alone may safely remove earwax.

The agency stated in the tentative final monograph that the use of an irrigation syringe in the ear should be limited as much as possible (47 FR 30018). The directions in § 344.50(d) for using a rubber bulb ear syringe are include in the monograph only to assist in the removal of any earwax that may

remain after 4 days of treatment with carbamide peroxide. The agency therefore objects to any labeling that might infer that a rubber bulb ear syringe must be used to remove earwax safely.

8. Two comments suggested that the warning in § 344.50(c)(3) that states "Do not use for more than 4 days; if excessive earwax remains after use of this product, consult a doctor" be revised because it does not indicate clearly that the 4-day limitation applies to each episode of excessive earwax. One comment pointed out that many individuals are subject to chronic accumulation of earwax and will, accordingly, use these products routinely for recurring accumulation. Therefore, the comments suggested that the warning be revised by adding a phrase such as "for each occurrence of accumulated earwax" or "during any episode" to make it clearer to the user that the 4-day limitation applies to each episode of excessive earwax.

The agency believes that the present warning in § 344.50(c)(3), concerning the limitation of use for not more than 4 days, in conjunction with the directions for use in § 344.50(d), which instruct consumers to use the product twice daily for up to 4 days, is adequate to inform consumers that the 4-day limitation applies to each episode of excessive earwax accumulation. The labeling of many OCT drug products contains limitations on the number of days that the product should be used, and the agency believes that it is reasonable to expect that consumers will understand that the 4-day limitation applies to each episode of excessive earwax.

9. One comment stated that anhydrous glycerin can cause a painful, burning sensation in the eyes, and suggested that the labeling instructions should anticipate accidental contact. The comment recommended that the proposed warning in § 344.50(c)(4) "Avoid contact with the eyes," be expanded by adding the following sentences: "If accidental contact occurs, wash eye with water. Consult physician if pain or irritation persists."

The agency concludes that it is not necessary to expand the warning in § 344.50(c)(4) because glycerin does not cause any serious effects. Although anhydrous glycerin can cause irritation and stinging of the eyes, anhydrous glycerin has accepted medical usage as an agent to facilitate ophthalmoscopic examination and to reduce corneal edema (Refs. 1, 2, and 3). Accordingly, the agency is not expanding the warning in the monograph as suggested by the comment. As long as the required warning appears on the products's label, the agency has no objection to the statements described in the comment also appearing in some other portion of the label.

Such information may not appear in any portion of the labeling that is required by the monograph.

References

(1) Smith, M. B., "Ocular Toxicity," Publishing Sciences Group, Acton, MA, p. 54, 1976.

(2) "AMA Drug Evaluations—1983," 5th Ed., American Medical Association, Chicago, IL, pp. 506–507, 1983.

(3) Gennaro, A., editor, "Remington's Pharmaceutical Sciences," 17th Ed., Mack Publishing Co., Easton, PA, p. 1308, 1985.

10. One comment stated that the directions for use of an ear syringe could be more instructive to the user and suggested that the directions in § 344.50(d) be worded as follows: "Any wax remaining after treatment should be removed once a day by gently flushing the ear with warm (body temperature) water, using a soft rubber bulb ear syringe. Place tip of washer at outer edge of ear canal."

The agency believes that the directions as proposed in the tentative final monograph are sufficient for OTC use of earwax removal aids. The agency does not agree with the comment's wording "Any wax remaining after treatment should be removed once a day . . ." because such information is misleading and implies that the ear syringe should be used each day after the treatment, whereas the ear syringe should only be used after treatment is completed if there is still wax remaining in the ear after 4 days of treatment.

In addition, the agency believes that the term "warm water" is understood by consumers and that it is not necessary to require in the monograph that the term "(body temperature)" be added to the directions. Manufacturers may, however, add terms such as "(body temperature)" to the directions of products if they believe that they enhance consumer understanding. They may also add additional information in the directions regarding the proper use of the bulb ear syringe, such as suggested by the comment, provided that the information is true and not misleading. Therefore, the agency's proposed directions in § 344.50(d) will be included in the final monograph without revision.

11. Three comments objected to the directions statement in § 344.50(d), "Children under 12 years of age: consult a doctor." The comments contended that the agency's basis for this age restriction, i.e., that the studies submitted in support of the use of carbamide peroxide in children were supervised by a physician (47 FR 30017), is not valid. The comments stated that all clinical studies are professionally supervised and that these studies were conducted under the supervision of a physician not because of safety concerns, but to assure that they were conducted under controlled conditions to support efficacy and to monitor any side effects that might occur. The comments contended that the studies demonstrate that earwax removal aid products can be safely used in children 2 to under 12 years of age.

One of the comments stated that restricting the use of carbamide peroxide in children under 12 years of age will force consumers to use primitive methods for removal of earwax in this age group. Another comment from a manufacturer stated that the Panel's and the agency's concerns that parents would unnecessarily use earwax removal aids to routinely clean the ears of their children are unfounded. The manufacturer explained that there is a target population of individuals who chronically accumulate earwax and who would derive benefit from cleaning the ears to prevent irritation and potential subsequent infection. The manufacturer submitted a summary of the results of a 1980 opinion poll which indicated that, in 5 percent of the surveyed families, earwax buildup occurred in children 12 years of age or under (Ref. 1). The manufacturer also stated that in the past 18 months it had received only one product-related report associated with the use of its earwax removal aid product in children per 2 million bottles sold and argued that "such a rate of reported occurrence does not indicate a need to restrict the use of the drug to adults and children 12 and over."

In the tentative final monograph for topical otic drug products, the agency stated that an earwax removal aid should not be used in children unless a physician has made a determination that there is a need to use such a product (47 FR 30017). This was based on the fact that earwax is derived from the watery secretions of the apocrine glands and the oily secretions of the sebaceous glands (Ref. 2) and on the fact that the apocrine glands are not active until puberty (42 FR 63558). Thus, these directions were proposed because excessive earwax is less likely to occur in children under 12 years of age, not because physicians had supervised the clinical studies and examined the ears of children as alleged by the comment.

The agency recognizes that some children under 12 years of age may have excessive earwax accumulation as indicated by the submitted opinion poll (Ref. 1). However, in cases where children under 12 years of age are suspected of having excessive earwax accumulation, a physician should be consulted to make a professional diagnosis and to recommend the proper treatment. A physician's diagnosis is particularly important in children under 12 years of age because young children may not often exhibit symptoms of serious ear problems or are unable to describe the symptoms of abnormal conditions to their parents. For example, the symptoms of otitis media (an inflammatory condition of the middle ear that occurs most often during childhood) include pain, hearing loss, and fever. However, in chronic serous otitis media there is impaired hearing, but the child may not have acute symptoms and pain is usually absent (Ref. 2). Such ear disorders would be difficult for parents to distinguish from excessive earwax. These ear disorders are serious and can result in hearing loss if untreated. Therefore, it is especially important for a physician to determine the appropriate treatment for the child's condition. The physician may recommend use of an OTC earwax removal aid if it is appropriate.

The agency does not believe that advising consultation with a doctor for children under 12 years of age, in the labeling of earwax removal aids, would force consumers to use primitive methods to remove excessive earwax in children in this age group. On the contrary, this direction should alert consumers to consult a physician before routinely cleaning the ears of children with an earwax removal aid, which might not be necessary and might delay needed medical attention. The direction thus promotes better ear care. Therefore, the agency is including in § 344.50(d) of this final monograph a direction restricting the use of an earwax removal aid to adults and children over 12 years of age.

References

(1) Comment No. C00009, Docket No. 77N-0334, Dockets Management Branch.

(2) Miller, K. O., "Otic Products," *in* "Handbook of Nonprescription Drugs," 7th Ed., American Pharmaceutical Association, Washington, pp. 402–403 and 406–408, 1982.

12. One comment disagreed with the proposed directions statement in § 344.50(d) for earwax removal aids that reads "Children under 12 years of age: consult a doctor." The comment suggested that the statement be revised to read: "Children under 12 should be supervised in the use of this product. For children under 2, there is no recommended dosage except under the advice and supervision of a doctor."

The agency does not agree with the comment's suggested revision. As stated in comment 11 above, earwax removal aids should not be used in children under 12 years of age except as recommended by a physician. If a physician recommends that an earwax removal aid be used in a child under 12 years of age, the agency expects that the child would be supervised in the use of the product.

## II. Summary of Significant Change From the Proposed Rule

In accord with the revised "exclusivity" policy, the agency is amending § 344.50(b) under the heading "Indications" to include some of the supplemental language that was previously included in the "Other Allowable Statements" section of the tentative final monograph (see comment 2 above). The resulting indication which includes the additional optional terms "soften" and "loosen" reads as follows: "For occasional use as an aid to" (which may be followed by: "soften, loosen, and") "remove excessive wax."

## III. The Agency's Final Conclusions on OTC Topical OTIC Drug Products

Based on the available evidence, the agency is issuing a final monograph establishing conditions under which OTC topical otic drug products are generally recognized as safe and effective and not misbranded. Specifically, the agency has determined that the only ingredient that has been determined to be monograph condition is carbamide peroxide 6.5 percent formulated in an anhydrous glycerin vehicle. Glycerin, antipyrine, and benzocaine, which were also considered in this rulemaking, have been determined to be nonmonograph ingredients. All other ingredients are considered nonmonograph ingredients. Any drug product marketed for use as an OTC topical otic drug that is not in conformance with the monograph (21 CFR Part 344) will be considered a new drug within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)) and misbranded under section 502(a) of the act (21 U.S.C. 352(a)) and may not be marketed for this use unless it is the subject of an approved NDA.

No comments were received in response to the agency's request for specific comment on the economic impact of this rulemaking (47 FR 30019). 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 topical otic 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 topical otic 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.

### List of Subjects in 21 CFR Part 344

OTC drugs, Topical otic drug products.

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 by adding new Part 344, to read as follows:

## PART 344—TOPICAL OTIC DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

### Subpart A—General Provisions

Sec.



### Subpart B—Active Ingredients



### Subpart C—Labeling



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 5.11.

## Subpart A—General Provisions

### § 344.1 Scope.

(a) An over-the-counter topical otic drug product in a form suitable for topical administration is generally recognized as safe and effective and is not misbranded if it meets each of the conditions in this part in addition to each of the general conditions established in § 330.1.

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

### § 344.3 Definitions.

As used in this part:

(a) *Anhydrous glycerin.* An ingredient that may be prepared by heating glycerin U.S.P. at 150° C for 2 hours to drive off the moisture content.

(b) *Earwax removal aid.* A drug used in the external ear canal that aids in the removal of excessive earwax.

## Subpart B—Active Ingredients

### § 344.10 Topical otic active ingredient.

The active ingredient of the product consists of carbamide peroxide 6.5 percent formulated in an anhydrous glycerin vehicle.

## Subpart C—Labeling

### § 344.50 Labeling of topical otic 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 an "earwax removal aid."

(b) *Indication.* The labeling of the product states, under the heading "Indication," the following: "For occasional use as an aid to" (which may be followed by: "soften, loosen, and") "remove excessive earwax." Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed above, may also be used, as provided in § 330.1(c)(2), 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 of 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) "Do not use if you have ear drainage or discharge, ear pain, irritation, or rash in the ear or are dizzy; consult a doctor."

(2) "Do not use if you have an injury or perforation (hole) of the ear drum or after ear surgery unless directed by a doctor."

(3) "Do not use for more than 4 days; if excessive earwax remains after use of this product, consult a doctor."

(4) "Avoid contact with the eyes."

(d) *Directions.* The labeling of the product contains the following statement under the heading "Directions": FOR USE IN THE EAR ONLY. Adults and children over 12 years of age: tilt head sideways and place 5 to 10 drops into ear. Tip of applicator should not enter ear canal. Keep drops in ear for several minutes by keeping head tilted or placing cotton in the ear. Use twice daily for up to 4 days if needed, or as directed by a doctor. Any wax remaining after treatment may be removed by gently flushing the ear with warm water, using a soft rubber bulb ear syringe. Children under 12 years of age: consult a doctor.

(e) *Optional wording.* The word "physician" may be substituted for the word "doctor" in any of the labeling statements in this section.

Dated: May 3, 1986.

Frank E. Young,

*Commissioner of Food and Drugs.*

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