21 CFR Part 330

[Docket No. 79N-0365]

Over-the-Counter (OTC) Category III Policy Intent To Revise Rule

AGENCY: Food and Drug Administration.

ACTION: Notice of intent to revise rule.

SUMMARY: The Food and Drug Administration intends to revise the procedural regulations governing the review and classification of over-the-counter (OTC) drug products to delete the term "Category III" and the provision that authorizes the marketing of a Category III condition in an OTC drug product after a final monograph. This notice is being issued to alert manufacturers of drug products with ingredients and claims recommended as Category III by an OTC Drug Advisory Review Panel or by the agency in a tentative final order that the agency will revise its regulations and procedures to conform to a recent court order.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Bureau of Drugs (HFD-510), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4960.

SUPPLEMENTARY INFORMATION: The Food and Drug Administration (FDA) intends to publish in the **Federal Register** in the near future proposed revisions to the OTC procedural regulations (21 CFR 330.10) to delete the term "Category III" and the provision that authorizes marketing of a Category III condition in an OTC drug product after a final monograph is established. This notice is being issued to alert manufacturers of drug products containing Category III conditions that FDA will revise its regulations to conform to the holding and order of the United States District Court for the District of Columbia in *Cutler* v. *Kennedy*, C.A. No. 77-0734 (D.D.C., July 16, 1979). This revision will affect the time period during which testing may be completed and new data submitted to FDA to support the inclusion in a final monograph of those conditions not classified in Category I in a proposed monograph or tentative final monograph.

Current Procedure

The OTC drug review was instituted to carry out FDA's statutory mandate to assure that OTC drugs are safe and effective for their intended use and not misbranded. The current approach involves the development of drug "monographs," in the form of regulations, which define conditions under which OTC drugs are generally recognized as safe and effective and not misbranded. Monographs list both acceptable ingredients and proper labeling for each of the different categories of OTC drugs. The procedures by which the monographs are developed involve several administrative steps, as set forth in 21 CFR 330.10. Advisory review panels comprised of scientific experts from outside the agency were appointed by FDA to review published and unpublished data and information, which the agency requested interested persons to submit, that is pertinent to a designated category of OTC drugs. Each panel also includes two nonvoting liaison members, a representative of consumer interests and a representative of industry. Each panel reviews the data submitted to it, and prepares a report containing its conclusions and recommendations to the Commissioner of Food and Drugs with respect to the safety and effectiveness of ingredients and labeling in a designated category of drug products. Each panel report may include a recommended monograph establishing conditions under which the drugs involved are generally recognized as safe and effective and not misbranded (Category I). In addition, each panel report includes a statement of all active ingredients, labeling claims or other statements, or other conditions reviewed and excluded from the monograph on the basis of the panel's determination that they would result in a drug not being generally recognized as safe and effective or would result in misbranding (Category II) and a statement of all such conditions reviewed and excluded from the monograph on the basis of the panel's determination that the available data are insufficient to classify such condition as Category I or Category II and for which further testing is required (Category III). FDA publishes the panel reports in the **Federal Register** and requests interested persons to comment. Additionally, because new data may be submitted in those comments, the OTC drug procedural regulations allow an additional 30 days after the comment period for the filing of reply comments. After considering these comments and reply comments, the agency publishes a tentative final order, proposing a monograph in the form of a regulation, which is subject to public objections and requests for a hearing. If the Commissioner finds reasonable grounds for so doing, an oral hearing before the Commissioner is scheduled. At the conclusion of these procedures, the agency publishes an order promulgating a final monograph. After publication of a final monograph, any product with a Category III condition may remain on the market or may be introduced into the market, provided FDA receives notification that studies will be undertaken to obtain the data necessary to resolve the issues that resulted in such classification. In promulgating the OTC drug procedural regulations, the agency concluded that Category III testing should not be required until after completion of the established OTC drug administrative procedures. Opportunity for public review and comment is provided at each stage of the administrative procedure, and the content of Category III and the testing period provided is thus not fixed until publication of the final monograph. Some manufacturers have, however, voluntarily begun the testing of Category III conditions prior to issuance of a final OTC drug monograph.

Court Opinion

On July 16, 1979, the United States District Court for the District of Columbia entered its opinion in the case of *Cutler* v. *Kennedy*, C.A. No. 77-0734 (D.D.C., July 16, 1979). Plaintiffs had alleged that 21 CFR 330.10 is unlawful to the extent that it authorizes the marketing of Category III drugs after publication of a final monograph. Plaintiffs claimed that, if a drug is determined to be in Category III, it necessarily lacks substantial evidence of safety or effectiveness, is a new drug, and cannot be marketed without an approved NDA. The Court concluded that "* * * the FDA may not lawfully maintain Category III in any form in which drugs with Category III conditions * * * are exempted from enforcement action," (*Cutler, supra*, slip op. at 38). The Court issued an order that declared the OTC drug regulations, 21 CFR 330.10, unlawful to the extent that they authorize the marketing of Category III drugs after a final monograph, and enjoined the FDA from implementing any portion of the regulations that authorizes such marketing. A copy of the memorandum opinion has been placed on display in the office of the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857.

The agency notes that an OTC advisory panel's use of the Category III classification to denote a certain quantum of evidence during the pendancy of the rulemking proceeding was not the subject of the court's decision. The challenge and court opinion were directed only toward the regulatory provision permitting marketing of a drug product containing a

Category III condition after publication of a final monograph.

Intent To Propose New Procedures

To carry out the court order, the agency intends to revise 21 CFR 330.10 to delete the provision permitting the marketing of Category III conditions in OTC drug products after a final monograph has been issued. Any data available to resolve the safety or effectiveness issues that resulted in a Category III classification will have to be submitted to FDA during the OTC drug administrative procedure, that is, before the establishment of a final monograph. The OTC drug review process itself provides extensive and adequate time for manufacturers to conduct studies and obtain the data necessary to resolve the issues that resulted in a Category III classification. Manufacturers interested in upgrading Category III conditions may wish to use the findings in a panel's report as a basis on which to plan and initiate the necessary studies. Past experience has shown that FDA has rarely disagreed with a panel's recommendation and upgraded a Category II or III condition without submission of additional data by a manufacturer. In the future, the agency will consider, in publishing a final monograph, only data submitted during the rulemaking period before the closing of the comment period for the tentative final monograph. Data submitted after the closing of the comment period for the tentative final monograph will be considered as a petition to amend the monograph and will be reviewed only after the final monograph is published in the **Federal Register**. The agency will meet with industry representatives at their request to advise them on the adequacy of their proposed protocols. FDA continues to encourages firms to cooperate and work with each other in arranging for the necessary study or studies to avoid unnecessary and repetitive human testing.

Although the court in *Cutler* did not object to use of the term "Cateogory III" during the course of the OTC drug review prior to publication of a final monograph, FDA intends to propose deleting the term wherever it appears in § 330.10. However, the agency believes it imporant that manufacturers know the distinction between the kind of safety or effectiveness issue that resulted in a Category I or II classification and that as to which the panel had insufficient data to make such a classification. In the latter case, the panel and the agency believe that further testing may upgrade the condition in question to Category I. Therefore, the agency intends to propose new language in the OTC regulations that will denote this distinction in the state of the evidence regarding a condition's classification during the rulemaking proceeding. The agency wants to make it clear that it intends to delete the term "Category III" from all future published tentative and final orders.

Under the revised procedure, any drug product that fails to conform to an applicable monograph after its effective date would be liable to regulatory action.

Elsewhere in this **Federal Register**, the agency is publishing notices to reopen the administrative record for three groups of drug products for which tentative final monographs with Category III conditions have been published. This is being done to permit manufacturers to submit new data prior to a final monograph demonstrating the safety and effectiveness of those conditions not classified as Category I.

Dated: October 19, 1979.

Sherwin Gardner,

Acting Commissioner of Food and Drugs.

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21 CFR Part 333

[Docket No. 75N-0183]

Topical Antimicrobial Products for Over-the-Counter Human Use; Reopening of the Administrative Record

AGENCY: Food and Drug Administration.

ACTION: Reopening of Administrative Record.

SUMMARY: The Food and Drug Administration is reopening the administrative record to permit interested persons to submit further data on those conditions classified in Category II or Category III in the published tentative final monograph establishing conditions for the safety, effectiveness, and labeling of over-the-counter (OTC) topical antimicrobial drug products for human use.

DATES: New data by March 26, 1980. Comments by May 27, 1980.

ADDRESS: Written data and comments to the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Bureau of Drugs (HFD-510), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4960.

SUPPLEMENTARY INFORMATION: The Food and Drug Administration (FDA) published a tentative final order on OTC topical antimicrobial drug products for human use on January 6, 1978 (43 FR 1210). Interested persons could have filed written objections and requested an oral hearing before the Commissioner of Food and Drugs by February 6, 1978. The tentative final order contained a tentative final monograph and a discussion of those conditions classified by the panel in Categories II and III. Under current procedures, a drug product with a Category III condition may remain on the market or may be introduced into the market, after the publication of a final monograph, provided FDA receives notification that studies will be undertaken to obtain the data necessary to resolve the issues that resulted in such classification.

Elsewhere in this issue of the **Federal Register**, FDA is publishing a notice of intent to revise the OTC drug procedural regulations in 21 CFR 330.10 to delete the term "Category III" and the provision that authorizes the marketing of an OTC drug product with a Category III condition after a final monograph is established. This action is being taken pursuant to an order of the United States District Court for the District of Columbia in *Cutler* v. *Kennedy*, C.A. No. 770734 (D.D.C., July 16, 1979). The Court concluded that "* * * the FDA may not lawfully maintain Category III in any form in which drugs with Category III conditions * * * are exempted from enforcement action," (*Cutler, supra*, slip op. at 38). The Court issued an order that declared the OTC drug regulations, 21 CFR 330.10, unlawful to the extent that they authorize the marketing of Category III drugs after a final monograph, and enjoined FDA from implementing any portion of the regulations which authorizes such marketing.

Under current procedures, the administrative record closes at the end of the comment period following publication of the panel's report and proposed monograph. Manufacturers wishing to submit data after that time may do so only if they file a petition to reopen the administrative record in accordance with 21 CFR 330.10(a)(10)(ii). Consistent with the court order and in order to simplify the procedures and permit the results of testing to be submitted to FDA as expeditiously as possible, the agency is reopening the administrative record for this category of products for a 5-month period from October 26, 1979 to March 26, 1980 to permit manufacturers to submit, prior to the establishment of a final monograph,