
CENTER FOR DRUG EVALUATION AND RESEARCH

Guidance for Industry

*The FDA published Good Guidance Practices in February 1997.
This guidance was developed and issued prior to that date.*

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, FOOD AND DRUG ADMINISTRATION

CHAPTER 32b - DRUGS - MISBRANDING

SUBJECT: OTC Drugs - General Provisions and Administrative Procedures for
Marketing Combination Products

BACKGROUND

The enforcement policy expressed in this document concerns the marketing of OTC drug products containing combinations of ingredients.

POLICY

An OTC drug listed in subchapter 21 CFR 330 is generally recognized as safe and effective and is not misbranded if it meets each of the conditions of 21 CFR 330.1 and each of the conditions contained in the specific final monograph(s). Following the establishment of a final monograph, any OTC drug that is subject to the conditions of a final monograph and fails to meet the requirements of that monograph and 21 CFR 330.1 will be regarded as misbranded (section 502 FD&C Act) and/or a new drug requiring an approved NDA before it can be marketed (section 505 FD&C Act).

In general, prior to final publication of a proposed monograph it is not appropriate to pursue regulatory action unless directed by headquarters.

REGULATORY ACTION GUIDANCE

1. Products Under the OTC Review - OTC drugs subject to a final monograph should be submitted for regulatory action consideration under sections 502 and 505 of the FD&C Act, only as the appropriate compliance program or program circular instructs.

OTC drug combinations that were commercially marketed in the United States on or before May 11, 1972, and that are not subject to a final monograph should not be sampled for regulatory action consideration on the basis of suspected labeling deficiencies unless there is a reasonable basis to conclude that the deficiency constitutes a potential hazard to health. Examples include: (1) documented consumer injuries; (2) drugs requiring the prescription legend marketed as OTC; and (3) unwarranted claims for the treatment of serious disease conditions which could preclude obtaining proper medical attention (see CPG 7132b.15).

2. OTC combination drug products not marketed on or before May 11, 1972, are subject to the following policy:

DATE 05/01/84

ISSUING OFFICE:

EDRO, Compliance Guidelines Branch, DFRG

AUTHORITY:

Associate Commissioner for Regulatory Affairs

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- A. Interim Marketing Permitted (at risk) - Marketing of a combination product not marketed on or before May 11, 1972, may begin if all of the following conditions are met:
- (i) Each of the active ingredients in the combination has been commercially marketed in the United States on or before May 11, 1972, and is subject to the OTC Drug Review;
 - (ii) Each of the active ingredients in the combination product has been classified by an OTC advisory review panel in Category I (generally recognized as safe and effective and not misbranded) in a published advance notice of proposed rulemaking;
 - (iii) The combination of ingredients has been classified by an OTC advisory review panel in Category I in a published advance notice of proposed rulemaking; and
 - (iv) The agency has not dissented from these panel recommendations.

Marketing of such a combination product must be in complete accord with all specifications in the advance notice of proposed rulemaking. In addition, such marketing is subject to the risk that the agency may subsequently adopt a different position that may require relabeling, recall, or other regulatory action. The Commissioner may state such position at any time by notice in the Federal Register, either separately or as part of another document; appropriate regulatory action may commence immediately and is not dependent on the publication of a final monograph.

- B. Interim Marketing Not Permitted (pending subsequent notice) - A combination product not marketed on or before May 11, 1972, is considered a new drug and/or misbranded and is subject to regulatory action if any one of the following applies:
- (i) A panel has recommended in a published advance notice of proposed rulemaking that the combination of ingredients or categories of ingredients be classified in Category I, and the agency has dissented from this recommendation;
 - (ii) A panel has recommended that the combination be classified as Category II (not generally recognized as safe and effective or misbranded) or Category III (available data insufficient to classify as either Category I or Category II);
 - (iii) A panel has recommended that one of the active ingredients in the combination be classified as Category II or Category III;
or

(iv) No OTC advisory review panel has considered the combination.

Any such combination product may be marketed only after (1) the Center for Drugs and Biologics or the Commissioner tentatively determines that the ingredients and the combination are generally recognized as safe and effective and the Commissioner states by notice in the Federal Register (separately or as part of another document) that marketing of the combination under specified conditions will be permitted; (2) the Commissioner determines that the combination is generally recognized as safe and effective and the combination is included in a published OTC drug final monograph; or (3) a new drug application for the product has been approved.

If no panel has considered the combination, the agency may propose to include the combination in a final monograph, but will allow a period for public comment. Ordinarily, such a proposal would not be made as a separate notice, but would be included at the next appropriate stage in the OTC Review rulemaking. Before marketing may begin, the comment period must have ended and a Federal Register notice must have been published setting forth the agency's determination concerning interim marketing.