

CHAPTER 61 - OTC DRUG EVALUATION

SUBJECT: OTC DRUG MONOGRAPH IMPLEMENTATION	IMPLEMENTATION DATE June 1, 2007
	COMPLETION DATE June 1, 2012
DATA REPORTING	
PRODUCT CODES	PRODUCT/ASSIGNMENT CODES
Use appropriate product coding for product/operation	61003

FIELD REPORTING REQUIREMENTS:

Submit to CDER, Office of Compliance (HFD-300), recommendations for regulatory action concerning OTC drugs that are suspected to be marketed in violation of final over-the-counter (OTC) Drug Monographs. Submit copies of enforcement-related correspondence (e.g., warning letters and untitled letters) issued and the firms' responses to the Division of New Drugs and Labeling Compliance (DNDLC) as soon as the documents are issued/received.

PART I - BACKGROUND

Because so few OTC drugs are the subject of new drug applications (NDAs), in 1972, FDA decided to review all OTC drugs for both safety and efficacy. A review on a drug-by-drug basis would have been impractical since there are an estimated 250,000 OTC drugs on the market. Therefore, FDA announced that the OTC Drug Review would occur on an ingredient and therapeutic-category basis. To accomplish this, FDA convened special review panels. The review procedure for drug products studied by these panels is set forth in 21 CFR Part 330.

Upon review of the recommendations made by the subject panel, FDA publishes a Federal Register announcement containing the Proposed Monograph (i.e., an Advanced Notice of Proposed Rule). After a period of review and comment, the agency then publishes a Tentative Final Monograph (Proposed Rule). Finally, after an additional review and comment period, the agency publishes a Final Monograph (Final Rule). The Final Monograph concerns general recognition of safety and efficacy for the class of OTC drugs that it covers. OTC drugs that deviate from a final monograph are not generally recognized as safe and effective and require approved applications before they can be marketed. But OTC drugs that comply with a Final Monograph do not need approved applications. During the development of the OTC Drug Review, the following categories were established:

Category I

Ingredients and claims that comply with the final monograph in all respects, i.e., those that are generally recognized as safe and effective and not misbranded.

Category II

Ingredients and claims that violate a final monograph. Products containing these ingredients and labeling claims are not generally recognized as safe and effective or are misbranded as specified in the preamble of the applicable monograph.

Category III

Ingredients and claims for which data are insufficient to place them either in category I or II.

PART II - IMPLEMENTATION

OBJECTIVES

To provide guidance to field offices on identifying and evaluating OTC drug products and assuring the products' compliance with applicable monographs.

To assure continuity and uniform and equitable enforcement while implementing OTC final monographs.

IMPORTANT

- Whenever a District determines that there are or may be violations of a Final OTC Monograph, it should consult with DNDLC before submission of any regulatory recommendations. Likewise, if a District believes that regulatory action is merited for a

product subject to a Tentative Final OTC Monograph, it should consult with DNDLC before submission of any regulatory recommendations. Inquiries should be directed to the OTC Drugs Team leader, currently Robert Heller (301) 827-8961.

FIELD RESPONSIBILITIES

- Review firm files before inspections to identify products that are subject to final monographs.
- By reviewing the labeling and formulations of OTC drug products, make a preliminary determination of their compliance with applicable OTC Final Monographs. We recommend that, when inspecting an OTC drug manufacturer/repacker, the District collect a representative sampling of the labeling for the firm's products, concentrating on those products for which OTC Final Monographs are in effect, especially those covered by Negative Final Monographs. The Final Monographs can be found at 21 CFR Parts 331 to 358, and Negative Monographs can be found at 21 CFR §§ 310.519-548. We note in particular that 21 CFR § 310.545 lists those active ingredients prohibited for use in the various OTC drug categories. Review of this labeling by the District should reveal obvious discrepancies with the corresponding Final Monographs, which the District may cite in Warning Letter recommendations. If this review raises questions or requires regulatory or policy guidance, Districts should contact the OTC Drugs Team.
- Continue to monitor the OTC drug industry as OTC drug monographs are finalized and published in the Federal Register. A complete list of the Federal Register documents published under the OTC Drug Review is found on the Office of Nonprescription Product's website under the heading "Rulemaking History for OTC Drug Products" at: <http://www.fda.gov/cder/Offices/OTC/industry.htm>

PART III - INSPECTIONAL

No special inspections are required under this program. DNDLC will, however, issue special assignments as needed.

The FDA conducts a significant number of current good manufacturing practice (GMP) inspections of OTC drug manufacturers. As part of these GMP inspections, Districts should check OTC final regulations, which are found at 21 CFR §§ 310.519-548 (Negative Monographs) and at 21 CFR Parts 331 to 358 (Final Monographs) in order to consider whether new drug and misbranding charges apply to the firm's OTC products. This avoids a listing of GMP violations for products that may not be marketed in any event because they are unapproved new drugs. We note, however, that labeling deficiencies for an OTC product might not preclude a GMP inspection. Please consult with the OTC Drugs Team as needed.

SAMPLE COLLECTION

The need for the collection of documentary samples to support a Warning Letter will be determined on a case-by case basis. The collection of labeling for each product to support any misbranding or new drug charges in a Warning Letter is essential. The labeling may be submitted as exhibits. Any questions regarding the need to collect documentary samples should be directed to the OTC Drugs Team.

IMPORTS

Imported OTC drug products are subject to the same monograph requirements as domestic products.

INTERNET

The Internet has become a marketing and promotional tool that gives marketers great visibility and reach. It is imperative that information found on the Internet be preserved when an OTC drug enforcement action is being contemplated. Internet websites can be used to document responsibility for illegal products and activities, and to establish the intended uses of an OTC product. When a product may be purchased from an Internet website, information contained on this Internet site can be defined as labeling, depending on the connection between the vendor and the promotional statements.

Therefore, the Internet must be considered as an integral part of all investigations and recommendations for enforcement actions against violative OTC drug products. Recommendations for enforcement actions must include copies of relevant pages from any Internet website that support a case. If no Internet website can be located concerning the firm or the products at issue, then a statement to that effect should be included in the enforcement recommendation's cover memo.

PART IV - ANALYTICAL

Samples will be collected and analyzed only upon assignments by DNDLC.

PART V - REGULATORY/ADMINISTRATIVE STRATEGY

Districts should not submit proposals for regulatory actions unless they have first consulted with the OTC Drugs Team. The initial action against violative products will generally be a warning or untitled letter.

Types of Firms Covered Under this Program

The following types of firms are eligible to receive warning letters and untitled letters: manufacturers, repackers, relabelers, and own-label distributors.

When more than one firm is responsible for a violative product, e.g., when a contract manufacturer makes a product and labels it according to specifications determined by an own-label distributor, both firms are legally responsible and each should be sent a warning or untitled letter.

A. Criteria to be considered in recommending an enforcement action follow:

1. Safety Risks:

Direct Health Hazard - An article presents a direct health hazard if it is likely to cause injury, death, or other serious adverse effects when used as directed or in a customary manner. Products that fit in this category are a top priority for enforcement.

Indirect Health Hazard – A health hazard is indirect when it does no direct harm to the person as a result of its use, but rather denies, delays, or interferes with effective treatment. An article presents an indirect health hazard if, as a result of reliance on the product, consumers are likely to delay or discontinue appropriate medical treatment. Products in this category have a lower enforcement priority than products presenting a direct health hazard.

2. Impact of Action on Industry:

The type and scale of promotion of a product should be considered in preparing an enforcement recommendation. Enforcement actions against highly visible products, e.g., those that are promoted widely on the Internet or by infomercials, can send a clear message that the agency is prepared to act against violative products.

3. Volume of Sales or Production:

A product's volume of sales or production can be a guide to the potential impact of a regulatory action. By considering sales volume or production, the agency can focus its enforcement priorities on products with larger market shares, thus providing broader consumer protection.

Large sales volume or production, however, is not required for enforcement action against products posing direct health hazards.

4. Risk to OTC Monograph or NDA Approval Process:

The agency has expended large amounts of resources through the OTC Drug Review and the NDA approval process to ensure that OTC drug products on the market are safe and effective, and not misbranded. It is important to maintain the integrity of these processes. Therefore, OTC products that do not conform to an appropriate Final Monograph, or that lack required NDA approval, may be enforcement priorities, especially when competitor products comply with a Final Monograph or obtain NDA approval.

B. Responses to enforcement related correspondence:

Copies of all responses are to be forwarded to DNDLC's OTC Drugs Team.

C. Follow-up to non-compliance with a warning or untitled letter shall be accomplished as required in the Regulatory Procedures Manual (RPM), with recommendations for further regulatory action submitted to the Office of Compliance. Districts should consult with the OTC Drugs Team regarding the types of regulatory actions to recommend.

RECALL

Districts are not to initiate recall recommendations under this program. Questions and recommendations regarding the need for recall, as well as health hazard evaluations, should be directed to the Recall Office (HFD-320) in accordance with RPM, Part 5 requirements.

IMPORTS

Imported OTC drug products are subject to the same monograph requirements as domestic products. There may be instances when importers should be notified of final OTC monograph

requirements for their products through the mechanism of "release with comment." This should first be addressed with the OTC Drugs Team. Subsequent shipments from the same manufacturer are to be detained if they do not comply with the monograph. If monograph deficiencies are not corrected for subsequent shipments, the District should consider submitting an Import Alert recommendation to Division of Import Operations and Programs.

PART VI - REFERENCES, ATTACHMENTS, AND PROGRAM CONTACTS

REFERENCES

- Title 21, Code of Federal Regulations
- CPG 450.200 (CPG 7132b.15)
- CPG 450.300 (CPG 7132b.16)
- Inspection Operations Manual, Chapter 5
- Regulatory Procedures Manual, Part 8.

CONTACTS:

Center for Drug Evaluation and Research (CDER)

Implementation

Division of New Drugs and Labeling Compliance
OTC Drugs Team (HFD-312)
Attention: Robert Heller
Telephone: 301-827-8961

Office of Regulatory Affairs (ORA)

1. Investigations Operations Branch (HFC-132)
DFI/ORO/ORA
301-443-3340
2. Analytical Problems
Division of Field Science (HFC-141)
DFS/ORO/ORA
Attn: Don Lech
Telephone: 301-827-1026
3. Imports
Division of Import Operations and Programs (HFC-170)
DIOP/ORO/ORA
Attn: John Verbeeten
Telephone 301-594-3853

PART VII - CENTER RESPONSIBILITIES

Division of New Drugs and Labeling Compliance/OTC Drugs Team

1. Based on agency policy, develops basic enforcement strategy and approves and directs regulatory action; coordinates with the Office of Nonprescription Products (HFD-560); and monitors and updates all compliance activities relating to OTC monograph compliance.
2. Advises firms and the field regarding the current marketing status of all OTC drugs, whether or not they are subject to a published final monograph.
3. Serves as a source of information for the field regarding compliance of OTC drugs.
4. Monitors effectiveness of compliance-related guidelines.
5. Advises districts of policy and/or significant status changes.
6. Resolves questions and makes final determinations concerning the applicability of compliance-related guidelines to OTC products.

Office of Nonprescription Products (HFD-560)

1. Coordinates advisory panel activities and data collection on drugs to be reviewed.
2. Writes proposed, tentative final, final monographs, and amendments to the final monographs, and provides technical assistance on compliance matters to the Office of Compliance, as required.