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Drugs

Drug Applications for Over-the-Counter Drugs

Over-the-counter (Nonprescription) drugs play an increasingly vital role in America's health care system. Today, six out of every ten medications bought by consumers are OTC drugs. OTC drugs are defined as drugs that are safe and effective for use by the general public without seeking treatment by a health professional. FDA's review of OTC drugs is primarily handled by CDER's Office of Drug Evaluation IV, Over-the-Counter Drug Products. The Nonprescription Drug Advisory Committee meets regularly to assist the Agency in evaluating issues surrounding these products. This committee has played a major role in the growth of prescription to OTC switches in recent years.

Because there are over 300,000 marketed OTC drug products, FDA reviews the active ingredients and the labeling of over 80 therapeutic classes of drugs, for example analgesics or antacids, instead of individual drug products. For each category, an OTC drug monograph is developed and published in the *Federal Register*. OTC drug monographs are a kind of "recipe book" covering acceptable ingredients, doses, formulations, and labeling. Many of these monographs are found in [section 300 of the Code of Federal Regulations](#)¹. Once a final monograph is implemented, companies can make and market an OTC product without the need for FDA pre-approval. New prescription drugs, on the other hand, require pre-approval before they can go on the market. These monographs define the safety, effectiveness, and labeling of all marketing OTC active ingredients. New products that conform to a final monograph may be marketed without further FDA review. Those that do not conform must be reviewed by the [New Drug Application](#)² process. A drug company may also petition to change a final monograph to include additional ingredients or to modify labeling.

For more information about non-prescription drugs, visit the [Office of Drug Evaluation IV home page](#)³. This page also contains documents that are frequently requested of the Division.

Guidance Documents

Guidance documents represent the Agency's current thinking on a particular subject. These documents are prepared for FDA review staff and applicants/sponsors to provide guidelines to the processing, content, and evaluation/approval of applications and also to the design, production, manufacturing, and testing of regulated products. They also establish policies intended to achieve consistency in the Agency's regulatory approach and establish inspection and enforcement procedures. Because guidances are not regulations or laws, they are not enforceable, either through administrative actions or through the courts. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. For information on a specific guidance document, please contact the originating office.

- [Over-the-Counter Drug Guidances](#)⁴
- Guidance for Industry: [National Uniformity for Nonprescription Drugs - Ingredient Listing for OTC Drugs](#)⁵ (Issued 4/1998, Posted 5/5/1998). Describes how active and inactive ingredients must appear on OTC labels.

Laws, Regulations, Policies and Procedures

Federal Register

In the *Federal Register* of February 27, 1997 (62 FR 9024), FDA proposed a rule that would establish a standardized format for the labeling of OTC drug products.

The rule is intended to make OTC drug product labeling easier to read and understand. The proposed rule includes a standardized format for listing the name and the quantity per dosage unit (or, when appropriate, the proportion) of each active ingredient. [Docket No. 98N-0337 Over the Counter Human Drugs Labeling Requirements](#)⁶ is a collection of comments on the proposed rule submitted by the public, as well as FDA responses, meeting minutes, and other related materials.

- [Over-The-Counter Human Drugs; Labeling Requirements: Final rule](#)⁷. Effective Date: April 16, 1999. This final rule establishes a standardized format and standardized content requirements for the labeling of OTC drug products. The rule is intended to assist consumers in reading and understanding OTC drug product labeling. All OTC drug products are required to carry the new, easy-to-read format and the revised content requirements within prescribed implementation periods.

Code of Federal Regulations

The final regulations published in the [Federal Register](#)⁸ (daily published record of proposed rules, final rules, meeting notices, etc.) are collected in the [Code of Federal Regulations](#)⁹. The *CFR* is divided into 50 titles which represent broad areas subject to Federal regulations. The FDA's portion of the *CFR* interprets the [Federal Food, Drug and Cosmetic Act](#)¹⁰ and related statutes. [Section 21 of the CFR](#)¹¹ contains all regulations pertaining to food and drugs. The regulations document all actions of all drug sponsors that are required under Federal law. Regulations of particular interest to OTC applicants include:

OTC Drug Products for existing Monographs

- [21 CFR Part 330 - Over the-Counter \(OTC\) Human Drugs Which are Generally Recognized as Safe and Effective and not Misbranded](#)¹². An OTC drug listed in subchapter 330 is generally recognized as safe and effective and is not misbranded if it meets the conditions of 330.1 and each of the conditions contained in the specific final monograph. As a basis for the scientific review of OTC ingredients, the CFR states definitions of safety, effectiveness, and labeling.

Monograph Changes

- [21 CFR Part 330.10](#)¹³ - Data regarding OTC monographs can be submitted by anyone- such as a drug company, health professional, consumer, or citizen's group. If the submission is a request to amend an existing drug monograph or is an opinion regarding a drug monograph, it needs to be submitted in the form of a citizen petition or as correspondence to an established monograph docket. However, if no monograph exists, data must be submitted in the format as outlined in the Code of Federal Regulations (CFR) section 330.1.

MAPPs (Manual of Policies and Procedures)

These documents are approved instructions for internal practices and procedures followed by CDER staff to help standardize the new drug review process and other activities. MAPPs define external activities as well. All MAPPs are available for the public to review to get a better understanding of office policies, definitions, staff responsibilities and procedures. MAPPs of particular interest to OTC applicants include:

- [6020.5R](#)¹⁴ Good Review Practice: OND Review Management of INDs and NDAs for Nonprescription Drug Products (Issued 7/13/2007, Posted 7/16/2007)
- [6532.1 Over-the-Counter \(OTC\) Labeling and Use Studies](#)¹⁵ Sponsors often conduct OTC drug actual use studies and OTC label comprehension studies for prescription-to-OTC switch candidates. Individual reviewing divisions have handled these studies differently. This guide describes standardized procedures to process documents related to OTC drug actual use and label comprehension studies.

Submissions Requesting Exemptions and Deferrals for Labeling Requirements

The Final rule for [Over-the-Counter Human Drugs Labeling Requirements, 21 CFR](#)

201.66¹⁶ provides for any manufacturer, packer, or distributor to submit a written request for exemption or deferral of one or more labeling requirements.

- [21 CFR 201.66\(e\)](#)¹⁷ Request for Exemption from OTC Labeling Format and Content Requirements. This section outlines the process for submission of exemption or deferral requests for drug products marketed under a monograph or an approved application.
- [21CFR 20.61](#)¹⁸. Trade secrets and commercial or financial information which is privileged or confidential. Anyone who submits records to the Government may designate part or all of the information exempt from disclosure under exemption 4 of the [Freedom of Information Act](#).¹⁹

An exemption and/or deferral request should include:

- A cover letter that includes the statement "Application for Exemption," and the NDA or ANDA number for approved drug products and a description of the drug product and shelf keeping unit(s) covered by the exemption request.
- A table of contents or index.
- A copy of the most recent marketed product label for products marketed under a monograph and the most recent approved labeling for drugs marketed under an NDA or ANDA.
- A complete listing of all requested exemptions from [21 CFR 201.66\(c\)](#) and [\(d\)](#)²⁰.
- An explanation why a particular requirement is inapplicable, impracticable, or is contrary to public health or safety. The sponsor should provide labeling in the Drug Facts format following [21 CFR 201.66](#)²¹ with annotation of the parts of the label where exemptions are requested.
- A representation of the proposed labeling, including any outserts, panel extensions, or other graphical or package techniques.
- The proposed labeling should include information on formatting, text style and text size as illustrated on 64 FR 13254 at 13293.

Submissions for Labeling Changes

For labeling changes submitted under [21 CFR 314.70 \(c\) or \(d\)](#)²², the sponsor should provide:

- A cover letter stating that the submission includes new labeling in the Drug Facts for the drug product and shelf keeping unit(s).
- A table of contents or index.
- The most recent approved labeling
- A representation of the proposed labeling, including and outserts, panel extensions, or other graphical or package techniques intended to be used with the product.
- The proposed labeling should include information on formatting, text type and text size as illustrated in 64 FD 13254 at 13293

Related Topics

- [Investigational New Drug Application \(IND\)](#)²³ Provides resources to assist drug sponsors with submitting applications for approval to begin new drug experiments on human subjects.
- [Abbreviated New Drug Application \(ANDA\)](#)²⁴ Provides resources to assist drug sponsors with submitting applications to market a generic drug.
- [Drug Application Regulatory Compliance](#)²⁵ The approval process for new drug applications includes a review of the manufacturer's compliance with Current Good Manufacturing Practice. This web page provides resources to help meet compliance.
- [Post Drug-Approval Activities](#)²⁶ The goal of CDER's post drug-approval activities is to monitor the ongoing safety of marketed drugs. This is accomplished by reassessing drug risks based on new data learned after the drug is marketed, and recommending ways of trying to most appropriately manage that risk.

- [Information for Clinical Investigators](#)²⁷ Provides regulations and guidelines to scientists who design and run experiments (clinical trials) to test the safety and effectiveness of new drugs on human subjects.
 - [Small Business Assistance Program](#)²⁸
 - [Electronic Regulatory Submission and Review \(ERSR\)](#)²⁹ Provides information on electronic drug applications, application reviews, Electronic Document Room, and other ERSR projects.
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Links on this page:

1. http://www.access.gpo.gov/nara/cfr/waisidx_99/21cfrv5_99.html
2. <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/NewDrugApplicationNDA/default.htm>
3. <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm093452.htm>
4. <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm065013.htm>
5. <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm078733.pdf>
6. <http://www.fda.gov/ohrms/dockets/dockets/98n0337/98n0337.htm>
7. http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=1999_register&docid=99-6296-filed.pdf
8. <http://www.gpoaccess.gov/fr/index.html>
9. <http://www.gpoaccess.gov/cfr/index.html>
10. <http://www.fda.gov/opacom/laws/fdactact/fdctoc.htm>
11. <http://www.access.gpo.gov/cgi-bin/cfrassemble.cgi?title=200921>
12. http://www.access.gpo.gov/nara/cfr/waisidx_09/21cfr330_09.html
13. http://www.access.gpo.gov/nara/cfr/waisidx_09/21cfr330_09.html
14. <http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/ucm082003.pdf>
15. <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/StaffPoliciesandProcedures/ucm082051.pdf>
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22. http://edocket.access.gpo.gov/cfr_2009/aprqttr/21cfr314.70.htm
23. <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm>
24. <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/default.htm>
25. <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/NewDrugApplicationNDA/default.htm>
26. <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/default.htm>
27. <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm>
28. <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/default.htm>
29. <http://www.fda.gov/FDAgov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm085324.htm>