OTC Monograph Reform Guidances: OMOR Format and Content & Electronic Submissions

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Learning Objectives

- Provide an overview of draft guidance for industry *Over-the-Counter Monograph Order Requests (OMORs): Format and Content*
  - Discuss FDA's recommendations on the format and content of the information that requestors should provide in an OMOR
  - Discuss the information that FDA may recommend for a sufficiently complete OMOR
- Provide an overview of draft guidance for industry *Providing Over-the-Counter Monograph Submissions in Electronic Format*
  - Describe examples of OTC monograph submissions that must be in electronic format
  - Discuss FDA's recommendations and other information on how to send OTC monograph submissions to FDA in electronic format

OTC Monograph Reform

- On March 27, 2020, the “Coronavirus Aid, Relief, and Economic Security Act” (CARES Act) was enacted

- CARES Act amended the Food, Drug & Cosmetic Act
  - Added Section 505G: modernizes the OTC drug review and OTC monograph drug development process
  - Added Section 744M: establishes an OTC monograph drug user fee program

- Over-the-Counter Monograph User Fee Program Performance Goals and Procedures Document
  - Specifies FDA and industry mutually agreed upon timelines

Administrative Order Process

- FDA can issue an administrative order that adds, removes, or changes generally recognized as safe and effective (GRASE) conditions for an OTC monograph drug
- Either industry or FDA can initiate the administrative order process

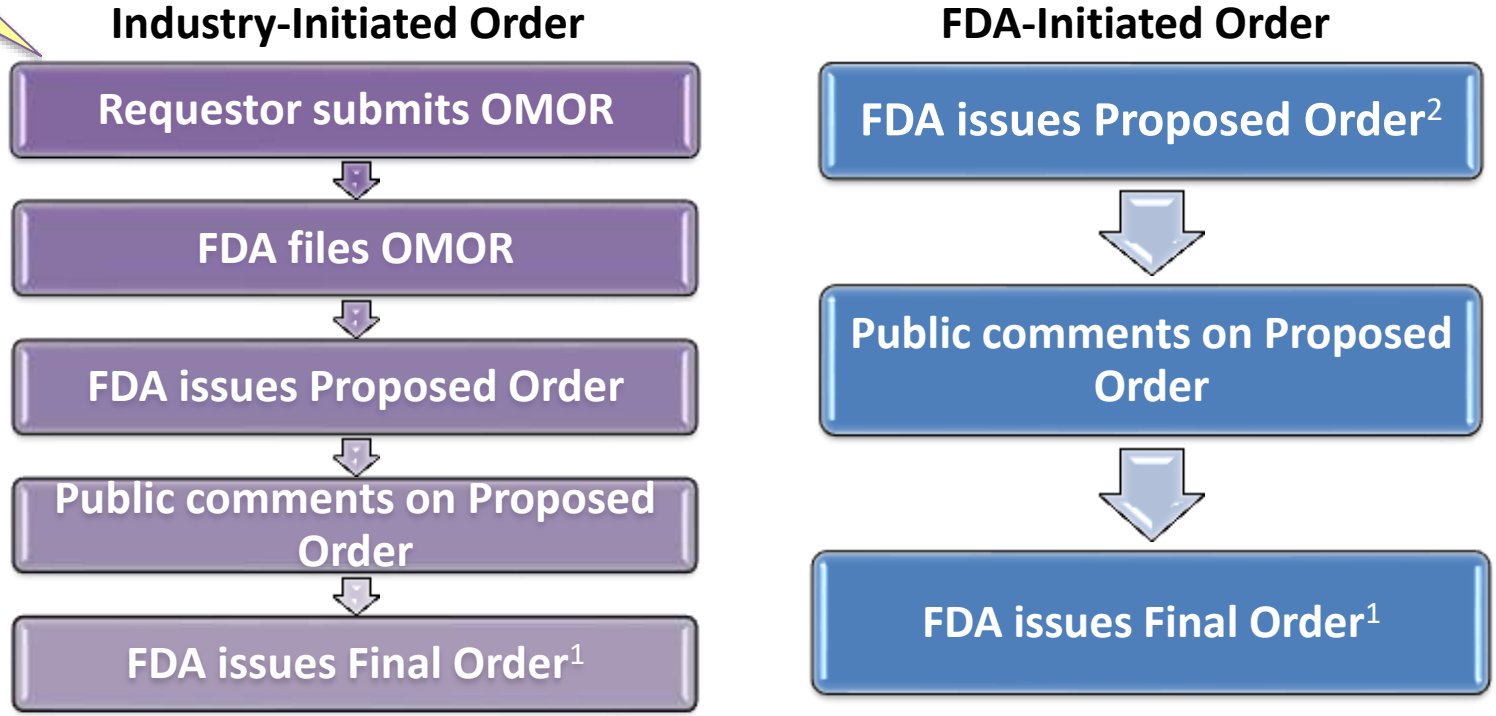
What is an OMOR?

Over-the-counter **M**onograph **O**rder **R**equest (OMOR) is a request for the issuance of an administrative order—

- determining whether a drug is generally recognized as safe and effective (GRASE), or
- determining whether a change to a condition of use of a drug is GRASE

Administrative Order Process

OMOR = OTC Monograph Order Request



[1] Final orders are final Agency actions subject to dispute resolution, administrative hearings, and judicial review.
[2] Or interim final order under an expedited procedure

OMORs

Tier 1 OMOR	Tier 2 OMOR
• Any request not determined to be a Tier 2 OMOR	• Reordering of existing information in the Drug Facts label (DFL) • Addition of information to the "Other Information" section of the DFL • Modification to the "Directions for Use" section of the DFL, consistent with a minor dosage form change • Standardization of the concentration or dose of a specific finalized ingredient within a particular finalized monograph • Change to ingredient nomenclature to align with nomenclature of a standards-setting organization • Addition of an interchangeable term consistent with 21 C.F.R. § 330.1 (or any successor regulations)

DRAFT GUIDANCE FOR INDUSTRY

OVER-THE-COUNTER MONOGRAPH ORDER REQUESTS (OMORS): FORMAT AND CONTENT

OMOR: Format and Content Draft Guidance

- Assist requestors in preparing OMORs to submit to FDA under section 505G FD&C Act.
- Provide FDA's recommendations on the format and content of the information that requestors should provide in an OMOR
- Identify other relevant guidance documents to assist requestors in preparing their OMORs

An OMOR must be:

- submitted in electronic format
- submitted to FDA in the form and manner specified by the Agency
- sufficiently complete and formatted to permit FDA to conduct a substantive review

OMOR: Format and Content Draft Guidance

- Provides an overview of the information that FDA recommends for a sufficiently complete OMOR
- **Is not** intended to indicate the studies and related information that a requestor must submit in a specific OMOR

Overview of OMOR: Format and Content Draft Guidance

I. Introduction

II. Background

III. The Common Technical Document Format and Content for a OMOR

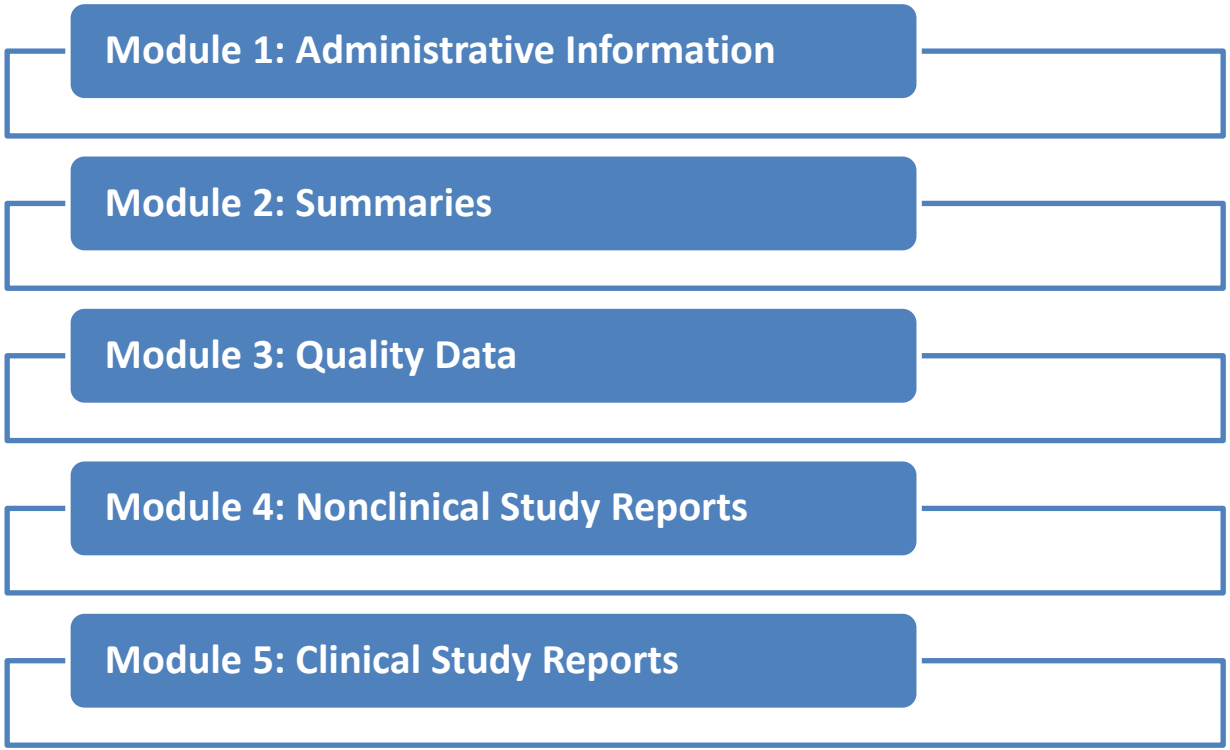
IV. General Considerations for an OMOR

V. Environmental Assessment

VI. Confidential Information

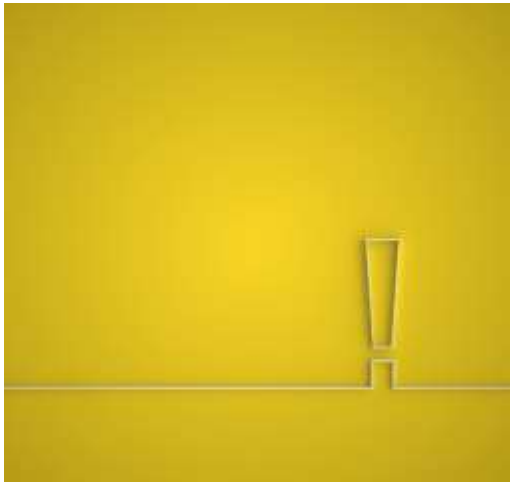
Organization of an OMOR

OMORs should follow the organizational structure and format outlined ***Common Technical Document for the Registration of Pharmaceuticals for Human Use (CTD)***



CTD Guidance Documents

- Refer to guidance documents that FDA issued specific to CTD for organizing certain applications that will be submitted to FDA
  - Recommendations provided in these guidance documents are also applicable to OMORs



- An OMOR may not need to include all the information identified for an applicable module, section, or subsection described in this guidance
  - In those circumstances, a requestor should indicate that no information is being submitted for a given module or a section or subsection of a module

Module 1: Administrative Information

Sections	Examples of Information to Include
Table of Contents	Comprehensive table of contents for entire submission
Cover Letter	Pertinent information that aids communication regarding the review of the OMOR
Administrative Information	Statement that all information considered by the requestor to be confidential has been identified in the OMOR; environmental assessment; statement of claimed exclusivity
References	Letters of authorization, Statement of right of reference; Previously submitted information to FDA
Meetings	Listing of all meetings with FDA, including complete copies of meeting materials and correspondence, pertaining to OMOR
Labeling	Proposed labeling and proposed OTC monograph that reflects OTC monograph conditions proposed in OMOR

Module 2: Summaries

- Module 2 summarizes the information that will be provided in the quality (Module 3), nonclinical (Module 4) and clinical (Module 5) modules of the OMOR
- Summaries should contain seven sections in the following order:
  - **2.1 Table of Contents**
  - **2.2 Introduction to the Summary Documents**
  - **2.3 Quality Overall Summary**
  - **2.4 Nonclinical Overview**
  - **2.5 Clinical Overview**
  - **2.6 Nonclinical Written and Tabulated Summaries**
  - **2.7 Clinical Summary**

Module 2: Summaries (cont'd)

Section	Summary Information	ICH Guidance for Industry Reference (if applicable)
2.1 Table of Contents	List all the documents provided in Modules 2- 5	N/A
2.2 Introduction to Summary Documents	Concise narrative summary of positive and negative safety and effectiveness data	N/A
2.3 Quality Overall Summary	Summary of all chemistry and manufacturing data	M4Q: The CTD — Quality
2.4 Nonclinical Overview	Integrated and critical assessment of the pharmacologic, pharmacokinetic, and toxicologic evaluation of the active ingredient or other conditions of use	M4S: The CTD — Safety
2.5 Clinical Overview	Integrated and critical assessment of all the clinical data	M4E(R2): The CTD — Efficacy
2.6 Nonclinical Written and Tabulated Summaries	Narrative summary and summary tables of all the nonclinical data	M4S: The CTD — Safety M4S: The CTD — Safety Appendices
2.7 Clinical Summary	Detailed, factual summary of all of the clinical information	M4E(R2): The CTD — Efficacy

Module 3: Quality Data Content

- Discuss the chemistry, manufacturing, and controls reports for both drug substance and drug product

- Refer to the ICH guidance for industry *M4Q: The CTD —Quality*

Module 3: Quality Data Format

- Module 3 should be organized according to the following general section outline:

  3.1 Module 3 Table of Contents

  3.2 Body of Data

  3.3 Literature References

- Refer to the ICH guidances for industry:
  - *M4Q: The CTD —Quality*
  - *M4: The CTD — Quality Questions and Answers/Location Issues*

Module 4: Nonclinical Study Reports Content

- Include data and reports from nonclinical studies such as:
  - pharmacology studies
  - general toxicity studies
  - toxicokinetic and nonclinical pharmacokinetic studies
  - reproduction toxicity studies
  - genotoxicity studies
  - an assessment of carcinogenic potential
- Refer to the ICH guidance for industry *M3(R2): Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals*

Module 4: Nonclinical Study Reports Format

- Should be organized according to the following general section outline:

  4.1 Module 4 Table of Contents

  4.2 Study Reports

  4.3 Literature References

- Refer to the ICH guidance for industry *M4S: The CTD — Safety*

Module 5: Clinical Study Reports Content

- Include full reports of:
  - all clinical effectiveness and safety studies and other clinical data
  - all clinical pharmacology and human toxicokinetic data
  - all consumer behavior studies
  - postmarketing experience
- Include other types of clinical data such as literature searches, scientific articles, and other published materials
- Refer to the ICH guidances for industry:
  - *M4E(R2): The CTD — Efficacy*
  - *E3 Structure and Content of Clinical Study Reports*

Module 5: Clinical Study Reports Content (cont'd)

- **Consumer behavior studies**

Label Comprehension Study
- Understanding the key label message

Self- Selection Study
- Choosing the right product

Actual Use Study
- Using according to labeled directions

Human Factors Study
- Interacting with the product

Module 5: Clinical Study Reports Content (cont'd)

- **Information demonstrating prima facie safe nonprescription marketing and use**
  - Required for an OMOR that proposes a drug is GRASE, if the drug contains an active ingredient not previously incorporated in a drug:
    - specified in section 505G(a)(1), (a)(2), or (a)(3) of the FD&C Act,
    - subject to a final order under section 505G(b) of the FD&C Act, or
    - subject to a final sunscreen order

Module 5: Clinical Study Reports Content (cont'd)

- **Information demonstrating prima facie safe nonprescription marketing and use (cont'd)**
  - For such OMORs, Module 5 must include information demonstrating prima facie safe nonprescription marketing and use, including the following, as applicable:

    (1) History of being marketed and safely used in the U.S. as a nonprescription drug under comparable conditions of use

    (2) If drug has not been previously marketed in the U.S. as a nonprescription drug, must include information sufficient for a prima facie demonstration that the drug was marketed and safely used under comparable conditions of marketing and use in a country listed in section 802(b)(1)(A) of the FD&C Act or designated by FDA in accordance with section 802(b)(1)(B) of the FD&C Act

    (3) If FDA determines (1) or (2) is not needed, requestor must submit other information FDA determines is sufficient for such purposes

Module 5: Clinical Study Reports Content (cont'd)

- **Information demonstrating prima facie safe nonprescription marketing and use (cont'd)**
  - If the OMOR fails to include such information, FDA will refuse to file the OMOR and require that the nonprescription marketing of the drug be pursuant to an approved application under section 505 of the FD&C Act

Module 5: Clinical Study Reports Content (cont'd)

- **Reports of postmarketing experience**
  - Summarize the marketing experience relevant to the OTC monograph condition of use proposed in the OMOR
  - Include available relevant postmarketing data, such as periodic safety update reports and adverse events
  - Discussions and analyses of the postmarketing data along with the conclusions and implications of the data as it pertains to the OTC monograph condition of use proposed in the OMOR
  - Relevant safety discussions and analyses from the literature, if available

Module 5: Clinical Study Reports Format

- Should be organized according to the following general section outline:

  5.1 Module 5 Table of Contents

  5.2 Tabular Listing of All Clinical Studies

  5.3 Clinical Study Reports

  5.4 Literature References

- Refer to the ICH guidance for industry *M4E(R2): The CTD — Efficacy*

General Considerations for an OMOR

- English language
- Easily legible (e.g., Times Roman 12-pt font)
- Formatted to standard U.S. letter paper size
- All documents should have page numbers
- Electronically searchable
- Include hyperlinks to full copies of referenced scientific articles or other published material

Environmental Assessment (EA)

- The National Environmental Policy Act of 1969 (NEPA) requires all Federal agencies to assess the environmental impacts of their actions and to ensure that the interested and affected public is informed of environmental analyses
- Requestor must accompany an OMOR with either an EA or a claim of categorical exclusion
- An adequate EA is one that contains sufficient information to enable FDA to determine whether the proposed action may significantly affect the quality of the human environment

Confidential Information

- In general, the OTC monograph order process is a public process
- Section 505G(d) of the FD&C Act limits the information that can remain confidential after submission to FDA in connection with proceedings on an order, including an OMOR
- FDA generally must make any information submitted by a requestor in support of an OMOR (e.g., the contents of the OMOR) available to the public not later than the date on which the proposed order is issued

Confidential Information (cont'd)

- The information will remain confidential if it:
  1. Information pertains to pharmaceutical quality information (unless such information is necessary to establish standards under which a drug is generally recognized as safe and effective)
  2. Information is of the type contained in raw datasets
  3. Information is submitted in a requestor-initiated request, but the requestor withdraws the request before FDA issues the proposed order; or
  4. FDA requests and obtains the information under section 505G(c) of the FD&C Act and the information is not submitted in relation to an order under section 505G(b)

DRAFT GUIDANCE FOR INDUSTRY

PROVIDING OVER-THE-COUNTER MONOGRAPH SUBMISSIONS IN ELECTRONIC FORMAT

Purpose of Draft Guidance

- Provide information on providing electronic submissions to FDA under section 505G of the FD&C Act (OTC monograph submissions)
- Intended to assist submitters by
  - describing the electronic OTC monograph submissions requirement in section 505G(j) of the FD&C Act
  - providing recommendations on how to send submissions in electronic format

OTC Monograph Submissions

- Section 505G(j) of the FD&C Act requires that all OTC monograph submissions must be in electronic format, including:
  - OTC monograph order requests (OMORs)
  - Public comments to a proposed or interim final administrative order
  - Formal meeting requests and meeting packages
  - Formal dispute resolution requests related to a final administrative order
  - Administrative hearing requests related to a final administrative order
  - Responses to record requests by FDA relating to minor changes
  - Updates to drug listing information for the drug in accordance with section 510(j) of the FD&C Act when a change is made to a drug subject to section 505G

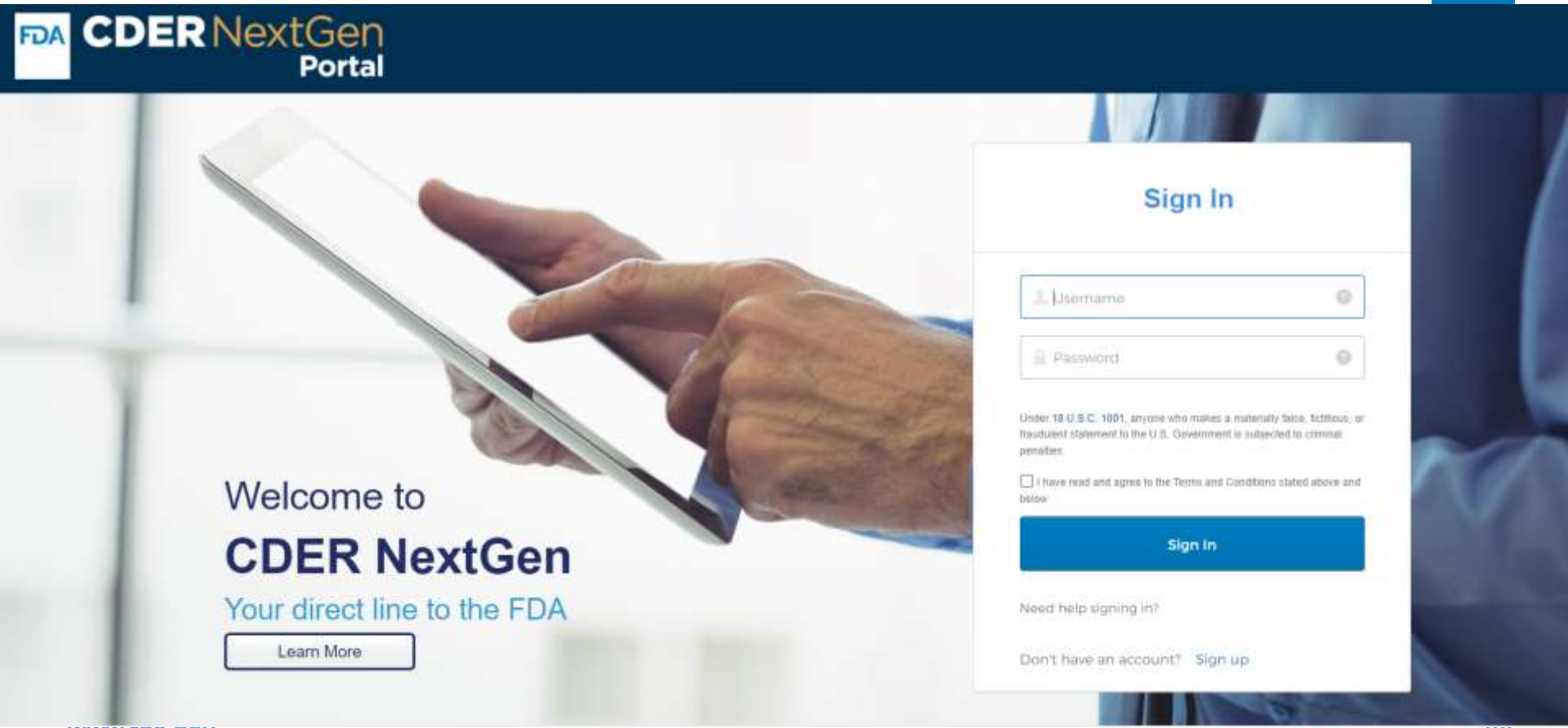
Where should OTC monograph submissions be submitted?

Depends on the type of submission

Submitting Electronic OTC Monograph Submissions

- Depending on the type of submission, OTC monograph submissions may be submitted to FDA through:
  - CDER NextGen Portal
  - OTC Monographs@FDA
  - Electronic Drug Registration and Listing System (eDRLS)

CDER NextGen Portal



CDER NextGen Portal Submissions

- Formal meeting requests and meeting packages
- OMORs
- Formal dispute resolution requests related to a final administrative order
- Administrative hearing requests related to a final administrative order
- Responses to record requests by FDA relating to minor changes

CDER NextGen Portal

- **Transmitting Electronic Submissions**
  - Submitters need to have a CDER NextGen Portal account to submit information to FDA
  - Provides for the secure submission of OTC monograph submissions.
  - Does not provide a means to edit OTC monograph submissions once they have been submitted.
  - For information related to file size limitations for OTC monograph submissions, contact CDER at EDMSupport@fda.hhs.gov.

CDER NexGen Portal (cont'd)

- **Receipt Date for an OTC Monograph Submission**
  - Date on which the request is deemed to have arrived at FDA
    - Determined only after the files in the submission have been validated (e.g., successful file size verification and virus scan)
  - After an OTC monograph submission has been successfully submitted
    - a confirmation will appear in the portal and
    - submitter will also receive an email notification from the portal confirming the submission is successful and establishing the submission's receipt date.

OTC Monographs@FDA

OTC MONOGRAPHS @ FDA

OTC Monographs@FDA provides a resource for the public to view Administrative Orders (Proposed, Final, and Interim Final Orders) for OTC Monograph Drugs and view OTC Monographs. OTC Monographs@FDA also facilitates the ability for the public to submit, search, and view comments and data for Proposed and Interim Final Administrative Orders, except if otherwise specified.

Some final orders incorporate by reference material that is available for inspection at FDA. For further information about inspecting incorporated material, contact druginfo@fda.hhs.gov.

Latest News

- **05/02/2023** - FDA posts remaining final administrative orders as deemed by the CARES Act on OTC Monographs@FDA. FDA also posts a revision to final Administrative Order OTC000024 Over-the-Counter Monograph M001: Antacid Products for Over-the-Counter Human Use **OTC Monograph Reform website**
- **05/02/2023** - FDA posts remaining five final administrative orders as deemed by the CARES Act: FDA also posts a revision to Final Administrative order OTC000024 Over-the-Counter Monograph M001: Antacid Products for Over-the-Counter Human Use **OTC Monographs@FDA**

OTC Monographs

Search OTC Monographs and Non-Monograph Conditions

Administrative Orders

Search proposed, interim final, or final administrative orders including supporting documents and public comments

Comment on Proposed or Interim Final Orders

Comment on administrative orders with open comment periods

OTC Monographs@FDA (cont'd)

Latest News

- **06/22/2023** - FDA issues draft guidance for industry **"Formal Dispute Resolution and Administrative Hearings of Final Administrative Orders Under Section 505G of the Food, Drug, and Cosmetic Act"**
- **05/02/2023** - FDA posts remaining final administrative orders as deemed by the CARES Act on OTC Monographs@FDA. FDA also posts a revision to final Administrative Order OTC000024 Over-the-Counter Monograph M001: Antacid Products for Over-the-Counter Human Use **OTC Monograph Reform website**

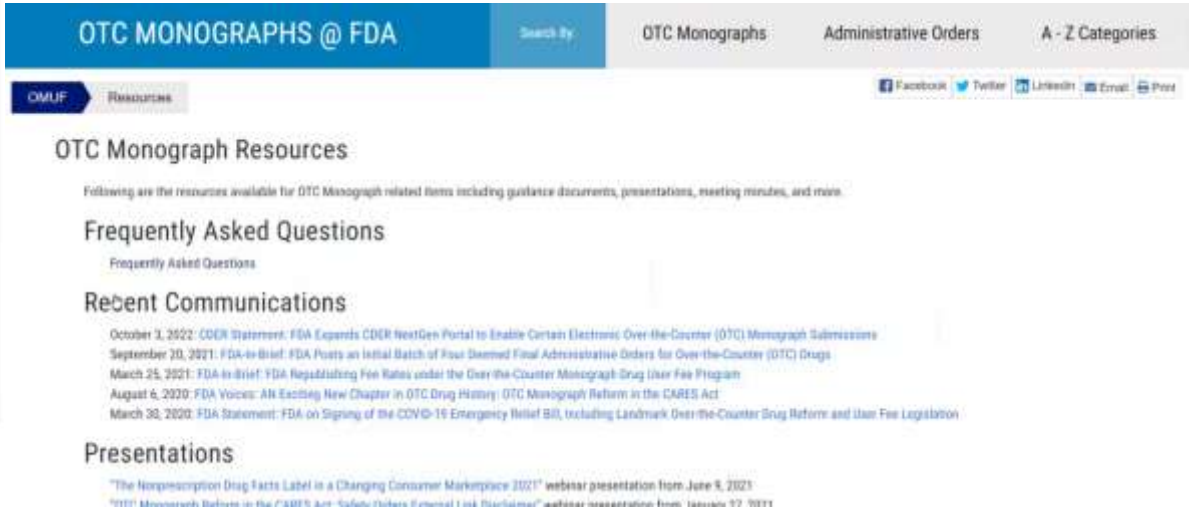
Read More...

Annual Forecast

Nonbinding list of planned OTC monograph activities that FDA intends to address over the next 3 years

OTC Monograph Resources

Guidance documents, presentations, meeting minutes, and regulatory information



OTC Monographs@FDA Submissions

- Data and information submissions to FDA data requests
- Public comments to a proposed order or interim final order

Electronic Drug Registration and Listing System (eDRLS)

- Sponsors submitting updates to drug listing information for a drug subject to section 505G in accordance with section 510(j) of the FD&C Act based on changes they have made to the drug should follow the general process for providing updated listing information

- Instructions can be found on FDA's Electronic Drug Registration and Listing System (eDRLS) web page

Challenge Question #1

Which of the following is an example of an OTC monograph submission that must be in electronic format?:

A. OTC monograph order requests (OMORs)

B. Public comments to a proposed administrative order or interim final administrative order

C. Formal meeting requests and meeting packages

D. All of the above

Challenge Question #2

Which of the following statements is NOT true?

A. Every OMOR must include all the information identified for each module, section, or subsection described in the OMOR: Format and Content draft guidance and other CTD guidance documents.

B. An OMOR should follow the CTD format.

C. FDA can refuse to file an OMOR that is not sufficiently complete and formatted to permit substantive review.

D. An OMOR should be submitted electronically through the CDER NextGen Portal.

Resources

- Over-the-Counter Monograph Order Requests (OMORs): Format and Content draft guidance
- Providing Over-the-Counter Monograph Submissions in Electronic Format draft guidance
- CTD guidance documents
- Formal Meetings Between FDA and Sponsors or Requestors of Over-the-Counter Monograph Drugs draft guidance
- CDER NextGen Portal
- OTC Monographs@FDA portal
- FDA's Electronic Drug Registration and Listing System (eDRLS)

Contact Us

- For General Questions on OTC Monograph Drugs: druginfo@fda.hhs.gov
- CDER NextGen Portal: EDMSupport@fda.hhs.gov
- User Fees (OMUFA): CDERCollections@fda.hhs.gov
- Small Business and Industry Assistance: cdersbia@fda.hhs.gov

U.S. FOOD & DRUG ADMINISTRATION

Questions?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