Over-the-Counter Monograph Order Requests: Format and Content

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

November 2026
Over-the-Counter

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Contains Nonbinding Recommendations

Over-the-Counter Monograph Order Requests: Format and Content Guidance for Industry[1]

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance is intended to assist requestors[2] in preparing over-the-counter (OTC) monograph order requests (OMORs)[3] for submission to FDA under section 505G of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355h). This guidance provides FDA's recommendations on the format and content of the information that requestors should provide in an OMOR and identifies relevant guidance documents to assist requestors in preparing their OMORs. However, because the type and quantity of data and information that would support a determination that a particular drug is generally recognized as safe and effective (GRASE) or a change to a condition of use of a drug is GRASE may vary, not all of the information described in this guidance may be relevant to each particular OMOR.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

[1] This guidance has been prepared by the Office of Nonprescription Drugs in the Center for Drug Evaluation and Research at the Food and Drug Administration.

[2] Under section 505G(q)(3) of the FD&C Act, the term *requestor* refers to any person or group of persons marketing, manufacturing, processing, or developing an OTC monograph drug.

[3] An OMOR is a request for an order submitted under section 505G(b)(5) of the FD&C Act. See also section 744L(7) of the FD&C Act.

II. BACKGROUND

Section 505G to the FD&C Act (21 U.S.C. 355h) sets forth the framework for the regulation of OTC monograph drugs. OTC monograph drugs may be marketed without an approved drug application under section 505 of the FD&C Act (21 U.S.C. 355) if they meet the requirements of section 505G of the FD&C Act, as well as other applicable requirements.

Under the process set forth in section 505G(b) of the FD&C Act, FDA has the authority to issue a final order that adds, removes, or changes GRASE conditions for an OTC monograph drug. Either FDA or a requestor can initiate the order process. A requestor can initiate the order process by submitting an OMOR with respect to certain drugs, classes of drugs, or combinations of drugs.[4] The OMOR may request issuance of an order determining the following: (1) whether a drug is GRASE or (2) whether a change to a condition of use of a drug is GRASE.[5]

The OMOR must be submitted to FDA in the form and manner specified by the Agency.[6] FDA will file the OMOR if FDA determines that the OMOR is sufficiently complete and formatted to permit FDA to conduct a substantive review.[7]

III. THE COMMON TECHNICAL DOCUMENT FORMAT AND CONTENT FOR AN OMOR

OMORs must be submitted in electronic format.[8] OMORs should follow the organizational structure and format outlined in the Common Technical Document (CTD) for the Registration of Pharmaceuticals for Human Use.[9]

An OMOR should be organized into five modules as follows:

- Module 1: Administrative Information
- Module 2: Summaries
- Module 3: Quality

[4] See section 505G(b)(5) of the FD&C Act.

[5] See section 505G(b)(5)(B) of the FD&C Act.

[6] See section 505G(b)(5)(B)(i) of the FD&C Act.

[7] See section 505G(b)(5)(A) of the FD&C Act.

[8] See section 505G(j) of the FD&C Act. See also the guidance for industry *Providing Over-the-Counter Monograph Submissions in Electronic Format* (July 2024), which provides information on how to electronically submit an OMOR. We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[9] The CTD format was developed by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) to streamline the submission requirements for Japan, the European Union, and the United States.

- Module 4: Nonclinical Study Reports
- Module 5: Clinical Study Reports

A. General Considerations

The CTD is designed for multiple types of regulatory applications. The CTD is sufficiently flexible to accommodate the types and sources of information that may be included in OMORs. FDA has issued guidance documents specific to CTD[10] for organizing certain applications that will be submitted to FDA. The recommendations provided in these guidance documents are also applicable to OMORs. Although, in general, requestors should follow the recommendations provided in previously issued CTD guidance documents, this guidance highlights additional format and content recommendations specific to OMORs.

The type and quantity of data and information capable of demonstrating that a drug or change to a condition of use of a drug is GRASE is specific to each OMOR. For example, the type and quantity of the data and information may vary depending on the request and whether the OMOR is a Tier 1 OMOR[11] or a Tier 2 OMOR.[12] Therefore, an OMOR may not include all the information identified for certain modules, section headings, or subsection headings described in this guidance or other CTD guidance documents if it is not applicable to that specific OMOR. In those circumstances, the requestor should indicate that no information is being submitted for a given module, section heading, or subsection heading.

Because the type and quantity of data and information to support a GRASE determination is specific to each OMOR, FDA encourages requestors to request a formal meeting with FDA to discuss the overall data recommendations before the initiation of an OMOR development program and during the course of the OMOR development program.[13] FDA also encourages requestors to request a meeting with FDA before the submission of an OMOR.

Upon submission, the OMOR must be sufficiently complete and formatted to permit FDA to conduct a substantive review.[14] In addition, the OMOR should include the relevant data and

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[10] For guidances for industry that address CTD, see the FDA guidance web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm. At this time, submission of OMORs should not be done through the electronic CTD (eCTD), which is the standard format for electronic regulatory submissions for NDAs, ANDAs, certain BLAs, and certain investigational new drug applications. See the guidances for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* (September 2024) and *Providing Regulatory Submissions in Electronic Format — Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act* (December 2014). See also section 745A(a) of the FD&C Act (21 U.S.C. 379k-1(a)).

[11] See section 744L(8) of the FD&C Act.

[12] See section 744L(9) of the FD&C Act.

[13] See the guidance for industry *Formal Meetings Between FDA and Sponsors or Requestors of Over-the-Counter Monograph Drugs* (July 2026).

[14] See section 505G(b)(5)(A) of the FD&C Act.

information even if they were previously submitted to FDA (e.g., as part of a new drug application (NDA) or an abbreviated new drug application (ANDA)). The OMOR should provide, not cross-reference, any such data or information previously submitted to FDA, except when referencing a drug master file (DMF).[15]

B. Module 1: Administrative Information

Module 1 should contain all administrative information, including the documents described below, if applicable. See also section III.A, General Considerations.

1. Format

Module 1: Administrative Information should contain six sections in the following order:

1.1 Table of Contents
1.2 Cover Letter
1.3 Administrative Information
1.4 References
1.6 Meetings
1.14 Labeling

2. Content

a. Table of contents

An OMOR should have a comprehensive table of contents for the entire submission. The comprehensive table of contents significantly enhances the usefulness of the document. It should include a complete list of all documents provided in the submission by module.

b. Cover letter

In general, the cover letter should contain pertinent information that aids communication regarding the review of the OMOR. At minimum, the cover letter should address the following:

- Indicate the applicable OTC monograph or request and rationale for creation of a new OTC monograph.

- Describe the change(s) to the OTC monograph condition(s) being proposed in the OMOR.

[15] For more information on DMFs, see the draft guidance for industry *Drug Master Files* (October 2019). When final, this guidance will represent the FDA's current thinking on this topic.

- Indicate the proposed classification of the OMOR as a Tier 1 or Tier 2 OMOR.[16]
- Provide the name and the full contact information of the requestor(s).
- Indicate the OMOR submission date.
- Provide information about the proposed OTC monograph condition, including active ingredient(s), pharmacological class, intended use, strength, specific dosage form, route of administration, directions for use, and any other pertinent information.
- Describe the data and information included in the OMOR to support the proposed change to the OTC monograph condition.
- Provide a certification that the requestor has submitted all evidence, both positive and negative, related to whether the drug or change to the condition or conditions of use of the drug that are the subject of the OMOR are GRASE.[17]
- Indicate whether the requestor is seeking market exclusivity under section 505(G)(b)(5)(C) of the FD&C Act for a change subject to a final order and provide the rationale.
- Indicate whether FDA reviewed any protocols or held formal meetings with the requestor during the development of the OMOR and, if so, indicate the date(s).
- Provide a statement listing the approximate size of the electronic submission (e.g., 2 gigabytes) and a statement that the submission is virus-free with a description of the software (name, version, and company) that was used to check the files for viruses.
- Provide the name, title, address, phone, email, and fax, if applicable, of the individual the Agency should contact about issues related to the submission. If there are separate regulatory and technical points of contact, include this information for both individuals.
- Provide the signatory's name and contact information.

c. Administrative information

Examples of administrative documents and information for inclusion in an OMOR include the following:

[16] This information is relevant to the requirements under sections 505G(b)(5)(A)(i) and 505G(b)(5)(C)(iv)(II) of the FD&C Act.

[17] See the Over-the-Counter Monograph User Fee Program Performance Goals and Procedures — Fiscal Years 2026–2030 document, which discusses content and format of OTC monograph submissions. The document can be accessed at https://www.fda.gov/media/182750/download.

- U.S. agent letter of appointment, if applicable.[18]

- An environmental assessment[19] or a claim of categorical exclusion[20] with a justification for the exclusion. A claim of categorical exclusion must (1) "include a statement of compliance with the categorical exclusion criteria" and (2) "state that to the applicant's knowledge, no extraordinary circumstances exist."[21]

- A financial certification (Form FDA 3454) and a financial disclosure (Form FDA 3455), if applicable.[22]

- Statement of claimed exclusivity.

d. References

The References section should include the following information, as applicable:

- Letter of authorization. If providing reference to information owned by a third party, (such as information in an NDA, ANDA, biologics license application (BLA), or DMF), the requestor should include letter(s) of authorization by the owner(s) of information giving authorization for the information to be used by the requestor in connection with the OMOR.[23]

- Statement of right of reference. If providing reference to a third party's NDA, ANDA, BLA, or DMF, the requestor should include a statement indicating the NDA, ANDA, BLA, or DMF to which the requestor has a right of reference and identify the section or sections of the OMOR for which the letter(s) of authorization are relevant.

- Previously submitted information to FDA, including the following:

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[18] If the requestor does not reside or have a place of business in the United States, an agent that resides or maintains a place of business in the United States should countersign the OMOR.

[19] See 21 CFR 25.20.

[20] 21 CFR 25.31.

[21] 21 CFR 25.15(a). See also section V, Environmental Assessment.

[22] 21 CFR 330.10(f); 21 CFR part 54. Form FDA 3454 Certification: Financial Interests and Arrangement of Clinical Investigators and Form FDA 3455 Disclosure: Financial Interests and Arrangements of Clinical Investigators are available on FDA's website Clinical Trial Forms, available at https://www.fda.gov/science-research/clinical-trials-and-human-subject-protection/clinical-trial-forms.

[23] When obtaining the letter of authorization, the requestor should make the owner of the information aware that in general the OTC monograph order process is a public process. Under this order 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. See section VI, Confidential Information.

- Indicate whether the OMOR includes data or information previously submitted to FDA in an NDA or ANDA, or licensed BLA, or cross-references any DMF, including the application or DMF number.[24]

- Indicate whether the OMOR includes relevant data or information previously provided to FDA, such as data submitted in support of another OMOR, public comments submitted on an order, or a citizen petition, including the submission date and file number.[25]

e. Meetings

The Meetings section should contain a listing of all meetings with FDA, including complete copies of meeting background materials and meeting correspondence, pertaining to the specific OMOR. The requestor should identify all meetings that pertain to the specific OMOR, if applicable.

f. Labeling

The Labeling section should include the following:

- An example of proposed labeling that reflects the OTC monograph condition(s) of use proposed in the OMOR

- The proposed OTC monograph that reflects the OTC monograph condition(s) of use proposed in the OMOR

C. Module 2: Summaries

Module 2 should include the summary documents described below, if applicable. See also section III.A, General Considerations.

1. Format

Module 2: Summaries should contain six sections in the following order:[26,27]

[24] The requestor should include in the appropriate module the complete data or information that was previously submitted to FDA if the data or information supports the GRASE determination. The requestor should not simply cross-reference the previously submitted data or information, except when referencing a DMF.

[25] The requestor should provide a complete copy of the previously submitted information in the appropriate module, except when referencing a DMF.

[26] The module numbers are consistent with the CTD hierarchy. Note that some module numbers, section heading, or section subheading in the CTD hierarchy may not be applicable.

[27] Module 2 does not need to include a quality overall summary of all chemistry and manufacturing data included in the submission.

2.1 Table of Contents
2.2 Introduction to the Summary Documents
2.4 Nonclinical Overview
2.5 Clinical Overview
2.6 Nonclinical Written and Tabulated Summaries
2.7 Clinical Summary

2. Content

a. Table of contents

The comprehensive table of contents should list all the documents provided in the OMOR for Modules 2 through 5.

b. Introduction to the summary documents

The Introduction to the Summary Documents section should provide a concise narrative summary of (1) the positive safety and effectiveness data supporting a determination that a specific drug, class of drugs, or combination of drugs with the proposed active ingredient or other condition is GRASE for the intended nonprescription use and (2) the negative safety and effectiveness data that are not supportive of a determination that the specific drug, class of drugs, or combination of drugs or other condition is GRASE. The introduction should clearly identify and address each of the major topics addressed in the submission. The introduction should include a summary table listing all studies included in the submission with their corresponding titles (as they appear in the study reports), study numbers, and location in the submission. There should be one clearly identified study number for each study submitted.

c. Nonclinical overview

The Nonclinical Overview section should present an integrated and critical assessment of the pharmacological, pharmacokinetic, and toxicological evaluation of the active ingredient or other conditions. Where relevant guidances on the conduct of studies exist, requestors should take these guidances into consideration and discuss any deviation from the recommendations in these guidances. The nonclinical testing strategy should be discussed and justified. There should be comments on the good laboratory practice status of the studies submitted, taking into consideration which studies are pivotal to support the safety of the active ingredient. Requestors should indicate any association between nonclinical findings and the quality assessment, the results of clinical studies, or the effects seen with related drug products or ingredients, as appropriate.

For content and structural format recommendations for the Nonclinical Overview section for an OMOR, refer to the ICH guidance for industry *M4S: The CTD — Safety* (August 2001).

d. Clinical overview

The Clinical Overview section should present an integrated and critical assessment of all the clinical data included in the OMOR (e.g., clinical effectiveness studies, biopharmaceutics, clinical pharmacology data, safety studies, consumer studies, and postmarketing safety data). The Clinical Overview section should provide the rationale for the OTC monograph drug development program and a succinct discussion and interpretation of the clinical findings together with any other relevant information (e.g., pertinent nonclinical data or drug product quality issues that may have clinical implications) necessary to present the conclusions and implications of the data. The Clinical Overview section should (1) present the strengths and limitations of the OTC monograph drug development program and study results, (2) analyze the benefits and risks of the conditions proposed in the OMOR for the OTC monograph drug for its intended use, and (3) describe how the study results support critical parts of the labeling.

For content and format recommendations for the Clinical Overview section for an OMOR, refer to the ICH guidance for industry *M4E(R2): The CTD — Efficacy* (July 2017).

e. Nonclinical written and tabulated summaries

The Nonclinical Written and Tabulated Summaries section should provide data summaries, not a complete exposition. Only in unusual cases should the narrative parts of the Nonclinical Overview section be the same as the summaries found in the nonclinical study reports in Module 4. In general, the narrative parts of the Nonclinical Written and Tabulated Summaries section should be different from those in the Nonclinical Overview section.

For recommendations on general presentation of this section such as the order of presentation of information within each section, use of tables and figures, length of written nonclinical summaries, and sequence of written summaries and tabulated summaries, refer to the ICH guidance for industry *M4S: The CTD — Safety*.

Nonclinical written summaries

The nonclinical written summaries should include a narrative summary of all the nonclinical data included in the submission. This includes nonclinical pharmacology, pharmacokinetics, and toxicology data.

For recommendations on the content for each nonclinical written summary, refer to the ICH guidance for industry *M4S: The CTD — Safety*. Requestors should modify the format, if needed, to provide the best possible presentation of the information and to facilitate the understanding and evaluation of the results.

Nonclinical tabulated summaries

Requestors should follow the order of presentation given for the nonclinical written summaries for the preparation of the tables for the nonclinical tabulated summaries.

For the recommended formats for summary tables for the nonclinical information submitted in an OMOR, refer to the ICH guidance for industry *M4S: The CTD — Safety*.

For the recommended formats for the tables in the nonclinical tabulated summaries, refer to Appendices B and C in the ICH guidance for industry *M4S: The CTD — Safety Appendices* (August 2001). However, requestors should use the format that provides the best presentation of the information and to facilitate the understanding and evaluation of the results.

f. Clinical summary

The Clinical Summary section should provide a detailed, factual summary of all of the clinical information in the OMOR. This includes information provided in clinical study reports; information provided in consumer study reports; information obtained from any meta-analyses or other cross-study analyses for which full reports have been included in Module 5; and postmarketing data for drugs that have been marketed in the United States or in other regions, including data from both the prescription and nonprescription settings. When summarizing postmarketing data for drugs that have been marketed in the nonprescription setting in other regions, the requestor should provide the regulatory status of the drug for each region, including information about whether there are limitations or restrictions on access (e.g., pharmacy only, pharmacist only, general sales).

For recommendations on the content and format for each subsection in the Clinical Summary section, refer to ICH M4E(R2).

D. Module 3: Quality Data

Module 3 should include relevant quality information, provided in the order described below. See also section III.A, General Considerations.

1. Format

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

3.1 Table of Contents[28]
3.2 Body of Data
3.3 Literature References

For recommendations on the format of information in Module 3 and its organizational placement within the module, refer to the ICH guidances for industry *M4Q: The CTD — Quality* (August 2001) and *M4: The CTD — Quality Questions and Answers/Location Issues* (June 2004).[29]

[28] The table of contents for Modules 3 should list all the documents provided in Module 3.

[29] We note the publication of the ICH draft guidance for industry *M4Q(R2) The Common Technical Document for the Registration of Pharmaceuticals for Human Use: Quality* (January 2026) that revises previous recommendations on the format and organization of the quality information to include in Modules 2 and 3 of the Common Technical Document. When final, this guidance will represent the FDA's current thinking on this topic.

2. Content

Module 3 should include quality information as described in section III.D for the proposed active ingredient and the drug product formulated using that active ingredient, as applicable. Such content should be appropriate for the nature of the request. Accordingly, this guidance recommends including only a subset of the information described in ICH M4Q. The quality information should be provided in the OMOR or, where applicable, be incorporated in the OMOR by reference to a DMF with a letter of authorization.[30]

Module 3 should include quality information about the active ingredient and the drug product incorporating that active ingredient in the dosage form consistent with the OTC monograph condition(s) proposed in the OMOR. Information about a drug product that incorporates the active ingredient can be important to support the OMOR, such as demonstrating that the active ingredient can be mixed with safe and suitable inactive ingredients[31] and maintain the integrity of the intended dosage form described in the proposed condition. Similarly, information about how the active ingredient and drug product are manufactured provides insight into factors such as the complexity of the manufacturing process operations, the need for any novel or proprietary equipment, controls requiring advanced analytical technology, or other aspects of the process that might not be readily replicated by other sponsors of OTC monograph drugs.

a. Active ingredient[32]

Quality information on the active ingredient that should be provided to support an OMOR includes, but is not limited to, how the active ingredient is manufactured and important quality attributes, such as the synthetic scheme, process controls, specifications, stability data, and compendial status.

- Synthetic scheme

[30] See section III.B.2.d, References, for information on a letter of authorization. When obtaining the letter of the authorization, the requestor should make the owner of the information aware that in general the OTC monograph order process is a public process. Under this order 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. See section VI, Confidential Information.

[31] A drug product marketed in conformance with section 505G of the FD&C Act must contain only suitable inactive ingredients which are safe in the amounts administered and do not interfere with the effectiveness of the preparation or with suitable tests or assays to determine if the product meets its professed standards of identity, strength, quality, and purity (21 CFR 330.1(e)).

[32] FDA's regulations define the term *active ingredient* as any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or other animals. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect (21 CFR 210.3(b)(7)).

- A flow diagram of the synthetic processes, including molecular formulas, chemical structures of starting materials, intermediates, reagents, and active ingredient reflecting stereochemistry, that identifies operating conditions and solvents.

- Process controls

  - A description of the manufacturing process and process controls, including the following:

    - Control of materials: This includes a tabulated list of materials used in the manufacture of the active ingredient (e.g., raw materials, starting materials, solvents, reagents, catalysts), identifying where each material is used in the process.

    - Control of critical steps and intermediates:

      - Tests and acceptance criteria performed at critical steps
      - Information on the quality and control of isolated intermediates, if applicable

- Specifications

  - The specifications, including a list of tests, analytical procedures, and acceptance criteria, for the active ingredient. Alternatively, a certificate of analysis containing a list of tests, acceptance criteria, and results for the active ingredient, along with a method validation report for the analytical procedures to demonstrate adequacy of the data provided in the certificate of analysis. For more information, see ICH guidances for industry *Q6A Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances* (December 2000), *Q3A(R2) Impurities in New Drug Substances* (June 2008), and *M7(R2) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk* (July 2023).

- Stability

  - Stability data to support an established retest date or shelf life of the active ingredient. For further information, see the ICH guidances for industry *Q1A(R2) Stability Testing of New Drug Substances and Products* (November 2003) and *Q1B Photostability Testing of New Drug Substances and Products* (March 1996).[33]

- Compendial status

[33] We note the publication of the ICH draft guidance for industry *Q1 Stability Testing of Drug Substances and Drug Products* (June 2025) that revises the Q1 series of ICH guidelines into a single guideline. When final, this guidance will represent the FDA's current thinking on this topic.

- The compendial status of the active ingredient(s) in the United States Pharmacopeia and National Formulary(USP-NF).

- For active ingredients without a USP monograph, requestors should include an update on any submission of a proposed monograph to USP in their OMOR. Requestors are encouraged to provide to USP detailed information regarding the active ingredient or ingredients sufficient to support development of a USP monograph.

b. Drug product[34]

The requestor should provide quality information for the drug product containing the proposed active ingredient in the dosage form consistent with the OTC monograph condition(s) proposed in the OMOR, if applicable. Relevant drug product information serves as a way to confirm that the active ingredient can be incorporated into a finished product manufactured using readily available processes and controls, such that products made under the proposed OTC monograph, if finalized, would be consistently safe and effective. Such information should include the composition, manufacturing process, process controls, specifications, and stability data.

- Composition

  - A list of all ingredients in the proposed drug product and their amount on a per-unit basis.

  - Information on the inactive ingredients, including justification for their use, their concentration, their compatibility with the active ingredient, their function (along with the characteristics that can influence drug product performance), and their applicable compendial standards.

- Manufacturing process

  - A flow diagram with the steps of the process and indicating where materials enter the process.

  - A narrative description of the manufacturing process, including packaging, that represents the sequence of steps undertaken and the scale of production. Requestors should describe novel processes or technologies and packaging operations that directly affect product quality with a greater level of detail. Requestors should, at a minimum, identify equipment by type (e.g., tumble blender, in-line homogenizer) and working capacity, where relevant.

- Process controls

[34] FDA's regulations define the term *drug product* to mean a finished dosage form, for example, tablet, capsule, solution, etc., that contains an active drug ingredient generally, but not necessarily, in association with inactive ingredients. The term also includes a finished dosage form that does not contain an active ingredient but is intended to be used as a placebo (21 CFR 210.3(b)(4)).

- The critical steps and points at which process controls, in-process tests, or final product controls are conducted should be identified.

- A description of process controls, including the following:

  - Control of critical steps: Tests and acceptance criteria performed at critical steps of the manufacturing process to ensure that the process is controlled.

  - Control of in-process materials: Information on the quality and control of in-process materials isolated during the process.

- Specifications

  - The specifications, including a list of tests, analytical procedures, and acceptance criteria, for the drug product that incorporates the proposed active ingredient. Alternatively, a certificate of analysis containing a list of tests, acceptance criteria, and results for the drug product that incorporates the proposed active ingredient, along with a method validation report for the analytical procedures to demonstrate adequacy of the data provided in the certificate of analysis. For more information, see ICH Q6A.

- Stability

  - Data to characterize the initial stability of the drug product (e.g., to demonstrate that the active ingredient will not aggregate, that the formulation does not show early signs of instability). Requestors should include data from testing of a drug product OTC monograph condition(s) proposed in the OMOR (final release testing), including stability data on an aged product after 3 months and 6 months. Requestors should summarize the types of studies conducted, protocols used, and the results of the studies. Requestors should present the results of the stability studies in an appropriate format such as tabular, graphic, or narrative. Requestors should include information on the analytical procedures used to generate the data. For further information, see ICH Q1A(R2), ICH Q1B, and the ICH guidance for industry *Q1C Stability Testing for New Dosage Forms* (November 1996).[35]

E. Module 4: Nonclinical Study Reports

Module 4 should contain the nonclinical study reports and related information provided in the order described below, if applicable. See also section III.A, General Considerations.

[35] We note the publication of ICH Q1, which revises the Q1 series of ICH guidelines into a single guideline.

1. Format

Module 4: Nonclinical Study Reports should be organized according to the following general section outline:

4.1 Table of Contents[36]
4.2 Study Reports
4.3 Literature References

For additional information on the structural format and organization of nonclinical study reports that may be helpful in preparing an OMOR, refer to the ICH guidance for industry *M4S: The CTD — Safety*.

2. Content

Module 4 should include data and reports from the nonclinical studies.

a. Nonclinical studies

The nonclinical studies that may be used to support an OMOR include the following: (1) pharmacology studies, (2) general toxicity studies, (3) toxicokinetic and nonclinical pharmacokinetic studies, (4) reproduction toxicity studies, (5) genotoxicity studies, and (6) an assessment of carcinogenic potential. Requestors should conduct other nonclinical studies, including those to assess phototoxicity, immunotoxicity, potential pediatric toxicity, and abuse liability on a case-by-case basis.

Module 4 should focus on nonclinical information on the active ingredient and specified impurities in the drug substance.[37] See the ICH guidance for industry *M3(R2) Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals* (January 2010), which provides recommendations on nonclinical safety studies and their relation to the conduct of human clinical studies.

Whether the studies are appropriate to qualify a drug substance impurity will depend on a number of factors, including the patient population, daily dose, route of administration, and duration of use. For more information, see ICH Q3A(R2), ICH M7(R2) and FDA's guidance on nitrosamine impurities[38] regarding qualification of DNA-reactive and carcinogenic impurities.

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[36] The table of contents for Modules 4 should list all the documents provided in Module 4.

[37] Specified impurity means an impurity that is individually listed and limited with a specific acceptance criterion in the new drug substance specification. A specified impurity can be either identified or unidentified. See ICH Q3A(R2).

[38] See the guidances for industry *Control of Nitrosamine Impurities in Human Drugs* (September 2024) and *Recommended Acceptable Intake Limits for Nitrosamine Drug Substance-Related Impurities* (NDSRIs) (August 2023). See also FDA's web page titled CDER Nitrosamine Impurity Acceptable Intake Limits, available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cder-nitrosamine-impurity-acceptable-intake-limits.

See also the recommendations in section III.F, Module 5: Clinical Study Reports, regarding potential clinical qualification methods.

We recommend that requestors request a meeting with FDA to discuss information related to drug substance impurities or the use of new approach methodologies[39] so that the appropriate studies can be conducted and submitted in an OMOR to support a GRASE determination.

b. Individual study reports

Each individual nonclinical study report should include its own table of contents and summary. Requestors should include complete datasets (not selected or summary data) in the submission.[40] Data from studies provided only in summary form may not be sufficiently informative to support a determination that the condition is GRASE.

F. Module 5: Clinical Study Reports

Module 5 should contain the clinical study reports and related information provided in the order described below, if applicable. See also section III.A, General Considerations.

1. Format

Module 5: Clinical Study Reports should be organized according to the following general section outline:

5.1 Table of Contents[41]
5.2 Tabular Listing of All Clinical Studies
5.3 Clinical Study Reports
5.4 Literature References

For recommendations on the specific organization and placement of clinical study reports and related information in Module 5, refer to ICH M4E(R2).

2. Content

Module 5 in the OMOR should include the following: (1) full clinical study reports of all clinical effectiveness and safety studies and other clinical data, (2) full clinical study reports of all

[39] See the draft guidance for industry *General Considerations for the Use of New Approach Methodologies in Drug Development* (March 2026). When final, this guidance will represent the FDA's current thinking on this topic.

[40] Although Standard for Exchange of Nonclinical Data datasets and CTD tables are not required for OMORs, we recommend that requestors submit both datasets and tables in their submissions to facilitate review of the data. See the FDA Data Standards Advisory Board web page at https://www.fda.gov/industry/fda-resources-data-standards.

[41] The table of contents for Modules 5 should list all the documents provided in Module 5.

clinical pharmacology and human pharmacokinetic data,[42] (3) full clinical study reports of all consumer studies, and (4) full reports of the postmarketing experience. In addition, the requestor should include all other types of clinical data (e.g., from literature searches, scientific articles, other published materials) in this module.[43]

a. Clinical studies and related information

For recommendations on the types of clinical studies and related information that can be included in Module 5 of an OMOR, refer to ICH M4E(R2).[44]

In addition to the clinical studies referenced in ICH M4E(R2), requestors may need to include consumer study reports or information demonstrating prima facie safe nonprescription marketing and use[45] in Module 5 of the OMOR.

Consumer Studies

Although not all consumer studies are clinical studies, all consumer study reports should be included in Module 5. Consumer studies may include label comprehension studies,[46] self-selection studies,[47] actual use studies, and human factors studies.[48]

Safe nonprescription marketing and use

Some OMORs may request that a drug be found GRASE, where that drug is a nonprescription drug that contains an active ingredient not previously incorporated in a drug that is (1) specified in section 505G(a)(1), (a)(2), or (a)(3) of the FD&C Act; (2) subject to a final order under section 505G(b) of the FD&C Act; or (3) subject to a final sunscreen order (as defined in section

[42] See the guidance for industry *Maximal Usage Trials for Topically Applied Active Ingredients Being Considered for Inclusion in an Over-The-Counter Monograph: Study Elements and Considerations* (May 2019) and the ICH guidance for industry *M12 Drug Interaction Studies* (August 2024).

[43] Requestors should include a hyperlink to a full copy of the referenced article or other referenced published material. If the scientific article or other published material is not accessible online, the requestor should include a complete copy in the submission.

[44] In addition, regarding drug substance impurities, whether previous human experience is appropriate for qualification will depend on a number of factors, including the target population, daily dose, route of administration, and duration of use. See ICH Q3A(R2) and ICH M7(R2), the latter regarding qualification of DNA-reactive and carcinogenic impurities. If a requestor proposes to use information on previous human experience to support a proposed drug substance impurity specification, evidence, such as batch data of impurity levels in the drug products to which humans were exposed, should be submitted to support that the previous human experience involved exposure to levels of impurities that are equal to or greater than the proposed specification.

[46] See the guidance for industry *Label Comprehension Studies for Nonprescription Drug Products* (August 2010).

[47] See the guidance for industry *Self-Selection Studies for Nonprescription Drug Products* (April 2013).

[48] See the guidance for industry and FDA staff *Application of Human Factors Engineering Principles for Combination Products: Questions and Answers* (September 2023).

586(2)(A) of the FD&C Act (21 U.S.C. 360fff)).[49] For such an OMOR to be filed, it must include certain information demonstrating prima facie safe nonprescription marketing and use, further described below.[50] The required information should be presented in Module 5.

Specifically, to satisfy the applicable statutory requirement, the OMOR must include one of the following:

1) Information sufficient for a prima facie demonstration that the drug has a verifiable history of being marketed and safely used by consumers in the United States as a nonprescription drug under comparable conditions of use.[51]

2) 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 (21 U.S.C. 382(b)(1)(A)) or designated by FDA in accordance with section 802(b)(1)(B) of the FD&C Act if the drug has not been previously marketed in the United States as a nonprescription drug.[52] The time period of marketing and use must provide reasonable assurances concerning the safe nonprescription use of the drug,[53] and during that time, the drug must have been subject to sufficient monitoring by a regulatory body considered acceptable by FDA for such monitoring, including for adverse events associated with nonprescription use of the drug.[54]

3) Other information FDA determines is sufficient for such purposes if FDA determines that information described in 1 or 2 above is not needed to provide a prima facie demonstration that the drug can be safely marketed and used as a nonprescription drug.[55]

[49] See section 505G(b)(6)(B) of the FD&C Act. We note that there are no final sunscreen orders as defined in section 586(2)(A) of the FD&C Act. That provision ceased to be effective at the end of fiscal year 2022, pursuant to section 586H of the FD&C Act. Prior to its sunset, no orders issued that meet its definition, which is limited to final orders reaching a positive conclusion. See Section 586(2)(A) ("the term ''final sunscreen order'' means an order published by the Secretary in the Federal Register containing information stating that a nonprescription sunscreen active ingredient or combination of nonprescription sunscreen active ingredients— (A) is GRASE and is not misbranded if marketed in accordance with such order".)

[50] See sections 505G(b)(6)(A) and 505G(b)(6)(C) of the FD&C Act.

[51] See section 505G(b)(6)(C)(i) of the FD&C Act.

[52] See section 505G(b)(6)(C)(ii) of the FD&C Act.

[53] See section 505G(b)(6)(C)(ii)(I) of the FD&C Act.

[54] See section 505G(b)(6)(C)(ii)(II) of the FD&C Act.

[55] See section 505G(b)(6)(C)(iii) of the FD&C Act.

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.[56]

b. Reports of postmarketing experience

For drug products or active ingredients that are currently marketed, Module 5 should include reports that summarize the marketing experience relevant to the OTC monograph condition proposed in the OMOR, including detailed information for relevant safety observations.

Module 5 should include all relevant postmarketing data available to the requestor (published and unpublished, including periodic safety update reports if available). The requestor should provide in Module 5 a tabulation of serious adverse events reported after the drug is marketed, including any potentially serious drug interactions. The requestor should describe any postmarketing findings in subgroups. The requestor should provide safety information from various safety databases such as the FDA Adverse Event Monitoring System, World Health Organization VigiBase, American Association of Poison Control Centers, another country's or region's safety database, or a requestor's (or their affiliate's) safety database.

If data are available for different combinations of active ingredients, different doses, different dosage forms, significantly different formulations, or different populations of use, the requestor should provide separate tabular summaries in Module 5.

The reports of postmarketing experience should include discussions and analyses of the postmarketing data along with the conclusions and implications of the data as it pertains to the OTC monograph condition proposed in the OMOR. The reports should also include any relevant safety discussions and analyses from the literature, if available.

Reports that are heavily redacted or do not provide clear drug product identification are unlikely to provide useful information.

c. Individual study reports

Each individual clinical study report should include its own table of contents and summary. The requestor should identify the drug products used in the study and include complete subject-level datasets (not selected or summary data). Each study should have its own datasets for efficacy and safety data, and there should be integrated datasets for safety and, if applicable, integrated datasets for efficacy. In general, we expect that data from studies provided only in summary form will not be sufficiently informative to support a conclusion that a drug, class of drugs, or combination of drugs is GRASE for the intended nonprescription use.

Each individual study should describe the statistical evaluation of clinical data (e.g., information concerning the description and analysis of each controlled clinical study and the documentation and supporting statistical analyses used in evaluating the controlled clinical studies; information

[56] See section 505G(b)(6)(A) of the FD&C Act.

concerning a summary of information about the safety of the drug, the documentation and supporting statistical analyses used in evaluating the safety information).

Each individual study report should include all necessary appendices including, but not limited to, study information (e.g., full protocols and protocol amendments, list of all independent ethics committees or institutional review boards consulted, documentation of statistical methods), patient data listings, and case report forms.

For additional guidance on the structure and content of clinical study reports, refer to the ICH guidance for industry *E3 Structure and Content of Clinical Study Reports* (July 1996).

IV. OTHER CONSIDERATIONS FOR AN OMOR

A. Language

The OMOR should be in the English language. If any portion of a submission is in a foreign language, the requestor should provide a complete and accurate English translation, including English translations of any references.

B. Fonts

Font size for text and tables should be of a style and size that is large enough to be easily legible, even after photocopying or when provided electronically. We recommend that narrative text be submitted in Times New Roman 12-point font. Generally, font sizes 9 to 10 points are considered acceptable in tables, but requestors should avoid fonts smaller than 12 points whenever possible. When choosing a font size for tables, it is important to balance the desirability of providing sufficient information on a single page to facilitate data comparisons with that of maintaining a font size that remains readable. If the font size is too large, data comparisons may be complicated because data may be presented in multiple tables. We recommend 10-point font for footnotes.

C. Paper Size

Generally, the requestor should format an OMOR to standard U.S. letter size paper (8.5 by 11 inches). Occasionally, a requestor may format individual pages larger than standard paper size to present a floor plan, synthesis diagram, batch formula, or manufacturing instructions.

D. Pagination

Page numbering should be at the document level and not at the module level. The entire submission should never be numbered consecutively by page. In general, all documents should have page numbers. Because the page numbering is at the document level, there should only be one set of page numbers for each document.

If the OMOR includes a document within a document, such as a protocol within a study report, the document to be included (in this case, the protocol) should be attached as an appendix.

E. OMOR Searchability

The entire OMOR submission should be electronically searchable. An OMOR should not contain nonsearchable text or images.

F. Hyperlinks to References

All items in reference lists and all in-text references citing scientific articles or other published materials should include a hyperlink to a full copy of the referenced article or other referenced published material. Requestors should place hyperlinks to scientific articles and other published materials in the relevant sections by subject.

V. ENVIRONMENTAL ASSESSMENT

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. FDA complies with NEPA by evaluating environmental impacts of agency action, such as decisions on applications or petitions, as a part of its regulatory process.

FDA's regulations in 21 CFR part 25 specify that environmental assessments (EAs) must be submitted as part of applications or petitions that request FDA action, unless the action qualifies for categorical exclusion.[57] Because an OMOR is a request for agency action analogous to an application or petition, the requestor must accompany such a request with either an EA or a claim of categorical exclusion. A claim of categorical exclusion must include a statement that to the applicant's knowledge, no extraordinary circumstances exist.[58]

Regulation 21 CFR 25.31 sets forth the classes of actions related to human drugs and biologics that are subject to categorical exclusions and, therefore, ordinarily do not require the preparation

[57] 21 CFR 25.15(a).

[58] Id. As stated in 21 CFR 25.15, "all applications or petitions requesting agency action require the submission of an EA or a claim of categorical exclusion." Under 21 CFR 25.31, the same categorical exclusion criteria apply to "actions on OTC monographs" as apply to applications like NDAs and ANDAs. See the final rule, "National Environmental Policy Act; Revision of Policies and Procedures" (NEPA final rule), published July 29, 1997 (62 FR 40570 at 40578). It follows that the requirement to submit an EA, when not categorically excluded, would similarly apply to requests for actions on OTC monographs. FDA "will treat like actions alike, regardless of the avenue through which the actions are requested" (NEPA final rule at 40578).

of an EA. Barring extraordinary circumstances,[59] the OMORs described below each would have a claim of categorical exclusion:

- The OMOR does not propose to increase the use of the active moiety.[60]
- The OMOR proposes to increase the use of the active moiety, but the estimated concentration of the substance at the point of entry into the aquatic environment will be below 1 part per billion.[61]
- The OMOR is for a substance that occurs naturally in the environment, and the OMOR does not propose to alter significantly the concentration or distribution of the substance, its metabolites, or degradation products in the environment.[62]

If none of these categorical exclusions apply, then the requestor must prepare an EA that addresses the relevant environmental issues and must include the EA in the OMOR.[63] 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.[64]

Requestors must comply with the requirements as set forth in 21 CFR 25. In addition, requestors should refer to the guidances for industry *Environmental Assessment of Human Drug and Biologics Applications* (July 1998) and *Environmental Assessment: Questions and Answers Regarding Drugs With Estrogenic, Androgenic, or Thyroid Activity* (March 2016) for general recommendations on how to prepare EAs for submission.[65]

VI. CONFIDENTIAL INFORMATION

In general, the OTC monograph order process is a public process. Under this order 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.

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[59] As described in 21 CFR 25.21, an EA is required for an action that ordinarily would be excluded if certain extraordinary circumstances indicate that the proposed action may significantly affect the quality of the human environment. When "extraordinary circumstances" exist, then the requestor of an OMOR that otherwise would be categorically excluded is required to submit an EA consistent with 21 CFR 25.21.

[60] 21 CFR 25.31(a).

[61] 21 CFR 25.31(b).

[62] 21 CFR 25.31(c).

[63] See 21 CFR 25.15(a), 21 CFR 25.21, and 21 CFR 25.31.

[64] 21 CFR 25.15(a).

[65] For further information, see FDA's website on Environmental Impact Review at CDER, available at https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/environmental-impact-review-cder.

In general, until disclosure is triggered under section 505G(d)(2) of the FD&C Act, any information, including reports of testing conducted on the drug or drugs involved, that is submitted by a requestor in connection with proceedings on an order under section 505G of the FD&C Act and is a trade secret or confidential information subject to 5 U.S.C. 552(b)(4) or 18 U.S.C. 1905 will not be disclosed to the public unless the requestor consents to that disclosure.[66] However, 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.[67] Nonetheless, the information will remain confidential if (1) the information pertains to pharmaceutical quality information, unless such information is necessary to establish standards under which a drug is GRASE; (2) the information is of the type contained in raw datasets; (3) the information is submitted in a requestor-initiated request, but the requestor withdraws the request in accordance with withdrawal procedures established by FDA 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) of the FD&C Act.[68]

[66] See section 505G(d)(1) of the FD&C Act.

[67] See section 505G(d)(2)(A)(i) of the FD&C Act.

[68] See section 505G(d)(2)(B) of the FD&C Act.

Guidance History*	Date	Description
Level 1 Final Guidance	November 2026	See notice of availability for more information.**
Level 1 Draft Guidance	April 2023	See notice of availability for more information.

* This table was implemented beginning November 2026, and previous guidance history may not be captured in totality.

** The notice of availability is accessible via the Search for FDA Guidance Documents web page at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.