POLICY AND PROCEDURES

OFFICE OF TRANSLATIONAL SCIENCES
OFFICE OF CLINICAL PHARMACOLOGY

Good Review Practices and Procedures: Clinical Pharmacology Review of New Drug Applications (NDAs) and Biologics License Applications (BLAs)

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PURPOSE

This Manual of Policies and Procedures (MAPP) establishes good review practices (GRPs) for the reviews of new drug applications (NDAs) and biologics license applications (BLAs) in the Office of Clinical Pharmacology (OCP), Office of Translational Sciences (OTS), Center for Drug Evaluation and Research (CDER). In general, the principles outlined herein may also be applicable to other submissions, as appropriate.

This MAPP describes OCP's integrated review procedure to evaluate NDAs and BLAs.

The GRPs and procedures described apply for all templates used to document the review.

BACKGROUND

Clinical pharmacology is a multidisciplinary science. OCP reviews of NDAs and BLAs are expected to synthesize information from all relevant clinical pharmacology knowledge areas, including drug disposition, pharmacology, biomarkers, quantitative methods, drug safety, pharmacotherapy, and clinical trial methods to inform regulatory decisions (e.g., approvability, labeling, and postmarketing requirements (PMRs) or

section 506B of the Federal Food, Drug, and Cosmetic Act postmarketing commitments (PMCs)). For each NDA or BLA submission, staff from various OCP units (divisions, groups, etc.) with expertise in relevant knowledge areas create a review team.[1] Once the review team is formed, team members work collaboratively within and outside of OCP to do the following:

- Identify issues that are important for the review of the application and subsequent regulatory action (including decisions on whether the application can be filed as well as key review questions)
- Assess information in the application along with previously established knowledge to address issues regarding dosage selection and optimization, therapeutic individualization, and benefit/risk balance
- Identify any critical gaps hindering the optimization of therapeutic use and recommend studies that can practically address those gaps
- Provide labeling recommendations for the safe and effective use of the drug or biological product by the health care provider as per regulations and current FDA guidance
- Determine if any PMRs and/or PMCs will be established
- Provide recommendations informed by current scientific thinking and guided by established regulatory policies and practices

This MAPP contains:

- Guiding principles for conducting and documenting OCP reviews
- Guiding questions for OCP reviews
- GRP within OCP

[1] See OCP website at https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/office-clinical-pharmacology, accessed September 22, 2026.

POLICY

The OCP review is based on the following guiding principles:

- Review recommendations and decisions will be clinically relevant, pragmatic, and take into consideration the specific therapeutic context (e.g., nature of disease, size of population, unmet medical need, available treatments). Reviewers will utilize a risk-based approach that incorporates the totality of evidence.

- The following four guiding review questions are important to inform the safe and effective use of all drugs in the general indicated population as well as in specific populations. These questions will be addressed during the clinical pharmacology review (refer to Attachment 1 for more details on the content expected in the response for each of these questions):

    1. To what extent does the available clinical pharmacology information provide evidence of effectiveness?

    2. Is the proposed dosage appropriate for the general patient population for which the indication is being sought?

    3. Is an alternative dosage and/or management strategy required for subpopulations based on intrinsic factors?

    4. Are there clinically relevant food-drug or drug-drug interactions, and what are the appropriate management strategies?

- Reviewers from different units in OCP with the expertise needed for the particular NDA or BLA submission will work collaboratively to review the submission and incorporate feedback.

- Reviewers will use the most current scientific and regulatory information available to ensure the highest quality reviews.

- Equal voice principles as outlined in MAPP 4151.8 Rev.2 will be employed for collaborative review and regulatory decision-making.

The following describe documentation principles:

- The OCP review team will use the review templates that are agreed upon by the CDER review team.

- Important findings and recommended regulatory actions will be clearly and succinctly communicated in reviews. The review will logically guide the reader through the thought process used to identify and address scientific, clinical, and regulatory questions and issues.

ROLES AND RESPONSIBILITIES

All OCP Review Team Members:

- All members of the OCP review team will work collaboratively and are jointly responsible for the stated OCP positions and recommendations.
- Review team members must participate in the following three ways to be listed as signatories:
    - Contribute to the formulation and/or design of the review questions, approach to addressing the review questions, and/or the analysis and interpretation of the data.
    - Draft the review or critically revised it for important content.
    - Approve the final version of the review to be entered into the regulatory record.
- Review teams consist of staff from various units in OCP, depending on the type of knowledge needed for the review. These areas may include drug- and disease-related clinical pharmacology, pharmacometrics, genomics and other biomarkers, pediatrics, biologics, labeling, life cycle management, guidance and policy implementation and development, and regulatory project management. Not all knowledge areas will be needed for every review.

OCP review team roles are listed below.

OCP Regulatory Project Manager:

- OCP Regulatory Project Managers (OCP RPMs) are the regulatory experts for the application. They are responsible for notifying the relevant review divisions within OCP of new molecular entity NDA and original BLA submissions. OCP RPMs coordinate OCP reviewer assignments and communicate the assignments to the Office of New Drugs, Office of Regulatory Operations RPMs (OND/ORO RPMs). OCP RPMs will ensure that appropriate experts, including labeling, pediatrics, life cycle management, as well as experts in biologics programs, guidance, and policy are consulted as required. OCP RPMs are responsible for scheduling and managing the OCP scoping and briefing meetings, capturing minutes of the discussion, and archiving minutes in accordance with current Records Management practices. They provide reviewer tools, templates, and knowledge management, and they promote consistent communication throughout the review of the application.

OCP Primary Reviewers:

- OCP primary reviewers are responsible for assessing information in the submission, analyzing and interpreting data, and completing individual study report reviews or integrated summaries of individual study reviews. The primary reviewers are responsible for authoring their respective parts of the integrated review and jointly communicating the overall OCP recommendations derived from the review. They will participate in internal FDA meetings, external meetings with applicants, and advisory committee meetings.

OCP Lead Author of the Integrated Review:

- The OCP review team will identify the lead author based on the clinical pharmacology issues identified for the submission. The lead author is responsible for integrating information from primary reviews and leading the completion of the issue-based, interdisciplinary review with input from other OCP reviewers. The lead author is usually the lead reviewer representing the OCP team at the CDER multidisciplinary review team meetings. The lead author will also ensure accurate representation of all OCP knowledge areas in the OCP review team in reviews, presentations, and communications related to the application.

OCP Team Lead (TL) and/or Secondary Reviewer:

- The OCP TLs or secondary reviewers are responsible for conducting secondary review to provide scientific and regulatory advice and input to primary reviewers, having appropriate discussions of key review issues, ensuring that a high-quality review is completed within agreed-upon timelines, ensuring that the summary of OCP's findings and regulatory recommendations are comprehensive and clear, and communicating with relevant parties within and outside OCP.

OCP Application TL:

- The OCP application TL is responsible for leading the review and overseeing the integrated review process to ensure overall review efficiency, quality, and consistency. The TLs and/or secondary reviewers work with each other to identify the application TL.

OCP Application Signatory:

- An OCP Division Director or their designee serves as the final review signatory and is responsible for ensuring that the official OCP positions on review issues (e.g., approvability, dosage, labeling, PMRs and/or PMCs) are clearly stated. They are also responsible for ensuring reviews are comprehensive and clearly written. They promote consistency in the review, ensure transparency in the decision-making process, and guide review teams on complicated or precedent-setting review issues that may have policy implications. They interact with OCP senior management, the OCP Director, and other CDER staff to identify issues in a timely manner and resolve them as needed. They will author an OCP Application Signatory Memorandum when situations outlined in PROCEDURES (See bullet 7) occur.

PROCEDURES

1. Reviewers in OCP will adhere to established goal dates.

2. Review teams will follow the most recent and up-to-date OCP Internal Quality Procedures.

3. Regulatory project management staff or other members of the review team should schedule additional formal meetings as needed (e.g., pre-filing meetings to gain alignment on potential filing issues from OCP's perspective, pre-mid-cycle/pre-briefing meetings to discuss clinical pharmacology issues, content, and deliverables before presenting these findings outside OCP).

4. Informal meetings and communication among OCP review team members and other discipline reviewers (e.g., clinical, biostatistics, pharmacology and toxicology, chemistry, manufacturing) are encouraged. Because participation in meetings is issue-based, keeping the entire OCP review team informed of key findings is important throughout the review process. Thus, important review findings that might influence approval or labeling decisions should be discussed among the OCP review team to gain alignment prior to engaging with other members of the CDER review team. Relevant outcomes of interactions with other disciplines outside of OCP that may be relevant to the OCP review should be shared with the rest of the OCP review team.

5. Reviewers in OCP will follow the review principles outlined in the POLICY section when documenting their reviews.

6. Differences in opinions with respect to review and/or process will be resolved among the OCP review team members. For unresolved issues,

Division leadership or the final OCP signatory will resolve the differences together with the review team and document the final decision in accordance with MAPP 4151.8 Rev.1.

7. A separate OCP Application Signatory Memorandum will be written when there is major disagreement within the OCP review team that cannot be resolved during review, when the application signatory does not agree with the final recommendations of the review team, when OCP is taking a precedential or controversial review position, or when the complexity of the review issues necessitates further written communication.

8. All communications with the sponsor will be made through the OND RPM. When questions to the applicant need to be sent in the form of an information request (IR), effort should be made to combine questions and input from all relevant OCP review disciplines.

REFERENCES

1. CDER MAPP 4151.8 Rev.2, Equal Voice: Collaboration and Regulatory and Policy Decision-Making in CDER (2025).

EFFECTIVE DATE

- This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
11/10/2026	Initial	N/A

ATTACHMENT 1: OCP-SPECIFIC ISSUE-BASED REVIEW GENERAL INFORMATION AND TEMPLATE

General Information

The purpose of the review template is to consistently ensure that critical information is presented by OCP review teams in a prioritized, issue-driven, and logical manner. The template provides standardization and consistency in the format and content of clinical pharmacology reviews and ensures that critical presentations and analyses will not be inadvertently omitted. The standardized structure also enables readers to readily locate specific information. As such, headings and subheadings are named, numbered, and ordered as stipulated in the template unless there is a compelling reason not to for a specific application.

Information should generally not be repeated within the review. Reviewers may refer the reader to relevant sections and use hypertext links where appropriate. Text, tables, and figures may be used to summarize information, but redundancy should be avoided. The approach that best ensures clarity and understanding should be used. Proper attribution regarding data sources and analyses is expected. Reviews should be clear as to which assertions, conclusions, and recommendations are those of the applicant and those of the review team. Coherent and concise writing is expected for all draft and final reviews.

The template may be modified by OCP review teams if deemed necessary to ensure clarity and cohesion for a given application; however, this scenario is expected to be a rare occurrence. The content of this template can easily be incorporated into other CDER integrated review team templates as appropriate.

Review Structure

The OCP integrated review consists of four sections. An overview of these four sections with a description of their target audiences is provided in **Table 1**.

- **Section 1. Executive Summary**: Summarizes OCP's position and final recommendations on key regulatory actions (e.g., approvability, dosing, labeling, need for PMR and/or PMC).

- **Section 2. Summary of Clinical Pharmacology Assessment**: Summarizes major clinical pharmacology information and analyses used to address issue-specific review questions.

- **Section 3. Comprehensive Clinical Pharmacology Review**: Contains more detailed information and explains the thought process for clinical pharmacology questions that are relevant to the application.

- **Section 4. Appendixes**: Includes individual study report reviews or integrated summary of individual study reviews, and/or analyses on various clinical pharmacology areas that inform key regulatory actions.

All four sections will be entered in the Center for Drug Evaluation and Research (CDER) review archival system as a complete clinical pharmacology review.

Table 1. Overall Structure and Target Audience for Integrated Clinical Pharmacology Reviews

OCP Integrated Review Section	Target Audience
Section 1 - Executive Summary	OCP, OND, and CDER Senior Leadership
Section 2 - Summary of Clinical Pharmacology Assessment	OCP, OND, and CDER Senior Leadership
Section 3 - Comprehensive Clinical Pharmacology Review	OCP staff and multidisciplinary review team members
Section 4 - Appendixes	OCP staff, multidisciplinary review team members, and regulatory scientists

OCP-Specific Issue-based Review Template

Office of Clinical Pharmacology (OCP) Review

NDA[1] or BLA[2] Number	
Link to EDR[3]	
Submission Date	
Submission Type	*[Indicate priority or standard review]*
Brand Name	
Established Name or Proper Name	
Dosage Form(s) and Strength(s)	
Route(s) of Administration	
Proposed Dosing	
Proposed Indication(s)	
Applicant	
Associated INDs[4]	*[INDs associated with MIDD Meetings[5], EOP2[6], Pre-NDA, and/or Pediatric Study Plan]*
OCP Review Team	*[List lead author first]*
OCP Final Signatory	*[Include name and title]*

[1] NDA: new drug application
[2] BLA: biologics license application
[3] EDR: electronic document room
[4] IND: investigational new drug application
[5] MIDD: model informed drug development
[6] EOP2: end of phase 2

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- **1.1 Recommendations**
- **1.2 Postmarketing Requirements and Commitments**

2 Summary of Clinical Pharmacology Assessment
- **2.1 Pharmacology and Clinical Pharmacokinetics**
- **2.2 Dosage and Therapeutic Individualization**
  - **2.2.1 General Dosage**
  - **2.2.2 Therapeutic Individualization**
- **2.3 Outstanding Issues**
- **2.4 Summary of Labeling Recommendations**

3 Comprehensive Clinical Pharmacology Review
- **3.1 Overview of the Product and Regulatory Background**

3.2 General Pharmacological and Pharmacokinetic Characteristics
3.3 Clinical Pharmacology Review Questions
3.3.1 To what extent does the available clinical pharmacology information provide evidence of effectiveness?
3.3.2 Is the proposed dosage appropriate for the general patient population for which the indication is being sought?
3.3.3 Is an alternative dosage and/or management strategy required for subpopulations based on intrinsic factors?
3.3.4 Are there clinically relevant food-drug or drug-drug interactions, and what is the appropriate management strategy?

4 Appendixes

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1 Executive Summary

The executive summary: (1) very briefly highlights the drug development program, intended place in therapy, or other relevant background information; (2) notes any novel, precedential, or controversial issues and how they were addressed; (3) highlight major review issues addressed; and (4) provides the positions/recommendations of the OCP review team.

1.1 Recommendations

The recommendations section is intended for the communication of OCPs positions and recommendations for regulatory action and key review questions as outlined below:

- The OCP review team will explicitly state OCP's position on approvability and the following key issues as appropriate: adequacy of dosage information, adequacy of risk management (if necessary), and adequacy of labeling and health communication.

- The OCP review team will recommend a complete response (CR) if there are major clinical pharmacology deficiencies that preclude safe and effective use and cannot be addressed by labeling, risk management options beyond labeling, or by conducting postmarketing studies.

- The OCP review team will use the table below to summarize OCP's recommendations and comments on key review issues.

Review Issue	Recommendations and Comments
Evidence of effectiveness	
General dosage instructions	
Dosing in patient subgroups (intrinsic and extrinsic factors)	
Labeling	
Bridge between the to-be-marketed and clinical trial formulations [1]	
Other (specify)	

[1]Refer to 21 CFR 320.21

1.2 Postmarketing Requirements and Commitments

If there is no need for a PMR or PMC, state that in this section.

Otherwise, describe the need for establishing PMRs and PMCs. Describe the issues to be addressed, the justification for the PMR and/or PMC, and the experimental/methodological approaches recommended using the table below (repeat rows as needed).

PMC or PMR	Key Issue(s) to be Addressed	Rationale	Key Considerations for Design Features
☐ PMC ☐ PMR			

2 Summary of Clinical Pharmacology Assessment

This section provides an integrated synopsis of the major clinical pharmacology issues dealt with in the course of a typical OCP review of an NDA, BLA, or OMOR. Only topline information should be presented in this section. Additional details are expected to be included in the section 3 Comprehensive Clinical Pharmacology Review.

The information in this section is organized into subsections 2.1 to 2.4 to address the following topics:

- Brief description of findings and conclusions in support of OCP recommendations

- Appropriateness of proposed dosage for the indication(s) sought
- Appropriateness of dosage and/or treatment in relevant patient subsets (e.g., molecularly defined, segmented by degrees of organ impairment)
- Presence or likelihood of clinically significant food-drug or drug-drug interactions and their clinical management strategies
- Other clinical pharmacology issues (e.g., available strengths, bridging of to-be-marketed formulations to clinical experience) relevant to the optimal use of the drug in populations or individuals
- Areas of uncertainty in the review (e.g., where assumptions were critical in filling information gaps)
- Important omissions from the application
- High-level labeling recommendations

Subsections 2.1 to 2.4 are described below.

2.1 Pharmacology and Clinical Pharmacokinetics

Provide topline information on the pharmacologic and pharmacokinetic (e.g., absorption, distribution, metabolism, and excretion) properties of the drug.

A detailed description is not necessary for clinical pharmacokinetic studies (e.g., single and multiple ascending doses, specific populations, drug interactions, relative bioavailability, and other studies).

2.2 Dosage and Therapeutic Individualization

2.2.1 General Dosage

Summarize the assessment and final recommended dosage recommendations for the general patient population for which the indication(s) are being sought. This includes a synopsis of the dosage finding strategy, how it led to the recommended dosage, and the reviewer's assessment on the adequacy of the dosage.

2.2.2 Therapeutic Individualization

Summarize the assessment and final recommendations on the dosage and/or the appropriateness of treatment in relevant patient subsets based on various intrinsic (e.g., organ impairment, genotype) or extrinsic (e.g., food, drug interactions) factors.

2.3 Outstanding Issues

Describe areas of uncertainty in the review and important omissions from the application. Describe high-level recommendations on preferred approaches to resolving these outstanding issues (e.g., PMR and PMC). Also note if the submission did not adequately address important biopharmaceutics and bioanalytical issues. State “None” if there are no outstanding issues.

2.4 Summary of Labeling Recommendations

Describe labeling recommendations at a high level, including areas of concurrence/disagreement. The information is captured in a narrative description of the labeling issues. Extensive redline/strike outs of the applicant's proposed labeling are generally not be included.

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3 Comprehensive Clinical Pharmacology Review

In subsequent subsections, integrate information across studies to address review questions that are most relevant to the application. Organize information under broad categories of questions in this section where appropriate.

State the answer to key review questions up front and provide details to support the conclusion. Regulatory recommendations, including the rationale for particular labeling recommendations, are clearly stated in the appropriate section.

3.1 Overview of the Product and Regulatory Background

Only relevant product information and regulatory history/activities (including key milestone discussions) that contribute to the clinical pharmacology assessment are described.

3.2 General Pharmacology and Pharmacokinetic Characteristics

Include a general overview of the drug’s non-clinical and clinical pharmacology information to provide a context for specific OCP recommendations. Briefly include information on the drug substance (note for BLAs, drug or drug substance means the therapeutic protein, terms which can be used interchangeably), drug product, and bioanalytical method if relevant to an important aspect of the review. Key information may be summarized in a table format.

3.3 Clinical Pharmacology Review Questions

This section addresses a series of clinical pharmacology questions that are relevant to the safe and effective use of all drugs. These questions should be answered explicitly and up

front.

3.3.1 Do the available clinical pharmacology data contribute to the evidence of effectiveness?

Clinical pharmacology information often provides substantial evidence of effectiveness in situations that involve extrapolation of findings of an approved product to a new population (e.g., adults to pediatric patients), a different dose, dosing regimen, or dosage form. In other situations, clinical pharmacology data may be considered confirmatory evidence of effectiveness or may otherwise contribute to the body of data providing substantial evidence of effectiveness. For more information, see the guidance for industry *Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products* (May 1998).[2] See also the draft guidances *Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products* (December 2019) and *Demonstrating Substantial Evidence of Effectiveness Based on One Adequate and Well-Controlled Clinical Investigation and Confirmatory Evidence* (September 2023).[3]

In general, a recap of efficacy results is not warranted, except in situations in which compelling clinical pharmacology information can be used to provide additional evidence of effectiveness for an NDA or BLA. Situations where the available clinical pharmacology data contribute to the evidence of effectiveness include, but may not be limited to:

- Providing mechanistic evidence of a drug's treatment effect that may be appropriate to be considered as confirmatory evidence to a single adequate and well-controlled trial (e.g., because of an effect on a relevant pharmacodynamic biomarker).

- Identifying subsets of patients with notably large treatment effects or favorable risk/benefit balance for a drug with significant toxicity or otherwise marginal average treatment effects.

- Contributing to evaluation of a biomarker as a fully validated surrogate or one reasonably likely to predict clinical benefit.

- Providing exposure-response information contributing to the understanding of drug effect in the intended population.

- Determining the individual contributions of components of a combination therapy (e.g., in the absence of a full factorial clinical trial).

[2] 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.

[3] When final, these guidances will represent the FDA's current thinking on these topics.

In general, safety of the drug should be discussed in section 3.3.2 as part of the risk-benefit assessment of the proposed dosing regimen for the general population. However, in rare instances, if there is a mechanistic basis for a significant safety concern that may outweigh the benefit of the drug's intended pharmacologic effect, it may be appropriate to include a brief statement of the risk in this section to provide proper context.

3.3.2 Is the proposed dosage appropriate for the general patient population for which the indication is being sought?

Provide an assessment of and final dosage recommendations for the general patient population for which the indication is being sought. This section could also include the details on the dose finding approach as well as the integrative approach taken (including pharmacokinetic, pharmacodynamic, efficacy, and safety information) to support the proposed dosing regimen. If necessary, this section should include revised dosing recommendations to be incorporated into labeling or proposal for further studies to resolve any unresolved issues related to dosing for the indication sought.

Information needed to address this question may include (but is not limited to):

- Dose-exposure-response analyses for drug activity, safety and/or efficacy, where available
- Therapeutic index of the drug if known
- Applicant's rationale to support dosing or labeling claims
- Additional analyses if OCP's conclusion is different from that of the applicant

3.3.3 Is an alternative dosing regimen and/or management strategy required for subpopulations based on intrinsic factors?

Provide an assessment of and final recommendations on dosage and/or the appropriateness of treatment in relevant patient subsets based on various intrinsic factors. Intrinsic factors include age, sex, race/ethnicity, genetics, body weight, organ impairment, etc.

If necessary, this section should include revised dosage recommendations to be incorporated into labeling or proposals for further studies to resolve any unresolved issues related to dosage in specific populations. The basis for alternative dosage recommendations in these populations should be explicitly described (e.g., average exposure matching, interpolation or extrapolation based on exposure-response analyses).

This section can provide information on:

- Intrinsic factors that influence exposure (pharmacokinetics of parent and/or relevant metabolites) and/or pharmacodynamics of the drug.

- Whether a dosage adjustment is warranted for a particular subpopulation and the nature of the data that support those conclusions.

- Applicant-proposed management strategies (if any).

- Review team-proposed management strategies (if different from the applicant).

- Rationale to support proposed management strategies (e.g., based on empirical results from dedicated standalone or nested studies, modeling, simulation, theoretical concerns).

- Whether intrinsic factors were adequately assessed and if such information is pertinent to safe and effective use of the drug.

- Intrinsic factors that were evaluated or considered but that do not influence exposure should be discussed. The adequacy of the data to support a negative finding should be discussed.

3.3.4 Are there clinically relevant food-drug or drug-drug interactions, and what is the appropriate management strategy?

Provide assessment of and final recommendations on dosage and/or therapeutic management strategies needed to address important food-drug (including beverage-drug) or drug-drug interactions. If necessary, this section includes revised management strategies to be incorporated into the labeling or proposals for further studies to resolve such clinically relevant interactions. The basis for alternative dosages under these conditions is explicitly described (e.g., average exposure matching, interpolation or extrapolation based on exposure/response analyses).

This section provides information on:

- The influence of food/diet, alcohol use, herbal supplements, and concomitant drugs on the exposure (pharmacokinetics of parent and/or relevant metabolites) and/or pharmacodynamics of the new drug.

- The new drug’s effect on the exposure and/or pharmacodynamics of concomitant drugs.

- Whether a dosage adjustment is warranted and the nature of the data that supports those conclusions.

- Applicant-proposed management strategies (if any).
- Review team-proposed management strategies (if different from the applicant).
- Rationale to support proposed management strategies (e.g., based on empirical results from dedicated standalone or nested studies, modeling, simulation, or theoretical concerns).
- Whether the impact of food/diet, alcohol use, and drug-drug interactions were adequately assessed and if such information is pertinent to safe and effective use of the drug.
- Interactions that were evaluated or considered but that do not influence exposure should also be discussed. The adequacy of the data to support a negative finding needs to be discussed.

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4 Appendixes

This section is organized to include key individual study report reviews or integrated summaries of individual study reviews and analyses on various clinical pharmacology areas that inform major decisions and recommendations. Subsections should be divided into informative topical subheaders.

Reviewers should take into account whether pivotal clinical pharmacology studies are fit for their intended purposes based on study design, data quality, and the appropriateness of the data analysis. Reviews may include independent OCP data analyses. This section, as with other sections of the review, should not include non-essential information. The review team should exercise judgment on the breadth and depth of information to be included in this section.

Examples of subheaders for this section are provided below:

4.1 Summary of Bioanalytical Method Validation and Performance

4.2 Clinical PK and/or PD Assessments

4.3 Population PK and/or PD Analyses

4.4 Exposure-Response Analyses

4.5 Enrichment, Stratification, and/or Biomarker-Based Assessment

4.6 Mechanistic Safety Assessment