POLICY AND PROCEDURES

OFFICE OF NEW DRUGS

Procedures and Responsibilities for Developing Postmarketing Requirements and Commitments

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PURPOSE

- The purpose of this Manual of Policies and Procedures (MAPP) is to:
  - Define **postmarketing requirements** (PMRs) and postmarketing commitments (PMCs) and describe the policies and procedures to be used by the Center for Drug Evaluation and Research (CDER) staff to develop PMRs/PMCs.[1]
  - Ensure consistency, clarity, and transparency of CDER's decision-making process for developing PMRs/PMCs by verifying that the rationale for PMRs/PMCs is well-documented and PMRs/PMCs are clearly described.
- This MAPP applies to the following:
  - The development of all reportable **506B PMCs** for drugs and licensed biological products regulated by CDER, and the communication of Chemistry,

[1] For the purposes of this MAPP, terms included in the Definitions section of this document are **bolded** the first time they are used.

Manufacturing, and Controls (**CMC) PMCs** between the Office of Pharmaceutical Quality (OPQ) and the Office of New Drugs (OND).[2]

– 506B PMRs for drugs approved under the Animal Efficacy Rule or accelerated approval, **studies** (either pediatric assessments or molecularly targeted pediatric cancer investigations) required under section 505B of the FD&C Act (commonly referred to as the Pediatric Research Equity Act (PREA)), and studies or **clinical trials** required under 505(o)(3) of the Food, Drug and Cosmetics Act (FD&C Act).

– The process of requiring PMRs or agreeing upon PMCs in writing at the time of drug approval during the first review cycle, as well as subsequent review cycles, or after approval.

BACKGROUND

- Before March 25, 2008, PMCs were conducted by the applicant after the Food and Drug Administration (FDA) approved a drug for marketing or licensing, and were intended to further refine the safety, efficacy, or optimal use of a drug, or to ensure consistency and reliability of drug quality. These PMCs were agreed upon by the FDA and the applicant or required by the FDA under the following authorities:

- Prior to March 25, 2008, FDA's authority to issue post-approval requirements was limited to the following authorities:

  – Accelerated approval (see current section 506(c) of the FD&C Act (21 U.S.C. 356(c))). FDA created the accelerated approval program by regulation (see 21 CFR 314.500 *et seq*. and 601.40 *et seq*.), but it was codified in the U.S. Code by the Food and Drug Administration Modernization Act (FDAMA, 1997) and amended by later legislation.

  – Deferred pediatric assessments required under PREA, which was enacted in 2003 and made permanent by the FDA Safety and Innovation Act (FDASIA) in 2012.

  – Animal Efficacy Rule Clinical Efficacy and Safety Studies (21 CFR 314.610(b)(1) and 601.91(b)(1)), where studies to demonstrate safety and efficacy in humans are required at the time of use.

[2] For the purposes of this MAPP, all references to "drugs" or "drug products" includes both human drugs and therapeutic biological products regulated by CDER.

- Section 506B of the FD&C Act provides FDA with additional authority to monitor the progress of PMCs by requiring the applicant to submit annual reports that provide information on the status of the PMCs. This report must also include the reasons, if any, for failure to complete the PMCs. The provision is implemented at 21 CFR 314.81(b)(2)(vii) and 601.70. [3,4]

- Effective March 25, 2008, section 901 of FDA Amendments Act (FDAAA, 2007) created section 505(o) of the FD&C Act authorizing the FDA to require postmarketing studies or clinical trials at the time of approval, or after approval if the FDA becomes aware of "new safety information."[5,6] The Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment for Patients and Communities (SUPPORT) Act of 2018 expanded FDA's authorities under 505(o)(3) to include requiring PMRs to study failure of expected pharmacological action of the drug, which may include reduced effectiveness under the conditions of use prescribed in the labeling of such drug, but which may not include reduced effectiveness that is in accordance with such labeling.[7]

  – Before a postmarketing study can be required under 505(o)(3), FDA must find that adverse event reporting under section 505(k)(1) of the FD&C Act and the active postmarketing risk identification and analysis (ARIA) system as available under section 505(k)(3) of the FD&C Act will not be sufficient to meet the purposes described below.[8]

  – Similarly, before requiring a postmarketing clinical trial (under 505(o)(3)), FDA must find that a postmarketing study or studies will not be sufficient to achieve these same purposes.[9]

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[3] Refer to the guidance for industry *Reports on the Status of Postmarketing Study Commitments – Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997* (February 2006). For the most recent version of a guidance, check the *Search for FDA Guidance Documents* webpage at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.

[4] *Postmarketing Requirements and Commitments Reports* website at https://www.fda.gov/drugs/postmarket-requirements-and-commitments/postmarketing-requirements-and-commitments-reports.

[5] Refer to the DEFINITIONS section for a definition of *studies* and *clinical trials* as they relate to the implementation of section 901 of FDAAA and this MAPP. Studies or clinical trials may be required under PREA (21 CFR 314.55(b) and 601.27(b)), the Animal Efficacy Rule (21 CFR 314.610(b)(1) and 601.91(b)(1)), accelerated approval (21 CFR 314.510 and 601.41), or FDAAA (section 505(o)(3)(A), 21 U.S.C.355(o)(3)(A)).

[6] Defined in section 505-1(b)(3) of the FD&C Act.

[7] Refer to the draft guidance for industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act* (October 2019). When final, this guidance will reflect the Agency's current thinking on this topic.

[8] Refer to section 505(o)(3)(D)(i) of the FD&C Act (21 U.S.C. 505(o)(3)(D)(i)).

[9] Refer to section 505(o)(3)(D)(ii) of the FD&C Act (21 U.S.C. 505(o)(3)(D)(ii).

– Section 505(o)(3)(B) provides that studies and clinical trials may be required for any or all of the following three purposes:

  - To assess a known serious risk related to the use of the drug involved.
  - To assess signals of serious risk related to the use of the drug.
  - To identify an unexpected serious risk when available data indicates the potential for a serious risk.

POLICY

- All PMRs/PMCs will be communicated using a standardized process as described in MAPP 6010.8 and as authorized under relevant Prescription Drug User Fee Acts (PDUFA) and Biosimilar User Fee Acts (BsUFA).[10] All **"anticipated" PMRs** will be communicated as per PDUFA VII and BsUFA III requirements and 506B PMCs may be communicated as appropriate.[11]

- For PMRs/506B PMCs, CDER Office of New Drugs (OND) will provide and review the rationale for each PMR/506B PMC and document each rationale in the PMR/PMC Development Template.[12]

  – PMRs must be required under one of FDA's four authorities identified above.

  – 506B PMCs must be agreed upon in writing between the FDA and the applicant and should be requested only if the objectives are important to further the knowledge of the effective use of the drug and do not fit the criteria for PMRs.

- For 505(o)(3) PMRs that are observational epidemiologic studies, ARIA sufficiency should be discussed during a Safety Assessment Meeting (SAM) and documented in an ARIA sufficiency memo before the PDUFA action date by

[10] Refer to CDER MAPP 6010.8. – *NDAs and BLAs: Communication to Applicants of Target Dates for Communicating Feedback Regarding Labeling, Anticipated Postmarketing Requirements (PMRs) and 506B Postmarketing Commitments (PMCs)*. For the most recent version of a MAPP, refer to the *CDER Manual of Policies & Procedures* website at https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cder-manual-policies-procedures-mapp.

[11] Under PDUFA VII, for new molecular entity (NME) NDAs and original BLAs, FDA will communicate anticipated PMRs for standard applications 8-weeks before the PDUFA goal and for priority applications 6-weeks before the PDUFA goal. Under BsUFA III, for original BLAs submitted under section 351(k) of the Public Health Service Act, the FDA must provide a target date for the OND review division to communicate feedback to the applicant regarding proposed PMRs/PMCs in the Day 74 letter.

[12] Throughout this document, "PMR/PMC Development Template" may be used to refer to either *PMR/506B PMC Development Template* or *CMC PMC Development Template* when appropriate.

CDER Office of Surveillance and Epidemiology (OSE).[13] OND will provide the proposed PMR description to OSE for feedback and inclusion in the ARIA sufficiency memo.

- For CMC PMCs, OPQ will:
  - Provide and review the rationale for each CMC PMC and document in the CMC PMC Development Template.
  - Provide CMC PMC descriptions and milestones to OND for inclusion in the approval letter.
- CDER will work with the applicant on the proposed timetable (**PMR/PMC schedule of milestones**) to reach agreement and ensure feasibility. However, for PMRs under 505(o)(3), if CDER and the applicant cannot reach agreement, CDER can require the applicant to submit a timetable.

RESPONSIBILITIES

- **PMR/PMC Development Coordinator**
  - Generally, this role is occupied by an OND review team member (e.g., Deputy Director for Safety (DDS), Associate Director for Safety (ADS)). In OPQ, this role is conducted by a CMC assessment team member (e.g., Application Technical Lead (ATL)).
  - Advises key stakeholders regarding development of PMRs/PMCs, including study or clinical trial description, milestones, and rationale.
  - Ensures that PMR/PMC development and communication procedures are followed by the review team.
  - Reviews and provides concurrence for the anticipated PMRs/PMCs proposed by the review team members and review team leader.
  - Reviews PMRs/PMCs before they are sent to the applicant and before letter issuance.
  - Reviews PMRs/PMCs to ensure the study/trial is feasible, clearly articulated, and the milestone schedule is appropriate, referring any concerns to the review team and management as necessary.

[13] Refer to footnote #7 [Guidance on PMR studies & clinical trials].

- Ensures PMR/506B PMC Development Template accuracy, completeness, and finalization.

- Receives, as appropriate, from OPQ any CMC PMCs and quality related PMRs for inclusion in an approval letter.

- Reviews documentation related to PMRs/PMCs and develops best practices to ensure the process is consistent within their OND review division.[14]

- Ensures any proposed 505(o)(3) PMR descriptions are provided to OSE for feedback and inclusion in the ARIA sufficiency memo, as appropriate.

- Clears the PMR/PMC section of the applicable NDA/BLA approval letter template.

- Clears and serves as signatory authority for the PMR/PMC Development Template.

- **PMR/PMC Program Manager and Team**

  - This role is occupied by Safety Policy Research Initiatives (SPIRIT) PMR/PMC Team Lead and Team in the OND Immediate Office.

  - Oversees the PMR/PMC program, policies, database, and website.

  - Ensures all PMR/PMC-related information is updated and made publicly available in the appropriate databases.

  - Performs regular quality checks on certain PMR/PMC data.

  - Supports OND and other CDER Office leadership, divisions, and review teams during the development of PMRs/PMCs.

  - Participates in policy and regulatory decisions related to PMRs/PMCs.

  - Supports the implementation of new regulations affecting the PMR/PMC Program.

  - Provides PMR/PMC-related updates to the leadership team.

[14] For the purposes of this MAPP, the term "OND review division" refers to the OND clinical review division or the OND pharm/tox review division, as appropriate.

- Reviews and clears PMR/PMC-related letters and memos as defined by internal process documents.

- Responds to PMR/PMC-related questions both from internal and external stakeholders.

- Provides updates to internal and external reports (e.g., Annual Reports on PMRs/PMCs to the *Federal Register*, Reports to Congress, Office of Inspector General (OIG) reports, General Accounting Office (GAO) reports).

- Provides PMR/PMC-related training to offices and divisions.

- Coordinates the development and revisions of PMR/PMC-related MAPPs, guidances, and other regulatory documents.

- **OND Safety Regulatory Project Manager (SRPM)**

  - Assists the review team in identifying when a 505(o)(3) PMR could be used to further evaluate or characterize a safety issue.

  - Communicates the criteria for establishing PMRs/PMCs to the review team, when necessary.

  - Ensures OSE is aware of the need for an ARIA sufficiency determination and ARIA memo for anticipated 505(o)(3) observational epidemiologic study PMRs, as appropriate.

  - Facilitates/participates in review team discussions with the applicant about PMRs/PMCs.

  - Ensures creation of PMRs/PMCs according to MAPPs and guidances.

  - Ensures that the PMR/PMC Development Template is correctly completed for each new PMR/PMC and uploaded into CDER's **Electronic Records Keeping Systems (ERKS)**.

  - Reviews and clears draft and final PMR/PMC descriptions with the PMR/PMC Development Coordinator (DDS/ADS, as appropriate) before including them in the approval/postapproval letter.

- Ensures that each PMR/PMC in the approval or postapproval letter is numbered sequentially and has a description that describes a study or clinical trial.[15]

- Ensures that there is at least one milestone in the schedule of milestones (e.g., a final protocol or final report submission milestone) and not more than one of each core milestone (e.g., draft protocol submission, final protocol submission, study/trial completion, and final report submission milestone).

- Creates PMR/PMC set numbers from ERKS if OND Office of Regulatory Operations (ORO) staff has not already created a new set.[16]

- Assists in communicating anticipated PMR/PMC information to applicants according to PDUFA VII and BsUFA III PMR-related requirements.

- Checks ERKS after either an approval or postapproval letter has been issued establishing new PMRs/PMCs to ensure that the PMRs/PMCs in the letter are accurately reflected in ERKS (including PMR/PMC descriptions and the schedule of milestones, as appropriate).

- **OND/Office of Regulatory Operations (ORO) Project Management Staff**

  - Coordinates with the review team and other CDER offices as appropriate and corresponds with the applicant regarding PMR/PMC issues and related PMR/PMC submissions.

  - Alerts/reminds OSE of the need for an ARIA sufficiency determination and ARIA memo for anticipated 505(o)(3) observational epidemiologic study PMRs as appropriate.

  - Provides the applicant with planned review timelines for the submission of original NDAs and BLAs and efficacy supplements related to PMRs/PMCs (Refer to MAPP 6010.8 for more information on communicating timelines to the applicant).

  - Communicates anticipated PMR/PMC information to applicants according to PDUFA VII and BsUFA III PMR-related requirements.

[15] For examples of PMR/PMC descriptions, please see the *PMR/506B PMC Development Template instructions* located in the internal *CDER Standard Templates (CST) Library*.
[16] For questions about when to create new PMR/PMC sets versus using existing PMR/PMC sets, contact the PMR/PMC Program Team.

- Ensures that each PMR/PMC in the approval letter is numbered sequentially and has a description that describes a study or clinical trial.

- Ensures that there is at least one milestone in the schedule of milestones (e.g., a final protocol or final report submission milestone) and not more than one of each core milestone (e.g., draft protocol submission, final protocol submission, study/trial completion, and final report submission milestone).

- Creates PMR/PMC set numbers from ERKS if the SRPM has not already created a new set or if there is no SRPM within the OND division.[17]

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- If there is no SRPM within an OND division, checks ERKS after either an approval or postapproval letter has been issued establishing new PMRs/PMCs to ensure that the PMRs/PMCs in the letter are accurately reflected in ERKS (including PMR/PMC descriptions and the schedule of milestones, as appropriate).

- **Office of Pharmaceutical Quality (OPQ)**

  - **Office of Program and Regulatory Operations (OPRO) Regulatory Business Project Management (RBPM) Staff**

    - Ensures with the OND ORO staff or SRPM that each CMC PMC in the approval letter is numbered sequentially and has a description that describes a PMC study.

    - Ensures that there is at least one milestone in the schedule of milestones (e.g., final report submission milestone) and not more than one of each core milestone (e.g., study completion, and final report submission milestone).

    - Creates CMC PMC set numbers from ERKS if the SRPM has not already created a new set, there is no SRPM within the OND division, or the submission is OPQ-managed (e.g., CMC supplement).[18]

  - **OPQ Assessor and OPQ Application Technical Lead (ATL)**

    - Ensures the accuracy, completeness, and finalization of the CMC PMC Development Template, and may submit it to the PMR/PMC Coordinator, as appropriate.

[17] Refer to Footnote #16 [contact the PMR/PMC Program Team].
[18] Ibid.

OND Reviewer

- This role is occupied by a discipline reviewer assigned to a drug (e.g., clinical, clinical pharmacology, nonclinical toxicology, safety-related discipline, product quality, biostatistics).

- Identifies potential PMR/PMC review issues and works with the review team and review management to discuss these issues. Recommends other discipline participation, as needed.

- Discusses with OSE, when there are considerations for an observational epidemiologic study to further evaluate serious safety risks as a 505(o)(3) PMR.

- Participates in the analysis and provides recommendations to inform decisions about PMRs/PMCs.

- Drafts a list of anticipated PMRs/PMCs for review and concurrence from the review team, review team leader, and PMR/PMC development coordinator.

- Ensures that PMR/PMC descriptions are clearly written and describe the study/trial and its objectives.

- Reviews and resolves any differences in the objectives and schedule of milestones between the draft and final list of PMRs/PMCs.

- Assists as needed in documenting the rationale for each PMR/PMC in the PMR/PMC Development Templates and other appropriate documents.[19]

- **Review Management**

  - Receives review updates from the review team leader and provides review oversight (e.g., ensures that PMRs/PMCs are clear and consistent with similar PMRs/PMCs).

- **Review Team Leader (TL), including the Cross-Disciplinary Team Leader (CDTL)**

  - Ensures that PMR/PMC development and communication procedures are followed by the review team.

[19] Use either the *CMC PMC Development Template* or *PMR-506B PMC Development Template* located in the internal *CDER Standard Templates (CST) Library*, as applicable.

  - Ensures that all appropriate disciplines and offices participate in the analysis and discussion of PMRs/PMCs (e.g., OSE is engaged in discussions when considering an observational epidemiologic study to further evaluate serious safety risks as a 505(o)(3) PMR).

  - Reviews and provides concurrence for the list of anticipated PMRs/PMCs proposed by primary reviewers before they are sent to the PMR/PMC Development Coordinator for final concurrence.

  - Reviews proposed and final schedule of milestones for completeness and feasibility.

  - Assists as needed in documenting the rationale for each PMR/PMC in the PMR/PMC Development Template.

  - Updates the supervisor who oversees the work of members of the review team, as applicable.

- **Review Team**

  - Adheres to standardized policies and procedures regarding PMR/PMC development.

  - Collaborates with other CDER offices as relevant to the PMR/PMC subject matter expertise.

  - Reviews the rationale for requiring a PMR/PMC in the appropriate Development Template.

  - Provides concurrence on PMRs/PMCs before letter issuance.

- **Senior Management (CDER Center Director/Deputy or CDER Office Directors)**

  - Receives updates from review management on PMR/PMC development process issues or changes on a periodic basis.

- **Signatory Authority —** For the purposes of this MAPP, signs regulatory letters related to PMRs/PMCs

PROCEDURES

Specific roles are not provided to allow for procedural flexibility within the OND review divisions. The following sections describe the general steps taken when establishing PMRs/PMCs. For CMC PMCs, these steps are performed by assigned OPQ staff.

1. **Identify all anticipated PMR/PMC review issues for internal discussion and inform the applicant as appropriate.**

   This section outlines initial steps for internal discussions once all anticipated PMR/PMC review issues have been identified, but a decision about whether a PMR or PMC is needed has not been made.

   a. Identify all anticipated PMR/PMC review issues and discuss with the review team.

   b. Ensure sound scientific basis for all anticipated PMRs/PMCs.

   c. Ensure that all anticipated PMR/PMC review issues are discussed internally and collaborate with other CDER offices as relevant to the PMR/PMC subject matter before the Mid-Cycle Meeting, if possible and/or applicable.

   d. If possible, start drafting all anticipated PMRs/PMCs to be sent to the applicant by 8 weeks (standard review) or 6 weeks (priority review) before the PDUFA or BsUFA goal date, utilizing the 8-/6- week PMR/PMC Communication Letter template.

   e. Discuss any anticipated PMRs/PMCs with the applicant during the pre-approval process, as appropriate.

2. **Decide whether PMRs/PMCs are necessary and prepare all anticipated PMRs/PMCs.**

   This section describes the procedures after initial discussion and review of any additional information submitted by the applicant that results in a decision to require a PMR or request a PMC.

   a. Decide whether PMRs/PMCs are necessary and meet the requirements for the specific statutory or regulatory authority or commitment (refer to the PMR/PMC Development Template for further information).

   b. For anticipated PMRs under section 505(o)(3) that are observational epidemiologic studies, a Sentinel ARIA Sufficiency Preliminary Review can

be completed by OSE, as applicable, to facilitate communication with the division that this type of anticipated PMR may be required.

c. During the review cycle, draft a description of each PMR/PMC, ensuring that it clearly communicates the objective and necessary study design details for applicant review.[20] [Note: the PMR/PMC description should start with a verb such as, "Complete the…" or "Conduct the…" when describing the study or trial. The PMR/PMC description should not be too general, nor too specific.][21]

d. Route the draft PMR descriptions to review management to ensure concurrence on PMR/PMC descriptions.

e. Document all anticipated PMRs/PMCs and their rationale in the written review/memo and other appropriate documents.

f. Review all anticipated PMRs/PMCs by each discipline reviewer for clarity, consistency, and feasibility (e.g., schedule of milestones).

g. Obtain concurrence from the appropriate review teams for the list of all anticipated PMRs/PMCs before ORO staff sends it to the applicant.

3. Communicate all anticipated PMRs/PMCs to the applicant and continue internal discussions.

This section addresses discussing anticipated PMRs/PMCs with the applicant during the mid-cycle and late cycle meetings. These discussions should include the goals and objectives of the studies or clinical trials.

a. Internally discuss PMR/PMC content and resolve any differences with the review team and applicant.

b. Draft the 8-/6- week PMR/PMC Communication letter and either email to the applicant or issue the letter via ERKS.

[20] Guidance for Review Staff and Industry – *Good Review Management Principles and Practices for PDUFA Products* (April 2005)

[21] Examples of standard descriptions for certain clinical pharmacology PMRs can be found in the *PMR/506B PMC Development Template instructions* located in the internal *CDER Standard Template (CST) Library*. For specific questions regarding PMR/PMC descriptions, please contact the PMR/PMC Program team.

c. Continue discussions about anticipated PMRs/PMCs with the applicant and internally with the review team.[22]

4. Finalize the list of PMRs/PMCs and schedule of milestones.

The schedule of milestones generally is proposed by the applicant and should be reviewed and evaluated by the review team. If the applicant has not previously proposed milestones, the review team should request a schedule of milestones from the applicant.

a. Draft a list of final PMRs/PMCs for review, including the schedule of milestones.

b. Ensure that the schedule of milestones includes only one of each core milestone (e.g., one draft protocol submission, one final protocol submission, one study/trial completion, and one final report submission milestone). If the study/trial is lengthy, consider adding a few interim report submission milestones to facilitate monitoring the progress of the study/trial.

c. Ensure that each PMR/PMC includes at least one milestone in the schedule (e.g., animal efficacy PMRs may include only a final protocol submission milestone).

d. Review final PMR/PMC descriptions and schedule of milestones for clarity, feasibility, and consistency with other similar PMRs/PMCs.

e. Ensure that each PMR/PMC description describes the study or clinical trial and action being requested (e.g., conducting or completing a study or completing an analysis of data).

f. Obtain concurrence for the list of final PMRs/PMCs, including the schedule of milestones, for inclusion in the approval/postapproval letter.

   i. For PMRs, send the final schedule of milestones to the applicant.

   ii. For PMCs, request the applicant's written agreement on the PMC description and schedule of milestones.

g. Draft the appropriate PMR/PMC Development Template including the rationale for each new PMR/PMC. Note that there is a specific CMC PMC development template for non-506B PMCs.

[22] Continued PMR/PMC discussions with the applicant, typically via emails, should be identified in ERKS by using the "PMR/PMC Discussion" code.

h. Ensure the appropriate PMR/PMC Development Template aligns with other regulatory documents. For instance:

   i. The information in all Development Templates should align with the related information in the approval letter.

   ii. For 505(o)(3) PMRs that are observational epidemiologic studies, the information in the PMR/506B PMC Development Template should align with the information in the ARIA Sufficiency Memo and in the approval letter, such as the type of serious safety risk, purpose, and rationale.

i. Identify unresolved issues that should be addressed by the review team and DDS/ADS or SRPM, as appropriate. Obtain concurrence of the final list of PMRs/PMCs as needed if unresolved issues arise.

j. Consult with the PMR/PMC Program Team in SPIRIT as needed to discuss PMRs/PMCs (e.g., PMR/PMC descriptions, schedule of milestones, how to complete the PMR/PMC Development Template).

k. Create a pre-assigned PMR/PMC set in ERKS, as needed.[23]

5. Include PMRs/PMCs in approval or postapproval letters.[24]

a. Ensure that each PMR/PMC is numbered sequentially in the letter, as needed. In postapproval letters, the PMR/PMC set number may be added as part of a pre-existing PMR/PMC set (special circumstances apply; consult the PMR/PMC Program Team when considering adding a new PMR/PMC to a pre-existing set).

b. Finalize the letter using the PMR/PMC-related content and format specified in the standardized letter templates.

c. Ensure that the rationale for each PMR/PMC is documented in the correct Development Template for each PMR/PMC.

d. Signatory authority (typically indicated in the cover page of the template) signs letter and appropriate Development Template in ERKS.

6. Ensure PMRs/PMCs are entered into ERKS.

[23] Refer to Footnote #16 [contact the PMR/PMC Program Team].

[24] Postapproval letters are those establishing PMRs or PMCs that are not included in approval or supplement approval letters. For example, *Acknowledge New PMR/PMC* letters and *Release and Reissue (Acknowledged New PMR/PMC)* letters located in the internal *CDER Standard Templates (CST) Library*.

a. Ensure the letter is processed correctly in ERKS.

b. Ensure that ERKS is populated with all PMRs/PMCs documented in the approval or postapproval letter, including the schedule of milestones as actual dates per the respective letter.

c. Contact the PMR/PMC Program Team in SPIRIT if any PMRs/PMCs have not been added to ERKS. There may be a few weeks before the PMR/PMC has been added to ERKS to allow for data integrity verification by the PMR/PMC Program Team.

REFERENCES

- Draft Guidance for industry – *Postmarketing Studies and Clinical Trials: Determining Good Cause for Noncompliance with Section 505(o)(3)(E)(ii) of the Federal Food, Drug and Cosmetic Act* (July 2023). When final, this guidance will represent the Agency's current thinking on this topic.

- Draft Guidance for Industry – *Pediatric Drug Development: Regulatory Considerations – Complying With the Pediatric Research Equity Act and Qualifying for Pediatric Exclusivity Under the Best Pharmaceuticals for Children Act* (May 2023). When final, this guidance will represent the Agency's current thinking on this topic.

- Draft Guidance for Industry – *Postmarketing Studies and Clinical Trials – Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act Guidance for Industry* (October 2019). When final, this guidance will represent the Agency's current thinking on this topic.

- Guidance for Industry – *Reports on the Status of Postmarketing Study Commitments — Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997* (February 2006).

- Draft Guidance for Industry and Review Staff – *Good Review Management Principles and Practices for New Drug Applications and Biological License Applications* (September 2018). When final, this guidance will represent the Agency's current thinking on this topic.

- CDER MAPP 6010.2 Rev.2, *Responsibilities for Tracking and Communicating the Status of Postmarketing Requirements and Commitments*, (04/13/2026).

- CDER MAPP 6010.8, *NDAs and BLAs: Communication to Applicants of Planned Review Timelines*, (09/19/2024).

- CDER MAPP 7600.11, *CDER Electronic Records Keeping Systems*, (08/04/2021).

- Postmarketing Requirements and Commitments Reports website at https://www.fda.gov/drugs/postmarket-requirements-and-commitments/postmarketing-requirements-and-commitments-reports.

- PDUFA VII Commitment Letter available at https://www.fda.gov/industry/prescription-drug-user-fee-amendments/pdufa-vii-fiscal-years-2023-2027.

- BsUFA III Commitment Letter available at https://www.fda.gov/industry/fda-user-fee-programs/biosimilar-user-fee-amendments.

DEFINITIONS

- **506B-Reportable Postmarketing Commitment (506B PMC)** – Postmarketing studies or clinical trials concerning clinical safety, clinical efficacy, clinical pharmacology, or nonclinical toxicology that applicants and the FDA have *agreed* to conduct in writing; and applicants are required to report on these PMCs in their PMR/PMC annual report (21 CFR 314.81(b)(2)(vii)(a), 21 CFR 601.70(b), and Section 506B the FD&C Act, *Reports of Postmarketing Studies*).[25,26]

- **Anticipated postmarketing requirement (PMR)/postmarketing commitment (PMC)** – The term "anticipated" refers to any study or clinical trial that is based on data received with the original submission of the application that an applicant may be required to conduct (PMR) or agrees upon in writing to conduct (PMC) after approval of a marketing or licensing application.

- **Clinical Trial** – Any prospective investigation in which the sponsor or investigator determines the method of assigning the investigational product or other interventions to one or more human subjects.

- **CMC Postmarketing Commitment (not reportable under section 506B of the FD&C Act)**– Commitments regarding chemistry, manufacturing, and controls

[25] Reportable 506B PMCs are listed on the FDA's *Postmarket Requirements and Commitments* website at https://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm.
[26] Refer to 21 CFR 314.81(b)(2)(vii).

(CMC) that applicants have agreed with FDA to conduct post-approval. CMC PMCs may also be referred to as quality postmarketing agreements (QPAs).[27]

Reports on the status of CMC PMCs are not subject to 506B reporting and 506B provisions concerning public disclosure, including disclosure on FDA's website and in the annual Federal Register reports; CMC PMCs and voluntary studies are subject to a separate reporting requirement (21 CFR 314.81(b)(2)(viii)).

- **Electronic Records Keeping Systems (ERKS)** – The authoritative data source for a given data element or piece of information within an information management system.

- **Molecularly Targeted Pediatric Cancer Investigations** – pediatric studies or trials required under section 505B(a)(1)(B) of the FD&C Act; see section 505B(a)(3)(A) for further description.

- **Pediatric Assessments** – pediatric studies or trials required under section 505B(a)(1)(A) of the FD&C Act; see section 505B(a)(2)(A) for further description.

- **PMR/PMC Postapproval letters** – Letters issued establishing PMRs or PMCs that are not included in approval or supplement approval letters. For example, *Acknowledge New PMR/PMC* letters and *Release and Reissue (Acknowledge New PMR/PMC)* letters.

- **PMR/PMC-related Submission** – A formal submission sent by the applicant to address an established PMR/PMC. Such submissions may include:

  – PMR/PMC protocols

  – PMR/PMC correspondence (e.g., requests for revised milestone dates)

  – Annual status reports

  – Final reports

  – Interim reports

  – Release requests

[27] The draft guidance for industry – *Benefit-Risk Considerations for Product Quality Assessments* (May 2022) uses the term quality postmarketing agreement (QPA) to mean CMC PMC synonymously. When final, this guidance will reflect the Agency's current thinking on this topic.

  - 180-day Accelerated Approval PMR Progress Reports
  - Supplemental applications submitted to address a PMR/PMC

- **PMR/PMC Schedule Of Milestones** – The specific milestone dates set forth as part of a PMR/PMC for conducting and completing a PMR/PMC that must be reported annually. The format for a milestone date should be MM/YYYY, which assumes that the milestone due date is the last day of the listed month. The following milestone dates should be included in the schedule and in the letter when the PMR/PMC is required or agreed upon:
  - Draft protocol submission date (optional but recommended as appropriate)
  - Final protocol submission date
  - Study/clinical trial completion date
  - Final report submission date
  - Interim report submission date (optional)

- **Postmarketing Requirement (PMR)** – Any study or clinical trial that an applicant is required to conduct after approval of a marketing or licensing application or a supplement. Studies or clinical trials may be required under PREA (21 CFR 314.55(b) and 601.27(b)), the Animal Efficacy Rule (21 CFR 314.610(b)(1) and 601.91(b)(1)), accelerated approval (21 CFR 314.510 and 601.41), or section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A).[28,29]

- **Study** – An investigation other than a clinical trial as defined above, such as an investigation in humans that is not a clinical trial as defined above (e.g., observational epidemiologic study or lactation study), nonclinical study, or laboratory experiment.

EFFECTIVE DATE

- This MAPP is effective upon date of publication.

[28] Refer to the draft guidance for industry *Pediatric Drug Development: Regulatory Considerations – Complying With the Pediatric Research Equity Act and Qualifying for Pediatric Exclusivity Under the Best Pharmaceuticals for Children Act* (May 2023). When final, this guidance will reflect the Agency's current thinking on this topic.

[29] Refer to the draft guidance for industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act* (October 2019). When final, this guidance will reflect the Agency's current thinking on this topic.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
03/09/2009	N/A	N/A
04/13/2026	1	Updated to align with current OND organizational structure, applicable UFA commitments, and contemporary CDER workflow procedures and best practices.