
POLICY AND PROCEDURES

OFFICE OF NEW DRUGS

**Responsibilities for Tracking, Monitoring, and Communicating the Status of
Postmarketing Requirements and Commitments**

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PURPOSE

- The purpose of this Manual of Policy and Procedures (MAPP) is to:
 - Define postmarketing requirements (PMRs) and postmarketing commitments (PMCs) and to describe the policies and procedures to be used by the Center for Drug Evaluation and Research (CDER) staff to track, monitor, and communicate information about PMRs and 506B PMCs.¹
 - Ensure consistency of CDER’s tracking, monitoring, and communicating of established PMRs/506B PMCs.
 - Ensure timely and accurate processing and review of PMR/506B PMC-related submissions received by the Food and Drug Administration (FDA).
 - Ensure that PMR/506B PMC statuses are accurate and updated in CDER’s electronic record keeping system (ERKS) in a timely manner.

¹ 506B PMCs are postmarketing studies or clinical trials concerning clinical safety, clinical efficacy, clinical pharmacology, or nonclinical toxicology that applicants and FDA have agreed to conduct in writing. 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).

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- This MAPP applies to the following:²
 - All reportable 506B PMCs for drugs and licensed biological products regulated by CDER.³
 - 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 safety studies or clinical trials required under 505(o)(3) of the Food, Drug and Cosmetics (FD&C) Act.
 - PMRs required and 506B PMCs agreed upon 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, all studies and trials were referred to as PMCs, which were conducted by the applicant after 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 either agreed upon by FDA and the applicant or required by FDA under 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.

² This MAPP does not apply to postmarketing commitments regarding chemistry, manufacturing, and controls (CMC) and certain product stability studies that applicants have agreed upon with FDA at the time of approval to be conducted during the commercial phase to ensure the consistency and reliability of drug quality (CMC commitments or PMCs). CMC PMCs may also be referred to as quality postmarketing agreements (QPAs). 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, are not applicable to these studies. CMC PMCs and voluntary studies are subject to separate reporting requirements under 21 CFR 314.81(b)(2)(viii).

³ For the purposes of this MAPP, all references to "drugs" or "drug products" include both human drugs and therapeutic biological products regulated by CDER.

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- 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.
 - 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.⁴ This report must also include the reasons, if any, for failure to complete the PMCs. This provision is implemented at 21 CFR 314.81(b)(2)(vii) and 601.70.⁵
 - Effective March 25, 2008, section 901 of FDA Amendments Act (FDAAA, 2007) created section 505(o) of the FD&C Act authorizing FDA to require postmarketing studies or clinical trials at the time of approval, or after approval if FDA becomes aware of “new safety information.”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
 - The Food and Drug Omnibus Reform Act (FDORA) of 2022, requires accelerated approval (AA) application holders to submit two 180-day AA PMR Progress Reports (hereafter, 180-day report) per year for each open study or clinical trial required under section 506(c) of the FD&C Act. Further, FDORA requires FDA to promptly publish on its website, in an easily searchable format, the information concerning the progress of any study or trial required under section 506(c) reported by the applicant.⁸

POLICY

- PMRs/506B PMCs are studies or clinical trials that are completed by the applicant after FDA has approved a drug for marketing or licensing. These studies or trials

⁴ The annual status reports required under section 130(a) of FDAMA are due each year within 60 days of the anniversary of U.S. drug approvals. The applicant must continue to report on the status of the PMR/PMC until it is notified in writing that the requirement or commitment has been fulfilled or released.

⁵ 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* (Feb 2006). For the most recent version of a guidance, refer to the *Search for FDA Guidance Documents* webpage at <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs>.

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

⁷ Defined at section 505-1(b)(1)(E) of the FD&C Act.

⁸ Reportable 506B PMCs are listed on the *Postmarketing Requirements and Commitments: Searchable Database* website at <https://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm>.

can be either required by regulation or statute (PMRs) or agreed upon in writing by FDA and the applicant (PMCs).

- CDER processes PMR/506B PMC-related submissions as they are received, verifies PMR/506B PMC status, communicates to the applicant any omissions and errors in PMR/506B PMC status reporting, and updates the ERKS accordingly.
- CDER communicates to the applicant missed milestone dates in a *Notification of Missed Milestones* letter.⁹ Generally, if missed milestone dates involve 505(o)(3) PMRs, CDER will make a good cause determination by evaluating an applicant's explanation of the circumstance(s) that led to the noncompliance and any other information deemed pertinent, if one is submitted.¹⁰ If no explanation is submitted by the applicant, CDER will generally determine that good cause for missing the milestone has not been demonstrated.
- CDER reviews PMR/506B PMC-related submissions according to relevant timelines.
 - *Protocols*: Upon receipt, all PMR/506B PMC protocols submitted by the applicant are reviewed and detailed feedback is provided as needed on noted deficiencies and suggested revisions if there are concerns with the submitted protocol design.

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised, as needed, to meet the goal of the study or clinical trial.

- *Annual status reports (ASR)*: CDER reviews ASRs and completes the *Annual Status Report Review Form PMR/PMC Summary* accordingly. FDA 3989 form entitled, "*PMR/PMC Annual Status Report for Drugs and Biologics*," includes fields in which applicants may provide ASR information on their PMRs and PMCs. Applicants may use the completed Form FDA 3989 to replace the content included in section 1.13.12, Status of Postmarketing Study Commitments and Requirements, in the electronic common technical document (eCTD).¹¹ The ERKS is reviewed to assess the current status of open PMRs/506B PMCs, and the regulatory record related to the application. After CDER verifies the information in ERKS, the PMR/506B PMC record is

⁹ All letters, templates, and forms referenced in this MAPP are located in the internal *CDER Standard Templates (CST) Library*.

¹⁰ 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.

¹¹ Guidance for Industry, *Annual Status Report Information and Other Submissions for Postmarketing Requirements and Commitments: Using Forms FDA 3988 and FDA 3989* (September 2023).

updated with the assessed status and the explanation of status as supported by the information provided by the applicant in the ASR and in ERKS.

- *180-day Accelerated Approval PMR Progress Report Submission (180-day report)*: The applicant is required to submit two 180-day reports per year for each open study or clinical trial required under section 506(c).¹² CDER reviews these submissions and completes the *180-day AA PMR Progress Report Review Form* accordingly.¹³
 - One report will be a standalone submission and the other report will be combined with an application's ASR as required under section 506B(a)(1) of the FDCA and 21 CFR 314.81(b)(2) (for NDAs) and 21 CFR 601.70 (for BLAs).
 - The standalone 180-day report will be due 180 days after the date of approval (with a 60-day grace period).
 - The subsequent 180-day report is to be submitted with the application's ASR. This report should be submitted as part of the PMR/PMC section of the annual report (section 1.13.12: *Status of Postmarketing Study Commitments and Requirements*).
 - Both 180-day reports are to be submitted each year until the final report for the corresponding study or clinical trial is submitted.
- *Final reports*:
 - A final report submitted as a supplemental application should be double coded in ERKS as a final report (*PMR/PMC/Clinical – Final Report or PMR/PMC/Non-Clinical – Final Report*) to open the *PMR/PMC Final Report* review goal and should be reviewed according to established review times for supplements.
 - A final report **NOT** submitted as a supplemental filing should be reviewed within 1 year of receipt.
 - In either case, CDER notifies the applicant in writing of the final fulfillment determination.

¹² Refer to Section 3210 of the 2022 Food and Drug Omnibus Reform Act (FDORA).

¹³ Refer to footnote #9. [CST library reference]

RESPONSIBILITIES¹⁴

- **PMR/506B PMC Tracking Coordinator**
 - This role is occupied by one or more Office of New Drugs (OND) review division staff members, generally an OND safety regulatory project manager (SRPM) or Office of Regulatory Operations (ORO) project management staff, in the absence of an SRPM or as designated by the division.¹⁵
 - Ensures that the review team is informed of PMR/506B PMC scheduled milestones.
 - Ensures that accurate PMR/506B PMC information is captured in ERKS (e.g., current status, scheduled milestones, explanation of status) and is reflected on the public website.¹⁶
 - Monitors whether PMR/506B PMC-related activities are conducted according to required timelines (e.g., review of PMR/506B PMC-related submissions, verification of PMR/506B PMC information in ASRs) and communicates deficiencies to the PMR/PMC Development Coordinator, review team leader, and others, as needed.
 - Ensures that staff adheres to standardized policies for PMR/506B PMC tracking and review.
 - Corresponds with the applicant regarding PMRs/506B PMCs.
- **OND/ORO Project Management Staff (ORO Staff)**
 - Provides information and support to the PMR/506B PMC Tracking Coordinator, as needed.
 - Usually serves as the OND review division's primary contact for internal activities related to PMR/506B PMC enforcement and compliance matters regarding PREA PMRs.
 - Validates receipt of expected submissions (e.g., the annual status reports, 180-day reports, and any other PMR/506B PMC-related submissions).

¹⁴ Refer to the RESPONSIBILITIES section in MAPP 6010.9, *Procedures and Responsibilities for Developing Postmarketing Requirements and Commitments*, as there may be overlap in each role. For the most recent version of a MAPP, refer to the *CDER Manual of Policies & Procedures* website available at <https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cder-manual-policies-procedures-mapp>.

¹⁵ 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.

¹⁶ Refer to footnote #8 [Searchable PMR/PMC database].

- Verifies contents of certain PMR/506B PMC-related submissions and sends them to the appropriate reviewer or review team (e.g., annual status report, release requests, deferral extension requests, and other PMR/506B PMC-related submissions).
 - Coordinates with the SRPM and review team regarding the evaluation of PMR/506B PMC-related submissions.
 - Drafts consults and letters and sends certain PMR/506B PMC content-related correspondence regarding PMR/506B PMC protocols to the applicant, as designated by the applicable OND review division, ensuring that the SRPM is aware of these communications.
- **OND Safety Regulatory Project Manager**
 - Generally, serves as the OND review division’s PMR/506B PMC Tracking Coordinator.
 - If ORO staff are designated as the PMR/506B PMC Tracking Coordinator, the SRPM provides information and support to the PMR/506B PMC Tracking Coordinator, as needed.
 - Serves as the OND review division’s primary contact for internal activities related to PMR/506B PMC enforcement and compliance matters regarding PMRs.
 - Ensures PMR/506B PMC ASRs are submitted for open PMRs/506B PMCs and ensures timely completion of the ASR review form.
 - Monitors and tracks PMR/506B PMC milestones and the applicant’s adherence to established milestones in coordination with ORO staff.
 - Communicates PMR/506B PMC deficiencies (e.g., missed review timelines) and statuses to their supervisor (i.e., Associate Director for Safety (ADS) or Deputy Director for Safety (DDS)), and review teams on a regular basis.
 - Contacts applicants regarding overdue PMR/506B PMC-related submissions and missed milestones.
 - Reviews PMR/506B PMC submissions, as assigned by ORO staff, to ensure that the submissions reflect PMR/506B PMC-related coding and to confirm that the appropriate PMR/506B PMC policies and procedures are followed.

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- Coordinates with ORO staff and SRPMs from other OND review divisions and consulting offices that have joint or team responsibility regarding the evaluation of PMR/506B PMC-related submissions.
 - Completes the correspondence and related forms or memos, using templates from the internal CST library.
 - Drafts consults and letters and sends certain PMR/PMC content-related correspondence regarding PMRs/506B PMCs to the applicant, as designated by the applicable OND review division, ensuring that ORO staff are aware, as appropriate.
 - **PMR/PMC Development Coordinator**
 - Generally, this role is occupied by an OND review division team member (e.g. ADS/DDS or their designee).
 - Provides information and support to the PMR/506B PMC Tracking Coordinator, as needed.
 - Participates in discussions and decisions regarding whether to release or fulfill a PMR/506B PMC.
 - **Review Team Leader or Cross-Disciplinary Team Leader (CDTL)**
 - Provides information and support to the PMR/506B PMC Tracking Coordinator, as needed.
 - Ensures that all appropriate disciplines and offices participate in the evaluation and discussion of PMR/506B PMC-related submissions (e.g., Office of Surveillance and Epidemiology (OSE) is engaged in discussions regarding observational epidemiologic studies required as a 505(o)(3) PMR).
 - Updates the supervisors who oversee the work of the review team members, as applicable.
 - **Reviewer**
 - This role is occupied by a discipline reviewer assigned to a drug (e.g., clinical, clinical pharmacology, nonclinical toxicology, safety-related disciplines, quality, biostatistics).
 - Identifies potential PMR/506B PMC review issues and works with the review team and review management to discuss these issues.
 - Recommends other discipline participation, if necessary.
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- Reviews PMR/506B PMC-related submissions according to stated review timelines.
 - Obtains appropriate review and sign-off as needed by the review team leader/CDTL, PMR/PMC development coordinator, and review management.
 - Collaborates on developing the appropriate communication regarding PMR/506B PMC-related submissions (i.e., related to a final protocol, interim report, or final report) and provides status updates to ORO staff and/or the PMR/506B PMC Tracking Coordinator.
 - **PMR/PMC Program Manager and Team**
 - This role is occupied by staff members in the OND Immediate Office/Safety, Policy, Research, and Initiatives (SPIRIT) PMR/PMC Program Team.
 - Oversees CDER’s PMR/PMC Program including all PMR/506B PMC data in ERKS and on the PMR/506B PMC public website.¹⁷
 - Reviews and clears PMR/506B PMC-related letters and memos.
 - Responds to PMR/506B PMC-related questions from internal and external stakeholders.
 - Clarifies PMR/506B PMC tracking and review processes to improve the quality and timeliness of status updates and submission review as appropriate.
 - Ensures data integrity for certain PMR/506B PMC data.
 - Provides updates to internal and external reports (e.g., Annual Reports on PMRs/506B PMCs to the Federal Register, Reports to Congress, Office of Inspector General (OIG) reports, and General Accounting Office (GAO) reports).¹⁸
 - Provides PMR/506B PMC-related training to other offices, divisions, and external stakeholders.
 - Coordinates and leads the development of and revisions to PMR/506B PMC-related MAPPs, guidances, and other regulatory documents.

¹⁷ Refer to footnote #8. [Searchable PMR/PMC database]

¹⁸ For the PMR/506B PMC annual reports and “Annual Report to Congress on the Backlog of PMRs and PMCs” refer to the Postmarketing Requirements and Commitments: Reports website at <https://www.fda.gov/drugs/postmarketing-requirements-and-commitments-introduction/postmarketing-requirements-and-commitments-reports>.

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- Supports the implementation of new regulations affecting the PMR/PMC Program.
 - Provides PMR/506B PMC-related updates to the leadership team.
 - **Office of Business Informatics (OBI)/Division of Data Management Services & Solutions (DDMSS)**
 - Updates the PMR/506B PMC data in ERKS based on outgoing PMR/506B PMC-related communications, ASR Review Forms, and 180-day AA PMR Review Forms, according to the current standard operating procedures.
 - Responds to questions related to PMRs/506B PMCs data in ERKS.
 - Collaborates with the PMR/PMC Program Team to manage the PMRs/506B PMC data in ERKS.
 - **Office of Program and Strategic Analysis/Analytics and Data Services Staff (ADSS)**
 - Generates internal PMR/506B PMC-related monthly reports from ERKS and disseminates for tracking purposes.
 - Provides PMR/506B PMC data for annual reports, quarterly updates, and internal and external requests for data.
 - **Review Management**
 - Receives updates on the review of applicants' submissions from the review team leader and provides review oversight (e.g., protocol submissions, interim report submissions, final report submissions).
 - **Senior Management (CDER Center Director/Office Directors)**
 - Ensures that adequate resources are allocated to develop and maintain PMR/506B PMC data in ERKS.
 - Receives updates on PMR/506B PMC-related policy issues (e.g. PMR reconsideration requests).
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PROCEDURES

OND review divisions monitor and track all established PMRs and 506B PMCs within their divisions, including all scheduled milestone dates and expected PMR/506B PMC-related submissions and take appropriate actions as needed.

1. Monitor Open PMRs/506B PMCs and Related Submissions

- a. Perform regular reviews of all open PMRs/506B PMCs:
 - i. Monitor receipt of expected submissions (e.g., protocols, ASRs, final reports) and ensures correct coding of the submission by verifying contents.
 - ii. Ensure the accuracy of the PMR/506B PMC status.
 - iii. Contact data entry or PMR/PMC Program team for discrepancies identified in ERKS.
- b. Monitor the status of PMRs/506B PMCs using the internal monthly reports and other information, as appropriate.

2. Timely Review of PMR/506B PMC-Related Submissions

- a. Review the contents of all PMR/506B PMC-related submissions.
 - i. Ensure that the submission is coded appropriately in ERKS based on its contents.
 - ii. Double code submissions that contain more than one document, (e.g., a labeling supplement and a final report) to indicate the inclusion of all documents.
 - iii. Assign the submission to the appropriate reviewers.
- b. Review PMR/506B PMC- related submissions within the internal review timelines.
 - i. PMR/PMC Final Report (goal without supplement: 12 months; goal with supplement: PDUFA supplement submission timeline).
 - ii. PMR/PMC Status Validation for Applicant's ASR (goal: 3 months).¹⁹

¹⁹ Refer to MAPP 6004.2, *Procedures for Completing and Processing the Form "Annual Report Review: Postmarketing Study Commitment Summary"*.

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- iii. 180-day Accelerated Approval PMR Progress Report (goal: 90 days).
 - iv. PMR/PMC Release Request (goal: 60 days).
 - v. Response to additional information requested for PMR/PMC release request (goal: 60 days).
 - vi. PMR/PMC Release Reconsideration Request (goal: 45 days).
 - vii. PREA Deferral Extension Request (goal: 45 days).
- c. Review PMR/506B PMC proposed revised milestones submitted by the applicant within a reasonable amount of time (may be submitted as a separate submission or within the ASR).
 - d. Monitor the progress of the review of PMR/506B PMC-related submissions.

3. Communicate Regarding PMRs/506B PMCs and Related Submissions

- a. Contact the applicant for resolution of discrepancies within PMR/506B PMC-related submissions, such as:
 - i. Missing or incomplete information related to the applicant's ASR.
 - ii. Lack of specific calendar dates for revised milestones.
- b. Draft PMR/506B PMC-related communication and obtain appropriate Safety Requirements Team (SRT) clearances as needed (e.g., *Acknowledge PMR-PMC Revised Milestones* (and communicate good cause) letter and memo).²⁰
- c. Issue appropriate PMR/506B PMC-related communication to the applicant. For instance:
 - i. Add PMR/506B PMC fulfilled language in the action letter or issue a separate *Fulfilled* letter if a submitted supplemental application for a PMR/506B PMC meets the objective of the PMR/506B PMC.
 - ii. Issue a *Notification of Missed Milestone* letter if a PMR/506B PMC-related milestone has been missed and the applicant has not communicated with the division.

²⁰ Refer to the internal *Postmarketing Requirements (PMRs) and 506B Postmarketing Commitments (506B PMCs)* site for a list of documents that require SRT review and clearance.

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- iii. Issue a *Notification of Missed Milestones* letter if a failure to demonstrate good cause determination is made regarding a 505(o)(3) PMR, to obtain additional information regarding the reason the milestone was missed.
 - iv. Issue a PREA Noncompliance letter consistent with 505B(d)(1) if the applicant failed to submit the required pediatric assessment by the final study report date.
- d. Issue the appropriate communication in response to an applicant's proposed revised milestones. Ensure that PMR/506B PMC-related communications and forms (e.g., ASR review form, fulfilled and release letters) are linked to the appropriate submissions, as applicable, to close related review goals.

4. Update the Status of PMRs/506B PMCs in ERKS

- a. Update the PMR/506B PMC data in ERKS regularly using PMR/506B PMC-related communications (e.g., ASR and 180-day AA PMR Progress Report review forms) and relevant applicant submissions.
- b. Perform regular quality checks to ensure the integrity of the PMR/506B PMC data in ERKS.
- c. Ensure that the correct incoming PMR/506B PMC document submission codes have been applied.

5. Report on PMRs/506B PMCs Internally and Externally

- a. Generate and disseminate PMR/506B PMC reports from ERKS for internal use.
- b. Provide PMR/506B PMC information publicly on FDA's PMR/506B PMC website, as mandated by statute:²¹
 - i. Quarterly update
 - ii. Annual Report on the Performance of Drugs and Biologics Firms in Conducting Postmarketing Requirements and Commitments and Federal Register Notice
 - iii. Report to Congress on the Backlog of Postmarketing Requirements and Commitments

²¹ Refer to the *Postmarketing Requirements and Commitments: Introduction* website available at <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/postmarketing-requirements-and-commitments-introduction>.

REFERENCES

- Guidance for Industry: *Annual Status Report Information and Other Submissions for Postmarketing Requirements and Commitments: Using Forms FDA 3988 and FDA 3989* (September 2023).
- 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: *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 represent the Agency's current thinking on this topic.
- Guidance for Review Staff and Industry: *Good Review Management Principles and Practices for New Drug Applications and Biologics License Applications* (September 2018).
- 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).²²
- CDER MAPP 6010.9 Rev.1: *Procedures and Responsibilities for Developing Postmarketing Requirements and Commitments* (04/13/2026).
- *Postmarketing Requirements and Commitments: Introduction* website (<https://www.fda.gov/drugs/guidance-compliance-regulatory-information/postmarketing-requirements-and-commitments-introduction>).

DEFINITIONS

- **506B-Reportable Postmarketing Commitment (506B PMC)** – Postmarketing studies or clinical trials concerning clinical safety, clinical efficacy, clinical pharmacology, or nonclinical toxicology that applicants have agreed in writing to conduct; 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).^{23,24}

²² Although the guidance refers only to postmarketing commitments, some of these commitments are required under PREA; 21 CFR part 314, subparts H and I; and 21 CFR part 601, subparts E and H.

²³ Refer to Footnote #8. [searchable PMR/PMC database].

²⁴ Refer to 21 CFR 314.81(b)(2)(vii).

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- **Clinical Trial** – Any prospective investigation in which the applicant or investigator determines the method of assigning the drug product(s) or other interventions to one or more human subjects.
 - **Electronic Records Keeping Systems (ERKS)** – The authoritative data source for a given data element or piece of information within an information management system. (Per 36 CFR 1236.2, an electronic information system is a “system that contains and provides access to computerized Federal records and other information.”).
 - **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.
 - **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).²⁵
 - **PMR/506B PMC-Related Submission** – A formal submission sent by the applicant to address an established PMR or 506B PMC. Such submissions may include:
 - Draft and Final protocols
 - PMR/PMC general correspondence (e.g., requests for revised milestone dates)
 - Annual Status Reports (ASRs)
 - Final reports
 - Interim reports
 - Release requests

²⁵ Draft Guidance for Industry, *Postmarketing Studies and Clinical Trials – Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act* (July 2023). When final, this guidance will reflect the Agency’s current thinking on this topic.

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- 180-day Accelerated Approval PMR Progress Reports
 - Supplemental applications submitted to address a PMR/PMC
 - **PMR/506B PMC Scheduled 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. At least one of 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)
 - **PMR/PMC Status Categories**
 - **Open Status Categories** – 506B of the FD&C Act requires applicants to report on the status of open PMRs/PMCs annually using the following categories:
 - *Pending* – The study or clinical trial has not been initiated (i.e., no subjects have been enrolled or animals dosed) but does not meet the criterion for delayed (i.e., the original projected date for initiation of subject accrual or initiation of animal dosing has not passed).
 - *Ongoing* – The study or clinical trial is proceeding according to, or is ahead of, the original schedule. FDA considers a study/clinical trial to be ongoing until a final report is submitted to FDA, as long as the activities are proceeding according to the original schedule. If subject accrual or animal dosing has started but is not complete, and the projected date for completion of that milestone has passed, the study/clinical trial should be categorized as delayed.
 - *Delayed* – The progression of the study/clinical trial is behind the original schedule. Delays can occur in any phase of the study/clinical trial, including subject enrollment, analysis of study/clinical trial results, or submission of the final report to FDA. Whereas the original schedule – not a revised schedule – serves as the basis for defining a study/clinical trial as delayed, each phase of the study/clinical trial will be considered in

its own right. If the applicant has one delayed phase, but gets back on schedule during the next phase, the delayed status will no longer apply.

- *Terminated* – The applicant ended the study/clinical trial before completion and has not yet submitted a final report to FDA.
- *Submitted* – The applicant has concluded or terminated the study/clinical trial and has submitted a final report to FDA, but FDA has not yet notified the applicant in writing that the PMR/PMC has been fulfilled or that the PMR/PMC has been released.

– **Closed Status Categories**

- *Fulfilled* – The applicant has submitted the final report for the PMR/PMC, and upon review of the final report, FDA has notified the applicant in writing that the terms of the PMR/PMC have been met.
 - *Released* – FDA has informed the applicant in writing that it has been released from its obligation to conduct the study/clinical trial because the study/clinical trial is either no longer feasible or would no longer provide useful information.
- **Study** – An investigation other than a clinical trial as defined above, such as an investigation with humans that is not a clinical trial (e.g., observational epidemiologic study or lactation study), nonclinical study, or laboratory experiment.

EFFECTIVE DATE

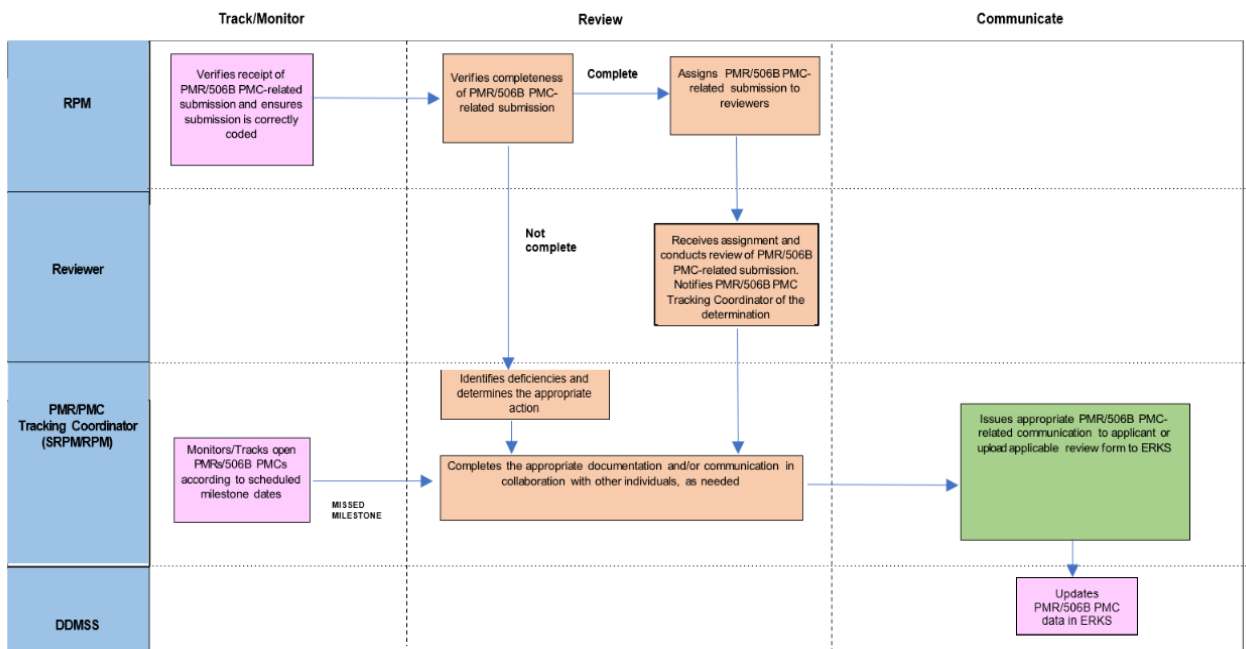
- This MAPP is effective upon date of publication.
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CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
10/01/1996	N/A	
07/28/2009	R1	
04/13/2026	R2	Updated to align with current OND organizational structure, any applicable user fee agreements (UFA) commitments, and contemporary CDER workflow procedures and best practices. Update to align background and definitions sections with MAPP 6010.9

ATTACHMENT 1: Process Flow for PMR/506B PMC Tracking, Monitoring, and Communicating

This flowchart reflects the processes and responsibilities by role for tracking and monitoring the progress of PMRs/506B PMCs, which includes reviewing PMR/506B PMC-related submissions and communicating with applicants regarding PMRs/506B PMCs.²⁶ The leftmost column shows the roles with the primary responsibility for tracking, monitoring/reviewing, and communicating with the applicant. The top row shows the processes from left to right starting with tracking/monitoring, reviewing, and communicating. The row or swim lane for each role contains relevant tasks associated with each of the processes.



- Tracking and monitoring activities
- Review activities
- Communication

²⁶ Roles and responsibilities may vary for each OND review division.