OFFICE OF NEW DRUGS

Responsibilities for Tracking and Communicating the Status of Postmarketing Requirements and Commitments

CONTENTS

PURPOSE

- The purposes of this MAPP are to define postmarketing requirements and commitments (PMRs/PMCs) and to describe the policies and responsibilities for the Center for Drug Evaluation and Research (CDER) staff to follow to:
  - Track and monitor status of established PMRs/PMCs, including proactive tracking of expected submissions
  - Ensure accurate processing of PMR/PMC-related submissions received by the Food and Drug Administration (FDA)
  - Track and monitor PMR/PMC-related submissions while under FDA review
  - Ensure review of PMR/PMC-related submissions
  - Verify PMR/PMC information provided in annual status reports, including applicant-reported status and explanation of status
  - Communicate to the applicant any comments or discrepancies in applicant-reported status following FDA review
  - Communicate to the applicant any content-related comments regarding PMR/PMC-related submissions following FDA review and when a PMR/PMC is fulfilled or released
  - Ensure that PMR/PMC statuses are updated in the database in a timely manner

- This MAPP applies to all reportable 506B PMRs/PMCs for drugs and licensed biologics regulated by CDER and to non-506B PMCs (i.e., chemistry, manufacturing, and controls and certain product stability studies).[1] This MAPP also applies to 506B PMRs for drugs approved under the animal efficacy rule or accelerated approval, studies required under the Pediatric Research Equity Act (PREA), and safety studies

[1] See the Definitions section.

or clinical trials required under the Food and Drug Administration Amendments Act (FDAAA). The responsibilities outlined in this MAPP do not apply to postmarketing studies or clinical trials conducted on an applicant's own initiative. This MAPP does not discuss policy and procedures for PMR/PMC development. That topic is described in MAPP 6010.9 *Procedures and Responsibilities for Developing Postmarketing Requirements and Commitments*.

BACKGROUND

- PMRs/PMCs are studies or clinical trials that are conducted by the applicant after the FDA has approved a drug for marketing or licensing.[2] These studies or trials can be either required by regulation or statute (PMRs) or agreed upon by the FDA and the applicant (PMCs).[3]

- Section 130(a) of the Food and Drug Administration Modernization Act of 1997 (FDAMA) amended the Federal Food, Drug, and Cosmetic Act (the Act) by adding a new provision requiring reports of certain postmarketing studies for human drug and biological products (section 506B of the Act (21 U.S.C. 356b)). Section 506B of the Act provides the FDA with additional authority to monitor the progress of a PMC that an applicant has been required or has agreed to conduct by requiring the applicant to submit an annual report that provides information on the status of the PMC. This report must also include the reasons, if any, for failure to complete the commitment. This provision is implemented at 21 CFR 314.81(b)(2)(vii) and 601.70. The regulations went into effect on April 30, 2001 (66 FR 10815).

- Effective March 25, 2008, section 901 of FDAAA created section 505(o) of the Act, which authorizes the FDA to require certain postmarketing safety studies/clinical trials and requires applicants to submit a timetable for completion of each study/clinical trial. Applicants are also required to periodically report on each safety study/clinical trial required or otherwise undertaken. Submission of the annual report on the status of PMRs/PMCs required under section 506B may also satisfy the periodic reporting requirements for PMRs under FDAAA. See the Definitions section for a definition of *studies* and *clinical trial* 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)).

- 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 PMC until it is notified in writing that the commitment has been fulfilled or that it has been released from the commitment.

[2] For the purposes of this MAPP, all references to *drugs* include both human drugs and therapeutic biological products unless otherwise specified.

[3] See the Definitions section.

- In February 2006, the FDA issued 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*. This guidance describes in detail the content, format, and timing of the reports required by section 506B of the Act.[4]

- The FDA reviews the annual status reports and then updates the status and other information in the PMR/PMC database.[5] The FDA uses the database to track PMR/PMC status and as a data source for certain information that is displayed on an FDA public Web site.[6] The FDA also publishes PMR/PMC data annually in the *Federal Register* to meet its obligations for public disclosure of information required under section 506B(b) and (c) of the Act.

- New amendments to the Act give the FDA authority to enforce the section 505(o)(3)(E)(ii) requirements for postmarketing studies and clinical trials. Violations include the applicant's failure to comply with the schedule milestones, periodic report submissions, and other requirements of section 505(o)(3)(E)(ii) unless the applicant demonstrates good cause for the noncompliance or violation. The FDA will determine what constitutes good cause. If the applicant is in violation of these requirements, the drug involved may not be introduced or delivered into interstate commerce. In addition, violations of the requirements for postmarketing safety studies and clinical trials may result in misbranding charges and civil penalties.

REFERENCES

- Federal Food, Drug, and Cosmetic Act, section 506B (http://www.fda.gov/opacom/laws/fdcact/fdcact5a.htm), and section 505(o)(3), created by section 901 of the Food and Drug Administration Amendments Act of 2007 (http://www.fda.gov/oc/initiatives/advance/fdaaa.html)

- 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* (http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm)

- Guidance for review staff and industry *Good Review Management Principles and Practices for PDUFA Products* (http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm)

[4] 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.

[5] The PMR/PMC database refers to the data management systems used in CDER to capture and track all PMRs/PMCs.

[6] See http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm.

- MAPP 6004.2 *Procedures for Completing and Processing the Form "Annual Report Review: Postmarketing Study Commitment Summary"* (http://www.fda.gov/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/default.htm)

- MAPP 6010.9 *Procedures and Responsibilities for Developing Postmarketing Requirements and Commitments* (http://www.fda.gov/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/default.htm)

- Postmarketing Requirements and Commitments public Web site (http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PostmarketingPhaseIVCommitments/default.htm)

- Independent Evaluation of FDA's Prescription Drug User Fee Act III — Evaluations & Initiatives: Postmarketing Commitments Study Final Report (conducted by Booz Allen Hamilton beginning 2006, published January 2008) (http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm119856.htm)

DEFINITIONS

- **506B-Reportable Postmarketing Requirements and Commitments —** Postmarketing studies or clinical trials concerning clinical safety, clinical efficacy, clinical pharmacology, or nonclinical toxicology that applicants have agreed upon in writing or are required to conduct.[7] Section 130 of FDAMA requires sponsors to submit annual status reports. The FDA is then required to make publicly available certain information about these studies/clinical trials.

- **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.

- **Postmarketing Commitment (PMC) —** Any study or clinical trial that an applicant has *agreed*, in writing, to conduct after approval of a marketing or licensing application or supplement that is *not* a PMR (see below).

- **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 FDAAA (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)).

[7] 506B reporting is described as *postmarketing study commitments*, even though some of these commitments are required under PREA and subparts H, E, and I. Similarly, this reporting often refers to *study*; FDAAA distinguishes between study and *clinical trial*. Finally, 506B reporting includes *clinical safety* PMCs; studies or clinical trials that concern serious safety risks will now be required under FDAAA. Section 130 of FDAMA amended the Federal Food, Drug, and Cosmetic Act to add section 506B and predates FDAAA. The definition of postmarketing commitments has been revised in accordance with FDAAA.

- **PMR/PMC Development Coordinator —**
  - An Office of New Drugs (OND) review team staff member, generally the OND deputy division director for safety, who has been assigned the responsibility of reviewing PMRs/PMCs before they are sent to the applicant and before a letter issues.

  - Participates in decisions regarding established PMRs/PMCs (e.g., decisions to consider whether a PMR/PMC is released or fulfilled).

  - Reviews the PMR/PMC rationale to ensure that it is sound and clearly articulated, the PMR/PMC is feasible, and the schedule of milestones is appropriate. Refers concerns about these components to the review team and review management for discussion.

- **PMR/PMC Program Manager —** Person in the OND Immediate Office with PMR/PMC database and Web site oversight responsibility who ensures that all PMR/PMC-related information is updated and made publicly available in the appropriate data management systems. The PMR/PMC Program Manager also provides support and training to offices and divisions included on review teams; coordinates the development and revisions of PMR/PMC-related MAPPs, guidances, and other regulatory documents; and periodically updates senior and review management on implementation issues as needed.

- **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
  - Annual status reports
  - Final reports
  - Supplemental applications submitted to address a PMR/PMC

- **PMR/PMC Schedule 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 following milestone dates should be included in the schedule and in the letter when the PMR/PMC is required or agreed upon.
  - Final protocol submission date
  - Study/clinical trial completion date or time related to the preceding milestone (e.g., X months after final protocol submission)
  - Final report submission date or time related to the actual completion date (e.g., within X months from completion)

- **PMR/PMC Status Categories**
  - **Open Status Categories —** 506B of the 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. The FDA considers a study/clinical trial to be *ongoing* until a final report is submitted to the 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 the 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 the FDA.

- *Submitted* — The applicant has concluded or terminated the study/clinical trial and has submitted a final report to the FDA, but the 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, the FDA has notified the applicant in writing that the terms of the PMR/PMC have been met.

- *Released* — The FDA has informed the applicant in writing that it has been released from its obligation to conduct the study/clinical trial.

- **PMR/PMC Tracking Coordinator —** One or more OND review division staff members, generally an OND review division safety regulatory project manager, with the role of ensuring that the review team is kept informed of PMR/PMC schedule milestones, verifying PMR/PMC information for accuracy, and monitoring whether expected activities are conducted according to the timelines specified in the letter and in CDER policy documents (e.g., applicant submissions and FDA review). The PMR/PMC tracking coordinator assumes primary responsibility for corresponding with the applicant regarding PMR/PMC **process** issues. The tracking coordinator's responsibilities generally occur after approval.

- **Quality Management Staff —** Staff in CDER's Office of the Center Director who initiate, conduct, and complete quality assurance assessments of Center-wide programs and processes.

- **Regulatory Project Manager (RPM) —** The OND division review team regulatory project manager (RPM) assigned to an application. The OND RPM has the primary responsibility for coordinating with the review team and corresponding with the applicant regarding PMR/PMC **content** issues.

- **Reviewer —** Discipline reviewer assigned to a drug (e.g., clinical, clinical pharmacology, nonclinical toxicology, safety-related disciplines, quality, biostatistics).

- **Review Management —** For the purposes of this MAPP, is defined as supervisors (e.g., from OND, the Office of New Drug Quality Assessment (ONDQA), Office of Biotechnology Products (OBP), Office of Surveillance and Epidemiology (OSE), Office of Biostatistics (OB), Office of Clinical Pharmacology (OCP)) who oversee the work of members of the review team. In general, a review team member's team leader will be primarily involved in review oversight and will inform and consult with upper management, including the signatory authority, and other disciplines as needed, and will ensure that other disciplines are included on the team as needed.

- **Review Team —** All RPMs, reviewers, review team leaders, review management, and senior management in OND, ONDQA, OBP, OSE, OB, OCP, and others, who are responsible for pre- and postapproval drug application and submission review.

- **Review Team Leader** including the Cross-Disciplinary Team Leader (CDTL) **—** A discipline review team member who provides secondary review for the primary discipline reviewer, or in the case of the CDTL, leads the review team for a drug.

- **Senior Management —** For the purposes of this MAPP, is defined as:
  - CDER Center Director or Deputy
  - CDER super-office directors and deputies, including but not limited to those from OND, OSE, Office of Pharmaceutical Science, and Office of Translational Sciences

- **Studies —** All investigations other than clinical trials as defined above, such as investigations with humans that are not clinical trials (e.g., observational epidemiologic studies), animal studies, and laboratory experiments.

POLICY

- The FDA review divisions will track all established PMRs and PMCs within their divisions, including all PMR/PMC scheduled milestone dates and all expected PMR/PMC-related submissions.

- The FDA will process PMR/PMC-related submissions as they are received, verify PMR/PMC status, communicate to the applicant omissions and errors in PMR/PMC status reporting, and update the PMR/PMC database in a timely manner.

- The FDA will communicate to the applicant missed submission dates, and will notify the Office of Compliance if missed dates involve FDAAA-related PMRs.

- The FDA will review PMR/PMC-related submissions according to the following timelines.
  - *Protocols* — The FDA will conduct a timely review of all PMR/PMC protocols submitted by the applicant. The FDA will provide detailed feedback on noted deficiencies and suggested revisions if there are concerns with the submitted protocol design.

  - *Annual status reports* — The FDA will review annual status reports and complete the summary sheet within 3 months of receipt. If the FDA does not agree with an applicant's categorization of the status and/or explanation of status of the PMR/PMC, the FDA will contact the applicant for clarification. After verification of the information submitted in annual status reports, the FDA database will be updated with the correct status and/or explanation of status as supported by the information provided by the applicant in the annual status report.

  - *Final reports* — A final report submitted as a supplemental application will be reviewed according to established review times for supplements. A final report submitted without a supplemental filing should be reviewed within 1 year of receipt. In either case, the FDA will notify the applicant in writing of the final fulfillment determination.

RESPONSIBILITIES

Responsibilities for the PMR/PMC tracking and communication process are described in Tables 1 through 8. The PMR/PMC tracking and communication process flow is illustrated in Attachment A.

Table 1. Overall Roles and Responsibilities for the PMR/PMC Tracking and Communication Process

Role	Responsibility
Senior Management	• Ensures that the PMR/PMC tracking and review process steps are implemented consistently and in a timely manner across the Center • Supports changes to the PMR/PMC tracking and review process that improve the quality and timeliness of status updates and submission review • Ensures that adequate resources are allocated to develop and maintain a PMR/PMC database with optimal tracking and reporting functionality • Provides a forum for review management to share summary updates on PMR/PMC status as well as tracking or review process issues or changes (e.g., as an agenda item at a standing meeting)
Review Management	• Ensures staff are aware of and adhere to standardized policies for PMR/PMC tracking and review • Ensures that PMR/PMC-related activities are completed according to stated review timelines (e.g., review of PMR/PMC-related submissions, verification of PMR/PMC information in annual status reports)
PMR/PMC Development Coordinator	• Provides information and support to the PMR/PMC tracking coordinator as needed • Participates in discussions and decisions regarding whether to release or fulfill a PMR/PMC
Review Team Leader/CDTL	• Provides information and support to the PMR/PMC tracking coordinator as needed • Ensures staff adhere to standardized policies for PMR/PMC tracking and review
Reviewer	• Reviews PMR/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 • Provides appropriate communication of deficiencies and status updates to the RPM and/or the PMR/PMC tracking coordinator
Regulatory Project Manager	• Facilitates compliance with responsibilities outlined in MAPP 6010.9 *Procedures and Responsibilities for Developing Postmarketing Requirements and Commitments* • Provides information and support to the PMR/PMC tracking coordinator as needed • Ensures that annual report submissions and other PMR/PMC-related submissions are distributed to the appropriate reviewers • Drafts and sends PMR/PMC *content*-related correspondence to the applicant with a copy to the PMR/PMC tracking coordinator

continued

Table 1, continued

Role	Responsibility
PMR/PMC Tracking Coordinator	• Ensures that accurate PMR/PMC information is captured in the PMR/PMC database (e.g., current status, schedule milestones, explanation of status) and is reflected on the public Web site • Monitors whether or not PMR/PMC-related activities are completed according to stated review timelines (e.g., review of PMR/PMC-related submissions, verification of PMR/PMC information in annual status reports) and communicates deficiencies to the development coordinator, review team leader, and RPM as needed • Issues PMR/PMC *tracking*-related correspondence to the applicant as appropriate with a copy of release or fulfillment letters to the RPM and pertinent review team members (e.g., PMR/PMC Dunner letters: letter notifying applicant of late PMR/PMC-related submission; letter notifying applicant of late annual status report submission; letter notifying applicant of PMR/PMC fulfillment or release) • Notifies the Office of Compliance when an applicant has missed, or is expected to miss, a scheduled milestone date or is late in submitting the annual status report • Includes the OND RPM and consulting offices and divisions that have joint or team responsibility for evaluation of the PMR/PMC-related submissions in the distribution list of key correspondence for the PMR/PMC
PMR/PMC Program Manager	• Establishes requirements for all necessary tracking elements, reports, and functionality in the PMR/PMC database • Works with the appropriate PMR/PMC tracking coordinator to ensure that quality checks of the data in the PMR/PMC database are performed and any discrepancies are resolved • Monitors whether offices and divisions are reviewing PMR/PMC-related submissions and verifying data in a timely fashion • Consults with the Division of Information Disclosure Policy on PMR/PMC information releasability issues • Provides training to staff across all offices and divisions on roles and responsibilities • Provides input and acts as a resource for policy issues related to PMR/PMC development, tracking, and review
Quality Management Staff	• Conducts periodic process audits to determine compliance with the defined policies and procedures

Table 2. Tracking Expected PMR/PMC-Related Submissions

Role	Responsibility
PMR/PMC Tracking Coordinator	• Actively monitors the PMR/PMC database in anticipation of expected submissions (e.g., protocol, annual status report, final report) • Verifies receipt of PMR/PMC-related submissions for all approved drugs within his or her division (e.g., using simple tracking sheet or PMR/PMC database reports in addition to routine notifications received from the document room staff and RPMs as described in Table 3), and requests updates on PMR/PMC-related issues from RPMs on a regular basis (e.g., monthly) • Serves as the primary point of contact for communications with applicants for *tracking*-related PMR/PMC issues • Generates PMR/PMC Dunner letters for overdue or incomplete PMR/PMC submissions (e.g., final reports and annual status reports) and copies the RPM; coordinates with the Office of Compliance for all deficiency communications related to safety PMRs under FDAAA • Notifies the Office of Compliance when an applicant has missed, or is expected to miss, a scheduled milestone date or is late in submitting the annual status report (applies only to safety PMRs under FDAAA)

Table 3. Processing PMR/PMC-Related Submissions

Role	Responsibility
Document Room Staff	• Processes all incoming submissions to investigational new drug applications, new drug applications, or biologics license applications that refer to PMRs/PMCs according to documented procedures • Ensures that incoming PMR/PMC document submission codes are accurately applied
Regulatory Project Manager	• Confirms that all PMR/PMC-related submissions are accurately coded in the document management system. If needed, updates the submission with the appropriate incoming PMR/PMC document submission code. • Conducts an administrative review of each annual status report for PMRs/PMCs to ensure they are: – Accompanied by Form FDA 2252 – Complete and do not contain any other type of notification or submission • Ensures that PMR/PMC-related submissions are routed to all appropriate reviewers. • Ensures the tracking coordinator is notified of receipt for all PMR/PMC-related submissions, or notifies tracking coordinator if the PMR/PMC status report is missing or incomplete so tracking coordinator can communicate with the applicant as needed (e.g., send Dunner letter).
PMR/PMC Tracking Coordinator	• Issues PMR/PMC Dunner letters when the annual status reports are missing or incomplete and copies the RPM when such letters are sent • Ensures that the data in the PMR/PMC database are quality checked (i.e., that the correct incoming PMR/PMC document submission codes have been applied) before periodic PMR/PMC-related submission reports are generated

Table 4. Tracking PMR/PMC-Related Submissions Currently Under Review

Role	Responsibility
PMR/PMC Tracking Coordinator	• Tracks the review progress of PMR/PMC-related submissions for all approved drugs in the division (e.g., using simple tracking sheet or PMR/PMC database report) • Actively monitors that PMR/PMC-related submissions are reviewed according to stated timelines for all approved drugs in the division • Confirms that applicant-reported statuses in the annual status report are verified by the reviewer • For PMRs/PMCs established with schedule milestone dates made in reference to other schedule milestone dates (e.g., final report to be submitted within 6 months of completion), ensures that the PMR/PMC database is populated with specific calendar dates that correlate with when these milestones are scheduled to occur or have actually occurred • Facilitates review team discussions with applicants to encourage compliance with PMRs/PMCs as needed (e.g., discuss modified schedules) • Coordinates the review of PMR/PMC-related submissions and communicates with the RPM as needed
Reviewer	• Communicates with the PMR/PMC tracking coordinator the progress and anticipated completion date for review of PMR/PMC-related submissions

Table 5. Reviewing PMR/PMC-Related Submissions and Verifying Status

Role	Responsibility
Reviewer	• Works with the PMR/PMC tracking coordinator and the RPM to coordinate an agreed-upon timeline for completing the review of PMR/PMC-related submissions. • Performs a complete technical, scientific, or clinical review of PMR/PMC-related submissions within the stated review timelines in consultation with the appropriate review team leader and review management. • Coordinates with the RPM to obtain consults as needed with other CDER review offices and/or divisions according to MAPP 6025.3 *Consultative Review of Drugs Regulated Within OND*. Incorporates the recommendations into the review and/or final fulfillment determination. • Evaluates the PMR/PMC protocol for its ability to meet the objectives of the PMR/PMC. • Reviews the annual status report and verifies whether or not the applicant-reported PMR/PMC status and explanation of status are accurate and consistent with the original schedule milestone dates. Documents discrepancies and works with the PMR/PMC tracking coordinator to resolve any discrepancies in applicant-reported status and/or explanation of status.

continued

Table 5, continued

Role	Responsibility
Reviewer (continued)	• Reviews the final report to determine whether or not the PMR/PMC has been fulfilled, with concurrence from the review team leader, review management, and the PMR/PMC development coordinator. Communicates the final determination of fulfillment to the PMR/PMC tracking coordinator. • Provides the PMR/PMC tracking coordinator with an update on the review progress when prompted. • Ensures that all PMRs/PMCs are still feasible and required or needed, with concurrence from the review team leader, review management, and the PMR/PMC development coordinator. If the PMR/PMC is no longer required, needed or feasible, documents the reason in a review, which should be reviewed and signed by the PMR/PMC development coordinator and review management, with a copy sent to the PMR/PMC tracking coordinator so that he or she may prepare a release letter to the applicant after the determination has been signed by the appropriate managers. • Sends any *content*-related questions or deficiencies to the RPM to communicate to the applicant.
Review Team Leader/CDTL	• Ensures that PMR/PMC study/clinical trial protocols are evaluated for their ability to meet the objective of the requirement or commitment • Ensures that the appropriate divisions and/or offices have been consulted for evaluation and review, and that the recommendations have been addressed and/or incorporated into the review • Participates in discussions and decisions pertaining to determination of PMR/PMC fulfillment or release • Conducts secondary reviews, as needed
PMR/PMC Development Coordinator	• Participates in discussions regarding the postmarketing studies/clinical trials (e.g., whether they remain necessary, are feasible, are fulfilled) and whether protocols meet the objective
Review Management	• Participates in discussions and decisions pertaining to determination of PMR/PMC fulfillment or release • Ensures that review goals for PMR/PMC submissions are met
PMR/PMC Tracking Coordinator	• Works with the review team to coordinate an agreed-upon timeline for the review of PMR/PMC-related submissions within the stated review timelines

Table 6. Communicating Deficiencies, Status Changes, or Fulfillment or Release Determination to the Applicant

Role	Responsibility
Regulatory Project Manager	• Drafts and sends PMR/PMC *content*-related correspondence (e.g., protocol deficiencies) to the applicant with a copy to the PMR/PMC tracking coordinator • If a supplemental application is submitted in response to a PMR/PMC and upon review meets the objective of the PMR/PMC, includes notification of fulfillment in the action letter and notifies the PMR/PMC tracking coordinator or ensures that the tracking coordinator issues a separate fulfillment letter
PMR/PMC Tracking Coordinator	• Contacts the applicant for resolution of discrepancies in applicant-reported status or explanation of status when the reviewer does not agree with the information reported by the applicant in the annual status report • Issues a letter, with a copy sent to the RPM, within 30 days of a division's determination of fulfillment for PMRs/PMCs or when the division has concluded that the applicant may be released from the commitment • For PMRs/PMCs where the final protocol was submitted and other PMR/PMC-related submission dates were dependent on that submission date, notifies the applicant of the specific calendar dates to which the FDA will be tracking the PMR/PMC-related submissions

Table 7. Updating Status of PMRs/PMCs in the PMR/PMC Database

Role	Responsibility
PMR/PMC Tracking Coordinator	• Processes the PMR/PMC annual status report verification form in accordance with MAPP 6004.2 *Procedures for Completing and Processing the Form "Annual Report Review: Postmarketing Study Commitment Summary"* • For PMRs/PMCs established with schedule milestone dates made in reference to other schedule dates, ensures that the PMR/PMC database is populated with specific calendar dates that correlate with when these milestones are scheduled to occur or have actually occurred via communication with the PMR/PMC Program Manager
PMR/PMC Program Manager	• Ensures that the PMR/PMC database is populated and updated according to the current operating procedures

Table 8. PMR/PMC Management Reports

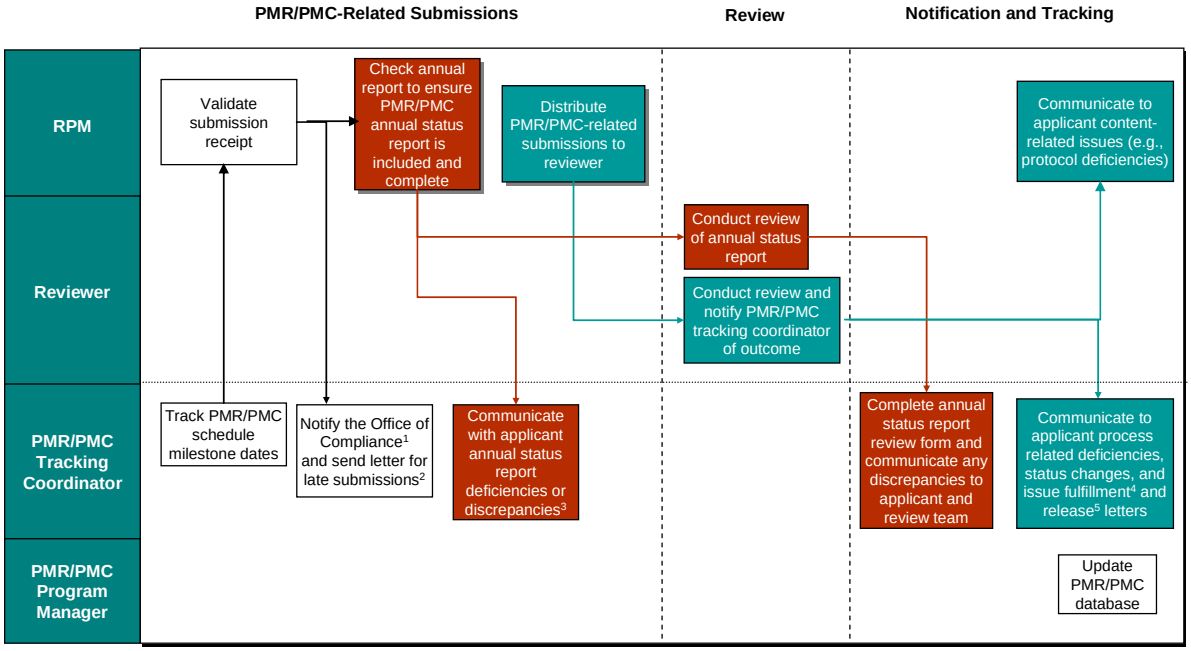
Role	Responsibility
Review Management	• Identifies a forum for reporting and reviewing PMR/PMC status at least quarterly (e.g., administration rounds)
PMR/PMC Tracking Coordinator	• Reports status of PMR/PMC-related submissions to be reviewed or currently under review to the PMR/PMC Program Manager on a regular basis (e.g., monthly or quarterly) • Conducts an annual review of the backlog of outstanding PMRs/PMCs in the division
PMR/PMC Program Manager	• Provides status reports from the PMR/PMC database to senior management and review management on a quarterly basis • Provides PMR/PMC information publicly as mandated (e.g., annual *Federal Register* report, public Web site)

EFFECTIVE DATE

- This MAPP is effective upon date of publication.

Attachment A: Process Flow for PMR/PMC Tracking, Communicating, and Reviewing

The processes and responsibilities by role for reviewing PMR/PMC-related submissions, tracking PMR/PMC progress, and communicating with applicants are illustrated below.



[1] Applies only to PMRs under FDAAA section 505(o)
[2] Dunner letter for failure to respond to PMRs/PMCs
[3] PMR/PMC annual status report missing or incomplete
[4] Letter communicating final PMR/PMC fulfillment determination
[5] Release from PMRs/PMCs

Tracking and review activities

Annual status report review activities

Protocol, final report, or other PMR/PMC submission review activities