Report to Congress

The Sixteenth Review of the Backlog of Postmarketing Requirements and Commitments

Submitted Pursuant to Section 505(k) of the Federal Food, Drug, and Cosmetic Act
(As Amended by Section 921 of Title IX of the Food and Drug Administration Amendments Act of 2007)

Executive Summary

On September 27, 2007, the President signed into law the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law 110-85). Under section 921 of this law, the Food and Drug Administration (FDA) is required to review, annually, the entire backlog of postmarketing requirements (PMRs) and postmarketing commitments (PMCs) to determine which PMRs/PMCs "require revision or should be eliminated."

FDA has performed this sixteenth review of the backlog consisting of all PMRs and PMCs that were open (i.e., not yet released or fulfilled) as of the date of enactment of FDAAA, which are considered the "backlog" for purposes of the section 921 review. For this review, FDA has identified 1,636 PMRs/PMCs[1] (1,553 in the Center for Drug Evaluation and Research (CDER) and 83 in the Center for Biologics Evaluation and Research (CBER)) that comprise the backlog to which section 921 applies.

The data available for review of the backlog of PMRs and PMCs are constantly changing as submissions are reviewed and statuses are updated. This sixteenth annual report shows that as of December 31, 2023, CDER completed the required review for 1,520 of the 1,553 PMRs and PMCs in the backlog. As of September 30, 2023, CBER completed the required review of 77 of the 83 PMRs and PMCs in the backlog.

The number of open PMRs and PMCs continues to decrease each year as applicants complete studies/trials and submit final reports and as FDA reviews the final reports and issues fulfillment and released letters.

[1] FDA originally identified 1,637 PMRs/PMCs in the backlog. However, two closed PMRs in the Center for Drug Evaluation and Research were administratively combined into a single PMR, reducing the total to 1,636. Please refer to footnote 9 in the report for more information.

Table of Contents

I. Introduction

On September 27, 2007, the President signed into law the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law 110-85). Section 921 of Title IX of FDAAA amended section 505(k) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(k)) by adding a provision requiring the Food and Drug Administration (FDA) to, "on an annual basis, review the entire backlog of postmarket safety commitments to determine which commitments require revision or should be eliminated, report to the Congress on these determinations, and assign start dates and estimated completion dates for such commitments."

The "backlog" consists of all postmarketing requirements (PMRs) and postmarketing commitments (PMCs) that were open (i.e., not yet released or fulfilled) as of the date of enactment of FDAAA.[2] PMRs and PMCs are studies or clinical trials required of or agreed upon in writing by an applicant and conducted after FDA has approved a product for marketing. These studies and clinical trials are intended to further define the safety, efficacy, or optimal use of a product and, therefore, play an important role in fully characterizing the product.

During the sixteenth review of the PMR/PMC backlog, FDA identified 1,636 PMRs/PMCs (1,553[3] in the Center for Drug Evaluation and Research (CDER) and 83 in the Center for Biologics Evaluation and Research (CBER)) that comprise the backlog to which section 921 applies. This is the sixteenth annual report on the review of the backlog of PMRs and PMCs. This report includes information about PMRs/PMCs in the backlog that remain "open" as well as those that were "closed." (See Appendix B for

[2] Before FDAAA, all postmarketing studies and clinical trials (both required and agreed upon) were referred to as "postmarketing commitments." Therefore, the backlog of PMCs includes required studies and clinical trials, as well as those studies/clinical trials an applicant agreed to, but was not required to, conduct. Since FDAAA, the terminology has been clarified to distinguish the studies/clinical trials that are required from those that are agreed upon.

[3] In the second annual backlog review, which was completed on March 12, 2010, the external contractor who conducted the review determined that the CDER backlog cohort consisted of 1,551 PMRs and PMCs. During the third annual review, CDER discovered one PMR/PMC that did not qualify as a PMR/PMC and was subsequently removed from this cohort. During the fourth annual review, CDER discovered four additional PMR/PMCs that had previously been excluded from the backlog (e.g., never entered into database). During the fifth annual review, one additional PMR/PMC was discovered; this PMR/PMC was subsequently determined to be a duplicate and was removed from the cohort during the seventh annual review. During the ninth annual review, CDER discovered that two closed PMRs had been administratively combined, in the CDER internal database, into a single PMR, decreasing the number of PMRs in the backlog by one (i.e., to 1,553).

these and other status definitions used in this report.) Past backlog reports are available at the links in Appendix C.[4]

This sixteenth annual report is based on data that had "data lock" dates of September 30, 2023 (CBER backlog) and December 31, 2023 (CDER backlog).[5]

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

[5] Because database updates were ongoing as of September 30, 2017, the data for the CDER backlog were locked and extracted as of December 31, 2017, to ensure the most current and accurate information for this review. Therefore, subsequent database updates for CDER are now locked and extracted on December 31.

II. Background

Section 130(a) of the Food and Drug Administration Modernization Act of 1997 (Public Law 105-115) amended the FD&C Act by adding a provision (i.e., section 506B of the FD&C Act (21 U.S.C. 356b)) requiring reports of certain postmarketing studies for human drug and biological products. Section 506B of the FD&C Act provides FDA with the authority to monitor the progress of a PMC by requiring the applicant to submit an annual report providing information on the status of the PMC, which was defined to include agreed-upon commitments and required studies (including clinical trials).[6]

The annual reports that applicants submit must also include the reasons, if any, for failure to satisfy the commitment. This provision is implemented per 21 CFR 314.81(b)(2)(vii) and 601.70.[7] Under section 506B(b) and (c), FDA is required to track these PMCs and report on them annually in the *Federal Register*.[8] As described previously, as of the date of enactment of FDAAA, there were 1,636 (CDER and CBER) open PMRs and PMCs that are considered the "backlog" for purposes of the section 921 backlog review.[9]

Before the passage of FDAAA, FDA required studies or clinical trials in the following situations:

- Subpart H and subpart E accelerated approvals for products approved under section 505(b) of the FD&C Act or section 351(a) of the Public Health Service

[6] See 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*, available at https://www.fda.gov/files/drugs/published/Reports-on-the-Status-of-Postmarketing-Study-Commitments-—-Implementation-of-Section-130-of-the-Food-and-Drug-Administration-Modernization-Act-of-1997.pdf.

[7] In addition, new drug application applicants are required by 21 CFR 314.81(b)(2)(viii) to report annually to FDA on postmarketing studies or clinical trials that are not 506B studies or clinical trials. Such studies or clinical trials are not required by statute, and they include both chemistry, manufacturing, and controls (CMC) commitments (i.e., CMC studies that applicants have agreed with FDA to conduct) and stability studies (i.e., product stability studies that applicants have agreed with FDA to conduct). The reporting requirement under 21 CFR 314.81(b)(2)(viii) also includes "any postmarketing study not included under [section 314.81](b)(2)(vii) . . . that is being performed by, or on behalf of, the applicant." Reports on the status of these types of studies are not required under section 506B.

[8] These annual reports are available on FDA's Postmarketing Requirements and Commitments Reports website at https://www.fda.gov/drugs/postmarket-requirements-and-commitments/postmarketing-requirements-and-commitments-reports.

[9] At the outset of this evaluation, CDER provided a list of 1,643 open PMRs and PMCs derived from the internal PMR/PMC tracking systems as of September 27, 2007. During the course of the annual reviews, CDER identified a number of PMRs/PMCs that were erroneously included in (e.g., duplicate entry, previously released/fulfilled study/clinical trial, non-PMR/PMC element from an action letter) or excluded from (e.g., never entered into database) this group. After these corrections were made, the CDER backlog consisted of 1,553 PMRs/PMCs. Together with the 83 CBER PMRs/PMCs, FDA identified a total of 1,636 PMRs/PMCs that are the subject of this report.

Act, respectively (commonly called “accelerated approval”). Accelerated approvals require postmarketing studies to verify clinical benefit (21 CFR 314.510 and 601.41, respectively);

- Deferred pediatric studies where studies are required under the Pediatric Research Equity Act (PREA); and

- Animal efficacy rule approvals where studies to demonstrate safety and efficacy in humans are required at the time of use (21 CFR 314.610(b)(1) and 601.91(b)(1)).[10]

Under FDAAA, FDA has been given additional authority to require applicants to conduct and report on postmarketing studies or clinical trials to assess a known serious risk, assess signals of serious risk, or identify an unexpected serious risk related to the use of a product. These required safety studies/clinical trials—as well as those required under accelerated approval, PREA, and the animal rule (as described above)—are now considered PMRs. Studies or clinical trials required after the passage of FDAAA are not included in the annual backlog review because the backlog has been interpreted in this context to refer to all required or agreed-upon studies or clinical trials that had not been released or fulfilled before the passage of FDAAA.

[10] PMRs for drugs approved under the animal efficacy rule (21 CFR 314.600 for drug products; 21 CFR 601.90 for biological products) are to provide a study of the safety and clinical benefit of the drug if circumstances arise in which a study would be feasible and ethical (i.e., if an emergency arises and the drug is used). In the absence of a public health emergency for which these drugs may be utilized, these studies or clinical trials will remain indefinitely open.

III. Methods

The first and second annual CDER reviews were conducted by an external contractor who reviewed internal FDA systems and documents to determine the status for all PMRs/PMCs. These reviews were accomplished by first identifying the status of each PMR/PMC listed in the internal PMR/PMC databases and comparing these statuses to the milestone dates established in each product's approval letter. When the milestone dates were inconsistent with the statuses in the PMR/PMC databases, the correct status was determined by examining existing documentation (e.g., PMR/PMC annual status reports, PMR/PMC final study/clinical trial reports, FDA-applicant communications, and internal FDA memos and reviews).

After the accurate statuses were determined, additional review of the backlog of PMRs/PMCs was performed to identify candidates for revision or release.[11] The PMRs/PMCs that were off schedule (i.e., delayed or terminated) or had no milestone dates were prioritized for review over those that were on schedule (i.e., pending, ongoing, or submitted) based on established milestone dates.

The contractor provided CDER with the results of the review as well as recommendations regarding potential re-evaluation or release of PMRs/PMCs in the backlog. CDER has conducted all subsequent annual reviews, including this sixteenth review, and continues to monitor the progress of the PMRs/PMCs recommended for revision or release in addition to assessing the current status for the entire backlog.

The data available for PMRs and PMCs in the backlog are constantly changing as submissions are reviewed and the statuses of the PMRs/PMCs are updated. CDER has policies and procedures to help ensure that its data on PMRs/PMCs, including the PMRs/PMCs in the backlog, are current and accurate. When identified, data discrepancies are addressed and/or corrected in later reports. The information in this report reflects the status information in CDER's database at the time the data were extracted and reflects CDER's data quality control processes.

CBER has a comprehensive module in its biologics license application database system for tracking PMRs/PMCs. Information from CBER's system is extracted monthly and quarterly, and the information is subjected to quality control processes external to the review offices for Centers' and FDA's reports. CBER's processes, along with clearly defined CBER staff responsibilities for managing PMRs/PMCs, help ensure that data available from the system are accurate and relatively current.

[11] There were 1,049 PMRs/PMCs that did not require a review because they were determined to be already fulfilled or released.

IV. Findings

A. CDER's Summary of Progress

The number of open PMRs/PMCs in the CDER backlog continues to decrease. The data show that as of December 31, 2023, 98 percent (1,520/1,553) of PMRs/PMCs have been closed (i.e., fulfilled or released). Of the 33 PMRs/PMCs that remain open, 91 percent (30/33) have studies/trials either in progress or completed (i.e., ongoing, delayed, or had final reports submitted) at the time of the sixteenth annual review.

The statuses of nine PMRs/PMCs were updated as a result of the study/trial being fulfilled, the final report being submitted, or PMRs/PMCs being released.

- Three were updated to fulfilled, four were updated to released, and two were updated to submitted. None were updated to pending, ongoing, or terminated.

- The PMRs/PMCs updated to fulfilled and released reflect the consistent efforts of the review divisions to either complete the reviews of the submitted final reports or assess the need/feasibility of current studies and trials.

B. CBER's Summary of Progress

The data show that as of September 30, 2023, 93 percent (77/83) of the PMRs/PMCs have been closed (i.e., fulfilled or released), and 83 percent (five/six) of the open PMRs/PMCs have studies/trials in progress or completed at the time of the sixteenth annual review. The data[12] show that the status of the backlog of PMRs/PMCs has remained unchanged from the previous year.

Of six open CBER PMRs/PMCs in the backlog, five (83 percent) have a study/clinical trial that is either in progress or delayed, and one is not yet underway.

[12] The Fifteenth Review of the Backlog of Postmarketing Requirements and Commitments is available at https://www.fda.gov/media/179430/download?attachment.

V. Conclusion

- Upon completion of the sixteenth annual review and as of December 31, 2023, 98 percent (1,520/1,553) of the PMRs/PMCs in the CDER backlog have been closed (i.e., fulfilled or released). As of September 30, 2023, 93 percent (77/83) of the PMRs/PMCs in the CBER backlog have been closed.

- Since the previous year, the number of open PMRs/PMCs in the CDER backlog decreased from 40 to 33 of 1,553 (two percent). The number of open PMRs/PMCs in the CBER backlog remained unchanged at six of 83 (seven percent).

- For CDER and CBER combined, 98 percent (1,597/1,636) of the PMRs/PMCs in the backlog have been closed (i.e., fulfilled or released), which is an increase from the previous year. For the two Centers combined, the number of open PMRs/PMCs has decreased slightly from 46 to 39 of 1,636 (two percent).

The number of open PMRs and PMCs is expected to continue to decrease each year as applicants complete studies/trials and submit final reports and as FDA reviews the final reports and issues fulfillment and released letters.

Appendix A: Tables & Figures

Table 1: CDER's PMR/PMC Statuses After Annual Reviews

This table shows the number of PMRs/PMCs by status in each annual review listed by year. The leftmost column lists the annual reviews starting with the first review. The top row shows the status, moving from left to right, of pending, ongoing, submitted, delayed, terminated, fulfilled, released, undetermined, and not available. The rightmost column provides the total for each row.

Copies of previous reports to Congress on the PMR/PMC backlog can be found on FDA's PMR/PMC Reports web page (available at https://www.fda.gov/drugs/postmarket-requirements-and-commitments/postmarketing-requirements-and-commitments-reports).

PMR/PMC Status by Review										
Review	**Pending[4]**	**Ongoing**	**Submitted**	**Delayed**	**Terminated**	**Fulfilled**	**Released**	**Undetermined[5]**	**Not Available[6]**	**Total**
First	208	212	565	225	16	209	47	39	30	**1,551**
Second	114	156	366	264	13	483	146	9	0	**1,551**
Third	93	132	197	223	13	701	191	0	0	**1,550**
Fourth[1]	77	106	113	199	10	827	222	0	0	**1,554**
Fifth[2]	51	71	79	171	11	900	272	0	0	**1,555**
Sixth	46	60	63	124	7	953	302	0	0	**1,555**
Seventh[3]	49	49	30	73	8	1,018	327	0	0	**1,554**
Eighth	32	37	15	65	10	1,050	345	0	0	**1,554**
Ninth	25	26	19	54	7	1,047[7]	375	0	0	**1,553**[8]
Tenth	6	22	22	32	3	1,076	392	0	0	**1,553**
Eleventh	6	17	15	30	4	1,087	394	0	0	**1,553**
Twelfth	5	11	13	29	4	1,094	397	0	0	**1,553**

PMR/PMC Status by Review										
Review	Pending[4]	Ongoing	Submitted	Delayed	Terminated	Fulfilled	Released	Undetermined[5]	Not Available[6]	Total
Thirteenth	5	6	13	24	3	1,103	399	0	0	**1,553**
Fourteenth	4	3	15	22	3	1,105	401	0	0	**1,553**
Fifteenth	3	3	11	21	2	1,111	402	0	0	**1,553**
Sixteenth	2	3	11	16	1	1,114	406	0	0	**1,553**

[1] During the fourth annual review, CDER discovered a total of four PMR/PMCs that had previously been excluded from the backlog (e.g., never entered into the database). After this correction was made, the CDER backlog consisted of 1,554 PMRs/PMCs.

[2] During the fifth annual review, CDER discovered one PMR/PMC that had previously been excluded from the backlog (e.g., never entered into a database). After this correction was made, the CDER backlog consisted of 1,555 PMRs/PMCs.

[3] During the seventh annual review, CDER discovered a duplicate PMR entry. After the duplicate entry was removed, the CDER backlog totaled 1,554 PMRs/PMCs.

[4] PMRs in pending status include those issued under the PREA and the animal efficacy rule (21 CFR 314.600 and 21 CFR 601.90). PREA PMRs are often deferred because the applicable drug product is ready for approval in adults before pediatric studies are complete. Initiation of the PREA studies may also be deferred because FDA finds that pediatric studies should be delayed until additional safety or effectiveness data have been collected. Postmarketing studies required under the animal efficacy rule are to provide a study of the safety and clinical benefit if circumstances arise in which a study would be feasible and ethical (i.e., if an emergency arises and the drug is used). In the absence of a public health emergency for which these drugs may be utilized, these studies/clinical trials will indefinitely remain pending.

[5] After the first and second annual reviews, the status of 39 and nine PMRs/PMCs, respectively, was undetermined because of insufficient documentation to determine the correct status at the time of the review. During the third annual review, CDER determined the status of the remaining 9 undetermined PMRs/PMCs.

[6] The status of 30 PMRs/PMCs was not available after the first annual review because the PMRs/PMCs had not been entered into the PMR/PMC database. These PMRs/PMCs were subsequently entered into the database and reviewed.

[7] During the ninth review, CDER determined that 12 PMRs/PMCs previously identified as fulfilled were released and that one PMR/PMC previously identified as released was, in fact, fulfilled.

[8] During the ninth annual review, CDER discovered that two closed PMRs had been administratively combined into a single PMR, decreasing the total number of PMRs in the CDER backlog to 1,553.

Figure 1: CDER's PMR/PMC Statuses After Annual Backlog Reviews

Figure 1 displays the data from Table 1 in graphical form and includes all years. The figure shows that the number of open (i.e., pending, ongoing, delayed, terminated, or submitted) PMRs/PMCs in the CDER backlog has progressively decreased.

Unknown = PMR/PMC status unknown or undetermined
Open = PMR/PMC status of pending, ongoing, delayed, submitted, or terminated
Closed = PMR/PMC status of released or fulfilled

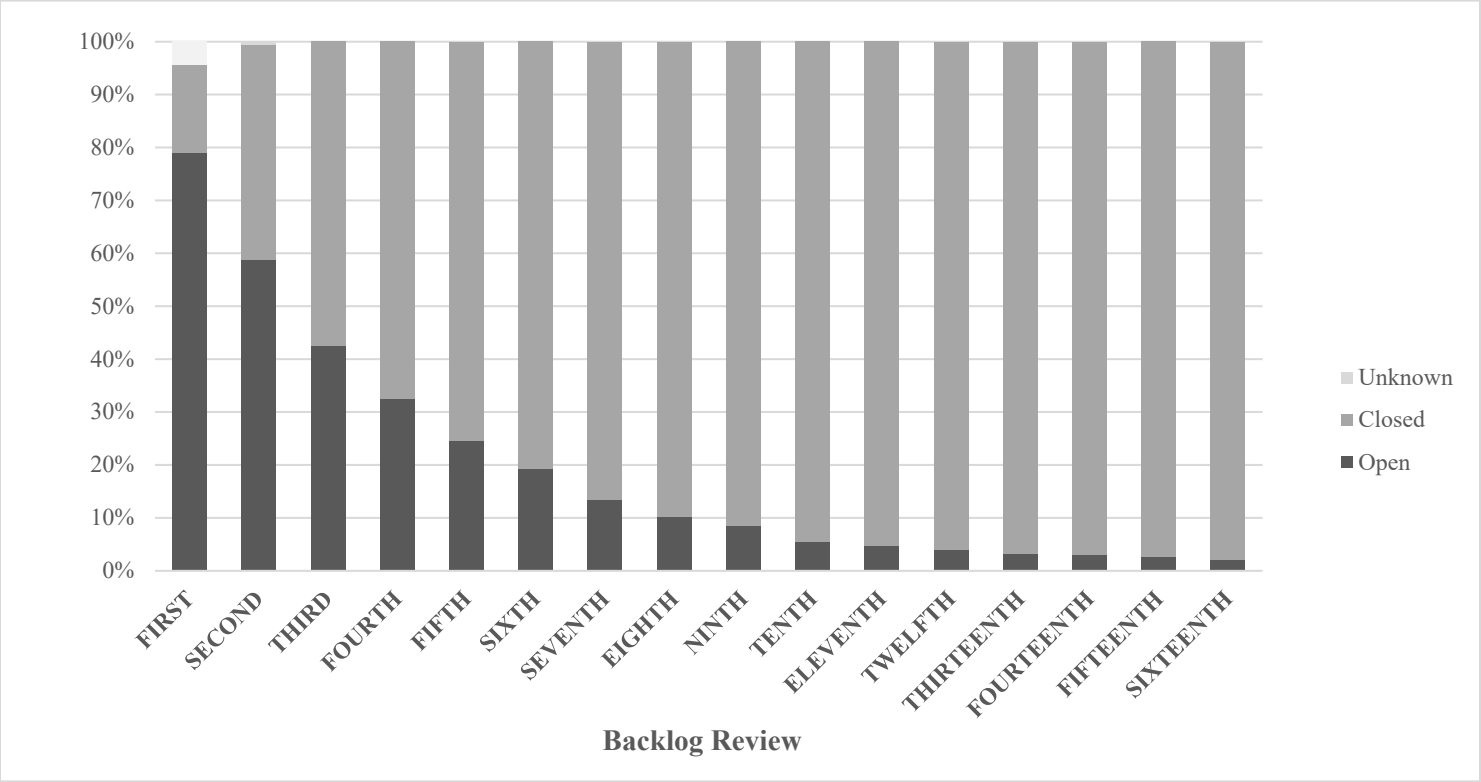


Table 2: **CBER's PMR/PMC Statuses After Annual Reviews**

This table shows the number of PMRs/PMCs by status in each annual review listed by year. The leftmost column lists the annual reviews starting with the first review. The top row shows the status, moving from left to right, of pending, ongoing, submitted, delayed, terminated, fulfilled, and released. The rightmost column provides the total for each row.

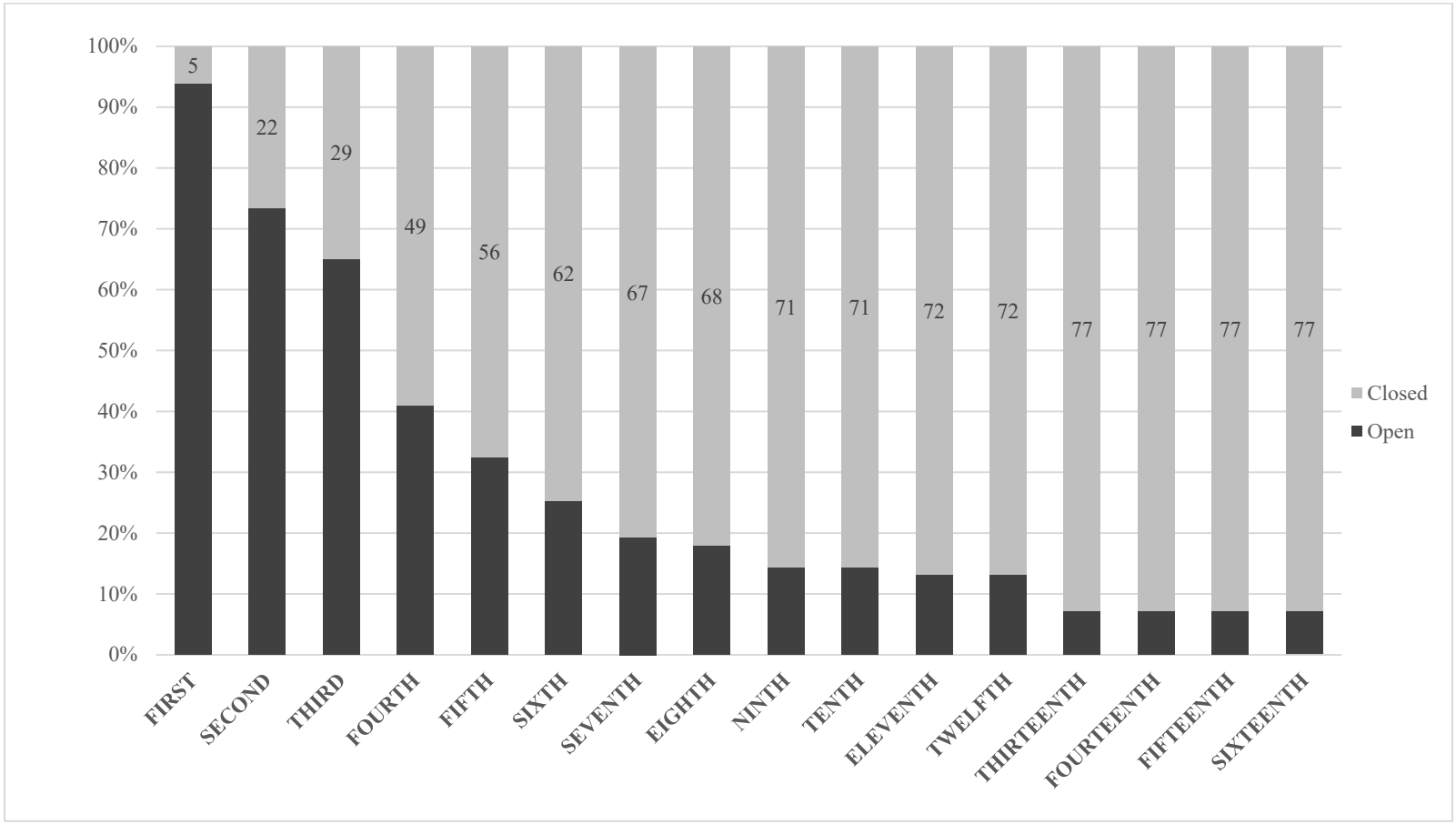
Copies of previous reports to Congress on the PMR/PMC backlog can be found on FDA's PMR/PMC Reports web page (available at https://www.fda.gov/drugs/postmarket-requirements-and-commitments/postmarketing-requirements-and-commitments-reports).

PMR/PMC Status by Review								
Review	**Pending**	**Ongoing**	**Submitted**	**Delayed**	**Terminated**	**Fulfilled**	**Released**	**Total**
First	10	21	24	23	0	5	0	**83**
Second	5	19	14	23	0	22	0	**83**
Third	4	18	14	18	0	29	0	**83**
Fourth	2	7	7	18	0	47	2	**83**
Fifth	2	4	8	13	0	54	2	**83**
Sixth	2	5	3	11	0	60	2	**83**
Seventh	1	5	3	7	0	65	2	**83**
Eighth	1	3	4	7	0	66	2	**83**
Ninth	2	3	0	7	0	69	2	**83**
Tenth	1	3	0	8	0	69	2	**83**
Eleventh	1	3	1	6	0	70	2	**83**
Twelfth	1	1	3	6	0	70	2	**83**
Thirteenth	1	1	0	4	0	75	2	**83**
Fourteenth	1	1	0	4	0	75	2	**83**

PMR/PMC Status by Review								
Review	**Pending**	**Ongoing**	**Submitted**	**Delayed**	**Terminated**	**Fulfilled**	**Released**	**Total**
Fifteenth	1	1	0	4	0	75	2	**83**
Sixteenth	1	1	0	4	0	75	2	**83**

Figure 2: CBER's PMR/PMC Statuses After Annual Backlog Reviews

Figure 2 displays the data from Table 2 in graphical form and includes all years. The figure shows that the number of open PMRs/PMCs in the CBER backlog remained unchanged between the end of FY 2022 and the end of FY 2023.



Appendix B: PMR/PMC Status Definitions

PMR/PMC Status	Definition
Pending*	The study/clinical trial has not been initiated but does not meet the criterion for “delayed.”
Ongoing*	The study/clinical trial is proceeding according to, or ahead of, the original schedule.
Submitted*	The study/clinical trial has been completed or terminated, and a final study report has been submitted to FDA.
Delayed*	The study/clinical trial is behind the original schedule.
Terminated*	The study/clinical trial was ended before completion, but a final study report has not been submitted to FDA.
Fulfilled	The final report for the study/clinical trial was submitted to FDA, and FDA notified the applicant, through written correspondence, that the commitment was fulfilled.
Released	FDA has informed the applicant in writing that it is released from its obligation to conduct the study/clinical trial because the study/clinical trial is no longer feasible, would no longer provide useful information, or the underlying application has been withdrawn.
Open	PMR/PMC status of pending, ongoing, delayed, submitted, or terminated.
Closed	PMR/PMC status of released or fulfilled.

* Adapted from 21 CFR 314.81.

Appendix C: PMR/PMC Backlog Reports

- First Annual Report
  http://wayback.archive-it.org/7993/20161022164917/http:/www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/UCM291522.pdf

- Second Annual Report
  http://wayback.archive-it.org/7993/20161022164918/http:/www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/UCM291520.pdf

- Third Annual Report
  http://wayback.archive-it.org/7993/20161022164919/http:/www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/UCM324917.pdf

- Fourth Annual Report
  http://wayback.archive-it.org/7993/20161022200658/http:/www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/UCM407411.pdf

- Fifth Annual Report
  http://wayback.archive-it.org/7993/20161022200647/http:/www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/UCM472975.pdf

- Sixth Annual Report
  https://www.fda.gov/media/94259/download

- Seventh Annual Report
  http://wayback.archive-it.org/7993/20161022200646/http:/www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/UCM472973.pdf

- Eighth Annual Report
  https://www.fda.gov/media/101945/download

- Ninth Annual Report
  https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/UCM579401.pdf

- Tenth Annual Report
  https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/UCM617801.pdf

- Eleventh Annual Report
  https://www.fda.gov/media/130519/download

- Twelfth Annual Report
  https://www.fda.gov/media/143984/download

- Thirteenth Annual Report
  https://www.fda.gov/media/154529/download

- Fourteenth Annual Report
  https://www.fda.gov/media/165051/download?attachment

- Fifteenth Annual Report
  https://www.fda.gov/media/179430/download?attachment

This report was prepared by FDA's Office of New Drugs in the Center for Drug Evaluation and Research. For information on obtaining additional copies, please contact:

U.S. Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993-0002

This report is available on FDA's home page at https://www.fda.gov/.