

**The Food and Drug Administration**  
**Report on the Performance of Drugs and Biologics Firms in Conducting Postmarketing**  
**Requirements and Commitments**  
**Fiscal Year 2018**

**I. Background**

A. Postmarketing Requirements and Commitments

A postmarketing requirement (PMR) is a study or clinical trial that an applicant is required by statute or regulation to conduct postapproval. A postmarketing commitment (PMC) is a study or clinical trial that an applicant agrees in writing to conduct postapproval, but that is not required by statute or regulation. PMRs and PMCs can be issued upon approval of a drug<sup>1</sup> or postapproval, if warranted.<sup>2</sup>

The Food and Drug Administration (FDA or Agency) can require application holders to conduct postmarketing studies and 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 drug product (section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(o)(3)), as added by the Food and Drug Administration Amendments Act of 2007 (FDAAA)).

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<sup>1</sup> For the purposes of this report, references to “drugs” or “drug products” include drugs approved under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and biological products licensed under the Public Health Service Act other than biological products that also meet the definition of a device in section 201(h) of the FD&C Act (21 U.S.C. 321(h)).

<sup>2</sup> The number of PMRs and PMCs issued varies from fiscal year to fiscal year due to a variety of factors, including but not necessarily limited to: (1) The number of applications approved in that year; (2) whether additional efficacy or clinical benefit issues needed to be evaluated postapproval; (3) if any drug-associated serious risk(s) were identified; and (4) whether or not FDA determined that a postmarketing study or clinical trial was necessary to further assess risk(s) or efficacy issues.

- Under the Pediatric Research Equity Act (PREA), to study certain new drugs for pediatric populations, when these drugs are not adequately labeled for children. Under section 505B(a)(3) of the FD&C Act (21 U.S.C. 355c), the initiation of these studies may be deferred until required safety information from other studies in adults has first been submitted and reviewed.
- To verify and describe the predicted effect or other clinical benefit for drugs approved in accordance with the accelerated approval provisions in section 506(c)(2)(A) of the FD&C Act (21 U.S.C. 356(c)(2)(A)) (21 CFR 314.510 and 21 CFR 601.41).
- For a drug that was approved on the basis of animal efficacy data because human efficacy trials are not ethical or feasible (21 CFR 314.610(b)(1) and 21 CFR 601.91(b)(1)). PMRs for drug products approved under the animal efficacy rule<sup>3</sup> can be conducted only when the drug product is used for its indication and when an exigency (or event or need) arises. In the absence of a public health emergency, these studies or clinical trials will remain pending indefinitely.

### B. Reporting Requirements

Under the regulations (21 CFR 314.81(b)(2)(vii) and 21 CFR 601.70), applicants of approved drugs and licensed biologics are required to submit annually a report on the status of each clinical safety, clinical efficacy, clinical pharmacology, and nonclinical toxicology study or clinical trial either required by FDA or that they have committed to conduct, either at the time of approval or after approval of their new drug application (NDA), abbreviated new drug application (ANDA), or biologics license application (BLA). Applicants are required to report to FDA on these requirements and commitments made for NDAs and ANDAs under

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<sup>3</sup> 21 CFR 314.600 for drugs; 21 CFR 601.90 for biological products.

§ 314.81(b)(2)(viii). The status of PMCs concerning chemistry, manufacturing, and production controls and the status of other studies or clinical trials conducted on an applicant's own initiative are not required to be reported under §§ 314.81(b)(2)(vii) and 601.70 and are not addressed in this report.

Section 505(o)(3)(E)(ii) of the FD&C Act requires an applicant to periodically report on the status of each PMR required under this authority. FDA considers the submission of the annual report required under section 506B of the FD&C Act and 21 CFR 314.81(b)(2)(vii) or 21 CFR 601.70, as applicable, as satisfying this periodic reporting requirement, if the elements listed in 505(o)(3)(E)(ii) and 21 CFR 314.81(b)(2)(vii) or 21 CFR 601.70, as applicable, are included in the annual report. To comply with section 505(o)(3)(E)(ii), the annual report must also include a report on the status of any other study or clinical trial undertaken to investigate a safety issue.

An applicant must report on the progress of the PMR/PMC on the anniversary of the drug product's approval<sup>4</sup> until the PMR/PMC is completed or terminated and FDA determines that the PMR/PMC has been fulfilled or that the PMR/PMC is either no longer feasible or would no longer provide useful information. The annual status report (ASR) must include a description of the PMR/PMC, a schedule for completing the PMR/PMC, and a characterization of the current status of the PMR/PMC. The report must also provide an explanation of the PMR/PMC status by describing briefly the progress of the PMR/PMC. A PMR/PMC schedule is expected to include the actual or projected dates for the following: (1) Submission of the final protocol to FDA; (2) completion of the study or clinical trial; and (3) submission of the final report to FDA.

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<sup>4</sup> An applicant must submit an annual status report on the progress of each open PMR/PMC within 60 days of the anniversary date of U.S. approval of the original application or on an alternate reporting date that was granted by FDA in writing. Some applicants have requested and been granted by FDA alternate annual reporting dates to facilitate harmonized reporting across multiple applications.

### C. PMR/PMC Status Categories

The status of the PMR/PMC must be described in the ASR according to the terms and definitions provided in §§ 314.81 and 601.70. For its own reporting purposes, FDA has also established terms to describe when the conditions of the PMR/PMC have been met, and when it has been determined that a PMR/PMC is no longer necessary.<sup>5</sup> The PMR/PMC status categories are summarized in the following list. As reflected in the definitions, the status of a PMR/PMC is generally determined based on the original schedule.<sup>6</sup>

- 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 criteria for delayed (i.e., the original projected date for initiation of subject accrual or initiation of animal dosing has not passed).<sup>7</sup>
- Ongoing: The study or clinical trial is proceeding according to or ahead of the original schedule.
- Delayed: The study or clinical trial is behind the original schedule.<sup>8</sup>
- Terminated: The study or clinical trial was ended before completion, but a final report has not been submitted to FDA.
- Submitted: The study or clinical trial has been completed or terminated, and a final report has been submitted to FDA.

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<sup>5</sup> See the guidance for industry entitled “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/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM080569.pdf>.

<sup>6</sup> The definitions for the terms “pending,” “ongoing,” “delayed,” “terminated,” and “submitted” are adapted from §§ 314.81 and 601.70; the definitions for the terms “fulfilled” and “released” are described in the guidance for industry entitled “Reports on the Status of Postmarketing Study Commitments — Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997.”

<sup>7</sup> It is important to note that PMRs/PMCs that are in pending status are not yet delayed; that is, per the milestones, the studies or clinical trials are indeed on schedule and are not expected to be underway yet.

<sup>8</sup> In some instances, an applicant may have justifiable reasons for delay of its PMR/PMC (see section I.D.).

- Fulfilled: The final report for the study or clinical trial was submitted to FDA and FDA notified the applicant that the requirement or commitment was fulfilled through written correspondence.
- Released: FDA has informed the applicant in writing that it is released from its obligation to conduct the study or clinical trial because the study or clinical trial is no longer feasible, would no longer provide useful information, or the underlying application has been formally withdrawn.

In addition to the above statuses, PMRs/PMCs may also be characterized as open or closed. Open PMRs/PMCs comprise those that are pending, ongoing, delayed, submitted, or terminated; whereas closed<sup>9</sup> PMRs/PMCs are either fulfilled or released. Open PMRs are also described by whether they are on- or off-schedule. On-schedule PMRs/PMCs are those that are pending, ongoing, or submitted. Off-schedule PMRs/PMCs are those that have missed one of the milestone dates in the original schedule and are categorized as either delayed or terminated.

#### D. Additional Requirements

If an applicant fails to comply with the original schedule for completion of postmarketing studies or clinical trials required under section 505(o)(3) of the FD&C Act (i.e., under the FDAAA authorities), or fails to submit periodic reports on the status of the studies or clinical trials, the applicant is considered to be in violation of section 505(o)(3), unless it has demonstrated good cause for its noncompliance or other violation. Failure to meet an original milestone and, as a result, falling behind the original schedule is one type of noncompliance with a PMR issued under FDAAA. In these circumstances, the FDAAA PMR is considered delayed, with or without good cause.

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<sup>9</sup> Previous FDA reports on the status of PMRs/PMCs used the term “completed” to refer to PMRs/PMCs that are closed.

Section 505B(a)(3)(B) of the FD&C Act, as amended by the Food and Drug Administration Safety and Innovation Act, authorizes FDA to grant an extension of the deferred pediatric assessments that are required under PREA.<sup>10</sup> On its own initiative or upon request, FDA may grant an extension of a pediatric assessment deferral, provided that certain applicable PREA criteria for deferral are still met and the applicant submits certain materials in support of the extension.<sup>11</sup> Applicants must submit requests for deferral extensions to FDA not less than 90 days before the date the deferral would otherwise expire. If FDA grants the extension of a pediatric study deferral, this new deferral date is considered the original due date of the PMR. Consequently, the status of PREA PMRs would be determined based on the new deferral date (and not the original PREA PMR schedule).

FDA may take enforcement action against applicants who are noncompliant with or otherwise fail to conduct studies and clinical trials required under FDA statutes and regulations (see, for example, sections 505(o)(1), 502(z), and 303(f)(4) of the FD&C Act (21 U.S.C. 355(o)(1), 352(z), and 333(f)(4))).

## **II. Understanding FDA's Data on Postmarketing Studies and Clinical Trials**

### **A. FDA's Internal PMR/PMC Databases**

Databases containing information on PMRs/PMCs are maintained at the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER). The information in these databases is periodically updated as new PMRs/PMCs are issued, upon FDA review of PMR/PMC ASRs or other PMR/PMC correspondence, upon receipt of final reports from completed studies and clinical trials, and after the final reports are reviewed and FDA determines that the PMR/PMC has been fulfilled, or when FDA determines that the

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<sup>10</sup> This provision does not apply to PMRs required under other provisions, or to PMCs.

<sup>11</sup> See section 505B(a)(3)(B) of the FD&C Act.

PMR/PMC is either no longer feasible or would no longer provide useful information. Because applicants typically report on the status of their PMRs/PMCs annually, and because updating the status of PMRs/PMCs in FDA's databases involves FDA review of received information, there is an inherent lag in updating the data (that is, the data are not real time). FDA strives to maintain as accurate information as possible on the status of PMRs/PMCs.

Both CDER and CBER have established policies and procedures to help ensure that FDA's data on PMRs/PMCs are current and accurate. When identified, data discrepancies are addressed as expeditiously as possible and/or are corrected in later reports.

#### B. Publicly Available PMR/PMC Data

FDA also maintains an online searchable and downloadable database that contains information about PMRs/PMCs that is publicly reportable (i.e., for which applicants must report on the status of the study or clinical trial, as required under section 506B of the FD&C Act (21 U.S.C. 356b)). The data are a subset of all PMRs/PMCs and reflect only those postmarketing studies and clinical trials that, at the time of data retrieval, either had an open status or were closed within the past year. Information on PMRs/PMCs closed more than a year before the date the data are extracted (i.e., September 30, 2018) are not included on the public website. The FDA website is updated quarterly.<sup>12</sup> The FDA website does not include information about PMCs concerning chemistry, manufacturing, and controls. It is FDA policy not to post information on the website until it has been verified and reviewed for suitability for public disclosure.

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<sup>12</sup> <https://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm>

### III. About This Report

This report is published to fulfill the annual reporting requirement under section 506B(c) of the FD&C Act. Information in this report covers any PMR/PMC that was made, in writing, at the time of approval or after approval of an application or a supplement to an application (see section I.A.) and summarizes the status of PMRs/PMCs in fiscal year (FY) 2018 (i.e., as of September 30, 2018). Specifically, the report summarizes the status of all open PMRs/PMCs through the end of the fiscal year, and the status of only those PMRs/PMCs that were closed in the fiscal year. If a requirement or commitment did not have a schedule, or an ASR was not received in the previous 12 months, the PMR/PMC is categorized according to the most recent information available to the Agency.<sup>13</sup>

This report reflects combined data from CDER and CBER. Information summarized in the report includes the following: (1) The number of applicants with open PMRs/PMCs;<sup>14</sup> (2) the number of open PMRs/PMCs; (3) the number of applications for which an ASR was expected but was not submitted within 60 days of the anniversary date of U.S. approval or an alternate reporting date that was granted by FDA; (4) FDA-verified status of open PMRs/PMCs reported in §§ 314.81(b)(2)(vii) or 601.70 ASRs; (5) the status of closed PMRs/PMCs; and (6) the distribution of the status by fiscal year of establishment<sup>15</sup> (FY2012 to FY2018) for PMRs and PMCs open at the end of FY2018, or those closed within FY2018. The tables in this report distinguish between all PMRs and PMCs, PMRs/PMCs for NDAs and BLAs, and on-schedule

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<sup>13</sup> Although the data included in this report do not include a summary of reports that applicants have failed to file by their due dates, the Agency notes that it may take appropriate regulatory action in the event reports are not filed on a timely basis.

<sup>14</sup> At the end of FY2018, there were no PMRs/PMCs for ANDAs that met the reporting requirements under the Food and Drug Administration Modernization Act of 1997. Therefore, this report reflects information for NDAs and BLAs only.

<sup>15</sup> The establishment date is the date of the formal FDA communication to the applicant that included the final FDA-required (PMR) or -requested (PMC) postmarketing study or clinical trial.



and off-schedule PMRs/PMCs, according to the original schedule milestones. Additional information about PMRs/PMCs is provided on FDA's website at

<https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm>.

Numbers published in this report cannot be compared with the numbers resulting from searches of the publicly accessible and downloadable database. This is because this report incorporates data for all PMRs/PMCs in FDA databases as of the end of the fiscal year, including PMRs/PMCs whose status and status explanation have not yet been verified for public posting on the FDA public searchable database. The publicly accessible and downloadable database includes a subset of PMRs/PMCs, specifically those that, at the time of data retrieval, either had an open status or were closed within the past 12 months. In addition, the status information in this report is updated annually while the downloadable database is updated quarterly (i.e., in January, April, July, and October).

#### **IV. Summary of Information on PMR/PMC Status**

This report provides information on PMRs/PMCs as of September 30, 2018 (i.e., for FY2018). It is important to note that a comparison of the number of open and on-schedule or off-schedule PMRs/PMCs from one time period to a later time period can be misleading because it does not take into account that the cohort of open PMRs/PMCs is not static from year to year. New PMRs/PMCs are continually being established for studies and clinical trials with varying start dates and durations; and other PMRs/PMCs are closed because they are either fulfilled or released. Therefore, the number of on- and off-schedule PMRs/PMCs can vary from year to year, and a year-to-year comparison of on- or off-schedule PMRs (e.g., to assess for a potential

trend) is not appropriate. Finally, due to rounding, the percentages in the tables may not add up to 100 percent.

#### A. Applicants with Open PMRs/PMCs

An applicant may have multiple approved drug products, and an approved drug product may have multiple PMRs and/or PMCs. Table 1 shows that as of September 30, 2018, there were 318 unique applicants with open PMRs/PMCs under 755 unique NDAs and BLAs. There were 226 unique NDA applicants (and 581 associated applications) and 92 unique BLA applicants (and 174 associated applications) with open PMRs/PMCs.

Table 1.—Applicants and Applications (NDA/BLA) With Open Postmarketing Requirements and Commitments  
[Numbers as of September 30, 2018]

	NDA <sup>1</sup>	BLA <sup>2</sup>	Total (NDA and BLA)
Number of unique applicants with open PMRs/PMCs	226	92	318
Number of applications with open PMRs/PMCs	581	174	755

<sup>1</sup> As of September 30, 2018, there was one NDA with associated PMRs/PMCs managed by CBER.

<sup>2</sup> Includes BLAs managed by both CDER and CBER.

#### B. Annual Status Reports Received

As previously mentioned, applicants must submit an ASR on the progress of each open PMR/PMC within 60 days of the anniversary date of U.S. approval of the original application or an alternate reporting date that was granted by FDA (§§ 314.81 and 21 CFR 601.70).<sup>16</sup> Table 2 shows that there were 719 NDAs and BLAs with an ASR due in FY2018 (569 NDAs and 150 BLAs).<sup>17</sup> Of the 569 NDA ASRs due in that fiscal year, 69 percent (390/569) were received on

<sup>16</sup> Some applicants have requested and been granted by FDA alternate annual reporting dates to facilitate harmonized reporting across multiple applications.

<sup>17</sup> The number of ASRs that were expected is different from the total number of unique applications with open PMRs/PMCs because not all applications had an ASR due during FY2018. Applicants with PMRs/PMCs associated with multiple applications may have submitted the ASR to only one of the applications. In addition, if all the

time, 13 percent (76/569) were received, but not on time, and 18 percent (103/569) were not received during FY2018. Of the 150 BLA ASRs due, 69 percent (103/150) were received on time, 11 percent (16/150) were received, but not on time, and 21 percent (31/150) were not received during FY2018.

Table 2.—Annual Status Reports Received  
[Numbers as of September 30, 2018]<sup>1</sup>

	Expected <sup>2</sup>	Received, on Time <sup>3</sup> (% of Expected)	Received, Not on Time <sup>4</sup> (% of Expected)	Expected but Not Received (% of Expected)
NDA	569	390 (69%)	76 (13%)	103 (18%)
BLA	150	103 (69%)	16 (11%)	31 (21%)
Total	719	493 (69%)	92 (13%)	134 (19%)

<sup>1</sup> Percentages may not total 100 due to rounding.

<sup>2</sup> ASR expected during fiscal year (within 60 days (before or after) of the anniversary of original approval date or alternate agreed-upon date).

<sup>3</sup> ASR was received within 60 days (before or after) of the anniversary of the original approval date or alternate agreed-upon date.

<sup>4</sup> ASR was received, but not within 60 days (before or after) of the anniversary of the original approval date or alternate agreed-upon date.

### C. Overview of On- and Off-Schedule Open PMRs/PMCs

Table 3 shows that as of September 30, 2018, most open PMRs (81 percent (1103/1368)) for NDAs and BLAs combined) and most open PMCs (80 percent (284/355)) for NDAs and BLAs combined) were progressing on schedule.

Tables 3.a. & 3.b.—Summary of On- and Off-Schedule Postmarketing Requirements and Commitments  
[Numbers as of September 30, 2018]<sup>1</sup>

Table 3.a.	Open PMRs		
	NDA (% of Open NDA PMRs)	BLA (% of Open BLA PMRs)	Total On- and Off-Schedule PMRs
On-schedule	824 (79%)	279 (86%)	1,103 (81%)
Off-schedule	221 (21%)	44 (14%)	265 (19%)

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PMRs/PMCs for an application were established in the preceding fiscal year, or if all PMRs/PMCs for an application were closed before the ASR due date, submission of an ASR would not have been expected.

Table 3.a.	Open PMRs		
	NDA (% of Open NDA PMRs)	BLA (% of Open BLA PMRs)	Total On- and Off-Schedule PMRs
Total	1,045	323	1,368

<sup>1</sup> Percentages may not total 100 due to rounding.

Table 3.b.	Open PMCs		
	NDA (% of Open NDA PMCs)	BLA (% of Open BLA PMCs)	Total On- and Off-Schedule PMCs
On-schedule	127 (76%)	157 (84%)	284 (80%)
Off-schedule	40 (24%)	31 (16%)	71 (20%)
Total	167	188	355

<sup>1</sup> Percentages may not total 100 due to rounding.

#### D. Open and On-Schedule PMRs

Table 4 shows that as of September 30, 2018, nearly half of the open NDA and BLA PMRs were pending (44 percent (464/1045) and 47 percent (152/323), respectively). PREA PMRs and FDAAA PMRs comprised 44 percent (271/616) and 48 percent (297/616) of pending PMRs, respectively. The next largest category of open and on-schedule PMRs comprised those that were ongoing (28 percent (288/1045) of NDA PMRs and 30 percent (97/323) of BLA PMRs).

Table 4.—Summary of Open and On-Schedule Postmarketing Requirements  
[Numbers as of September 30, 2018]<sup>1</sup>

Reporting Authority/PMR Status	NDA N = 1,045 (% of Open NDA PMRs)			BLA N = 323 (% of Open BLA PMRs)			Total Open and On-Schedule PMRs
	Pending	Ongoing	Submitted	Pending	Ongoing	Submitted	
Accelerated approval	16 (2%)	20 (2%)	1 (<1%)	18 (6%)	12 (4%)	2 (1%)	69 (5%)
PREA <sup>2</sup>	214 (20%)	137 (13%)	17 (2%)	57 (18%)	27 (8%)	10 (3%)	462 (34%)
Animal	5 (<1%)	0 (0%)	1 (<1%)	9 (3%)	0 (0%)	0 (0%)	15 (1%)

Reporting Authority/PMR Status	NDA N = 1,045 (% of Open NDA PMRs)			BLA N = 323 (% of Open BLA PMRs)			Total Open and On-Schedule PMRs
	Pending	Ongoing	Submitted	Pending	Ongoing	Submitted	
efficacy <sup>3</sup>							
FDAAA safety (since March 25, 2008)	229 (22%)	131 (13%)	53 (5%)	68 (21%)	58 (18%)	18 (6%)	557 (41%)
Total Open and On-Schedule	464 (44%)	288 (28%)	72 (7%)	152 (47%)	97 (30%)	30 (9%)	1,103 (81%)

<sup>1</sup> Percentages may not total 100 due to rounding.

<sup>2</sup> Many PREA studies have a pending status. PREA studies are usually deferred because the drug product is ready for approval in adults. Initiation of these studies may be deferred until additional safety information from other studies has first been submitted and reviewed before beginning the studies in pediatric populations.

<sup>3</sup> PMRs for drug products approved under the animal efficacy rule (21 CFR 314.600 for drugs; 21 CFR 601.90 for biological products) can be conducted only when the drug product is used for its indication and when an exigency (or event or need) arises. In the absence of a public health emergency, these studies or clinical trials will remain pending indefinitely.

#### E. Open and Off-Schedule PMRs

Table 5 provides additional information on the status of open and off-schedule PMRs (i.e., delayed and terminated). At the end of September 30, 2018, 21 percent (221/1045) of the open NDA PMRs and 14 percent (44/323) of the open BLA PMRs were off schedule. Of the off-schedule NDA PMRs, 98 percent (217/221) were off schedule because they were delayed and the remaining 2 percent (4/221) were terminated. Most off-schedule BLA PMRs were delayed (98 percent (43/44)) and one was terminated.

In certain situations, the original PMR schedules were adjusted for unanticipated delays in the progress of the study or clinical trial (e.g., difficulties with subject enrollment in a clinical trial for a marketed drug or the need for additional time to analyze results). In this report, study or clinical trial status reflects the status in relation to the original<sup>18</sup> study or clinical trial schedule

<sup>18</sup> With the exception of PREA PMRs for which a deferral extension of the final report submission date has been granted.

regardless of whether FDA has acknowledged that additional time was required to complete the study or clinical trial.

Table 5.—Summary of Open and Off-Schedule Postmarketing Requirements  
[Numbers as of September 30, 2018]<sup>1</sup>

Reporting Authority/PMR Status	NDA N = 1,045 (% of Open NDA PMRs)		BLA N = 323 (% of Open BLA PMRs)		Total Open and Off-Schedule PMRs
	Delayed	Terminated	Delayed	Terminated	
Accelerated approval	11 (1%)	1 (<1%)	4 (1%)	0 (0%)	16 (1%)
PREA	101 (10%)	3 (<1%)	12 (4%)	0 (0%)	116 (8%)
Animal efficacy	0 (0%)	0 (0%)	1 (<1%)	0 (0%)	1 (<1%)
FDAAA safety (since March 25, 2008)	105 (10%)	0 (0%)	26 (8%)	1 (<1%)	132 (10%)
Total Open and Off-Schedule	217 (21%)	4 (<1%)	43 (13%)	1 (<1%)	265 (19%)

<sup>1</sup> Percentages may not total 100 due to rounding.

#### F. Open On-Schedule and Off-Schedule PMCs

Table 6 provides the status of open on-schedule and off-schedule PMCs. As of September 30, 2018, most open, on-schedule NDA PMCs were pending (49 percent; 82/167) and most open, on-schedule BLA PMCs were ongoing (36 percent; 68/188). Fewer open NDA and BLA PMCs were considered off schedule (24 percent (40/167) and 16 percent (31/188), respectively). The majority of off-schedule NDA and BLA PMCs were delayed according to the original schedule milestones.

Table 6.—Summary of Open Postmarketing Commitments  
[Numbers as of September 30, 2018]<sup>1</sup>

	NDA N = 167 (% Open NDA PMCs)	BLA N = 188 (% Open BLA PMCs)
<b>On-Schedule</b>		
Pending	82 (49%)	54 (29%)
Ongoing	28 (17%)	68 (36%)
Submitted	17 (10%)	35 (19%)
Total	127 (76%)	157 (84%)
<b>Off-Schedule</b>		
Delayed	38 (23%)	30 (16%)
Terminated	2 (1%)	1 (<1%)
Total	40 (24%)	31 (16%)

<sup>1</sup> Percentages may not total 100 due to rounding.

#### G. Closed PMRs and PMCs

Table 7 provides details about PMRs and PMCs that were closed (fulfilled or released) within FY2018. The majority of closed PMRs were fulfilled (55 percent of NDA PMRs and 77 percent of BLA PMRs) at the end of FY2018. Similarly, the majority of closed PMCs were fulfilled at the end of FY2018.

Table 7.—Summary of Closed<sup>1</sup> Postmarketing Requirements and Commitments  
[Numbers as of September 30, 2018]<sup>2</sup>

	NDA	BLA
<b>Postmarketing Requirements</b>		
Closed PMRs (% of Closed PMRs)	<u>N = 200</u>	<u>N = 43</u>
Requirement met (fulfilled)	110 (55%)	33 (77%)
Requirement not met (released and new revised requirement issued)	30 (15%)	0 (0%)
Requirement no longer feasible or drug product withdrawn (released)	60 (30%)	10 (23%)
<b>Postmarketing Commitments</b>		
Closed PMCs (% of Closed PMCs)	<u>N = 39</u>	<u>N = 30</u>
Requirement met (fulfilled)	35 (90%)	27 (90%)
Requirement not met (released and new revised requirement issued)	0 (0%)	1 (3%)
Requirement no longer feasible or drug product	4 (10%)	2 (7%)

	NDA	BLA
withdrawn (released)		

<sup>1</sup> The table shows data for those PMRs/PMCs that were closed (fulfilled or released) within FY2018. Therefore, data for PMRs/PMCs that were closed in prior fiscal years are not included.

<sup>2</sup> Percentages may not total 100 due to rounding.

#### H. Distribution of the Statuses of PMRs and PMCs

Tables 8 and 9 show the distribution of the statuses of PMRs/PMCs as of September 30, 2018, presented by the years that the PMRs/PMCs were established<sup>19</sup> (FY2012 to FY2018).<sup>20,21</sup> Note that the data shown for closed (fulfilled or released) PMRs/PMCs are for all PMRs/PMCs that were closed as of FY2018. Therefore, data for PMRs/PMCs that were closed in prior fiscal years are included.

Based on the data shown in Table 8, an average of 272 PMRs were established each year since FY2012. Most PMRs that were established in the earlier years were either fulfilled or released. For example, as of September 30, 2018, 51 percent (112/220) of the PMRs that were established in FY2012 were fulfilled, and 17 percent (38/220) were released. The majority of PMRs that were established in more recent years were either pending (i.e., not yet underway) or ongoing (i.e., still in progress and on schedule). For example, as of September 30, 2018, 94 percent (259/277) of the PMRs established in FY2018 were pending, and 2 percent (5/277) were ongoing. Overall, of the PMRs that were pending as of September 30, 2018, 82 percent (495/602) were created within the past 3 years (FY2016, FY2017, and FY2018). Finally, based

<sup>19</sup> The establishment date is the date of the formal FDA communication to the applicant that included the final FDA-required (PMR) or -requested (PMC) postmarketing study or clinical trial.

<sup>20</sup> Tables 8 and 9 include data for only the past 7 fiscal years. Data on the distribution of statuses for PMRs/PMCs established in FY2011 and as of FY2017 are presented in the FY2017 status of postmarketing requirements and commitments report (83 FR 58259) (<https://www.federalregister.gov/documents/2018/11/19/2018-25128/report-on-the-performance-of-drug-and-biologics-firms-in-conducting-postmarketing-requirements-and>).

<sup>21</sup> The total number of PMRs/PMCs established in FY2012 through FY2018 reflects the data in FDA's databases as of September 30, 2018. Because of data corrections and improvements in ascertaining the PMR/PMC establishment date, some of the total numbers of PMRs/PMCs established in each fiscal year are different from those reported in the prior fiscal year's (FY2017) *Federal Register* report.



on the data in Table 8, on average, 10 percent (195/1906) of the PMRs established since FY2012 were delayed as of September 30, 2018.

Table 8.—Summary of Status of Postmarketing Requirements Established<sup>1</sup> Between FY2012 and FY2018<sup>2</sup>  
[Numbers as of September 30, 2018]<sup>3</sup>

PMR Status as of FY2018 (% of Total PMRs in Each Establishment Year)	Fiscal Year of PMR Establishment						
	2012	2013	2014	2015	2016	2017	2018
Pending	10 (5%)	15 (5%)	34 (11%)	48 (17%)	69 (25%)	167 (60%)	259 (94%)
Ongoing	27 (12%)	43 (16%)	56 (19%)	68 (24%)	76 (28%)	34 (12%)	5 (2%)
Submitted	3 (1%)	9 (3%)	17 (6%)	23 (8%)	17 (6%)	12 (4%)	2 (1%)
Delayed	29 (13%)	40 (15%)	35 (12%)	34 (12%)	30 (11%)	24 (9%)	3 (1%)
Terminated	1 (<1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Released	38 (17%)	59 (22%)	47 (16%)	29 (10%)	40 (15%)	15 (5%)	6 (2%)
Fulfilled	112 (51%)	108 (39%)	107 (36%)	84 (29%)	41 (15%)	28 (10%)	2 (1%)
Total <sup>4</sup>	220	274	296	286	273	280	277

<sup>1</sup> The establishment date is the date of the formal FDA communication to the applicant that included the final FDA-required (PMR) or -requested (PMC) postmarketing study or clinical trial.

<sup>2</sup> The table shows data for PMRs that were closed (fulfilled or released) as of FY2018. Therefore, data for PMRs that were closed in prior fiscal years are included.

<sup>3</sup> Percentages may not total 100 due to rounding.

<sup>4</sup> The total number of PMRs/PMCs established in FY2012 through FY2018 reflects the data in FDA's databases as of September 30, 2018. Because of data corrections and improvements in ascertaining the PMR/PMC establishment date, some of the total numbers of PMRs/PMCs established in each fiscal year are different from those reported in the prior fiscal year's (FY2017) *Federal Register* report.

Table 9 provides an overview of PMCs in a similar format as Table 8 for PMRs. Based on the data shown in Table 9, an average of 61 PMCs were established each year since FY2012. Most PMCs that were established in the earlier years were either fulfilled or released. For example, as of September 30, 2018, 73 percent (30/41) of the PMCs that were established in FY2012 were fulfilled, and 5 percent (2/41) were released. The majority of PMCs that were established in more recent years were either pending (i.e., not yet underway) or ongoing (i.e., still in progress and on schedule). For example, as of September 30, 2018, 86 percent (78/91) of the PMCs established in FY2018 were pending, and 5 percent (5/91) were ongoing. Overall, of

the PMCs that were pending as of September 30, 2018, 93 percent (119/128) were created within the past 3 years (FY2016, FY2017, and FY2018). Finally, based on the data in Table 9, on average, 7 percent (28/427) of the PMCs established since FY2012 were delayed as of September 30, 2018.

Table 9.—Summary of Status of Postmarketing Commitments Established<sup>1</sup> Between FY2012 and FY2018<sup>2</sup>  
[Numbers as of September 30, 2018]<sup>3</sup>

PMC Status as of FY2018 (% of Total PMCs in Each Establishment Year)	Fiscal Year of PMC Establishment						
	2012	2013	2014	2015	2016	2017	2018
Pending	0 (0%)	0 (0%)	4 (7%)	5 (8%)	10 (16%)	31 (46%)	78 (86%)
Ongoing	2 (5%)	10 (21%)	15 (27%)	13 (21%)	18 (29%)	11 (16%)	5 (5%)
Submitted	1 (2%)	1 (2%)	5 (9%)	4 (6%)	7 (11%)	6 (9%)	3 (3%)
Delayed	6 (15%)	2 (4%)	0 (0%)	5 (8%)	5 (8%)	9 (13%)	1 (1%)
Terminated	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Released	2 (5%)	4 (9%)	0 (0%)	3 (5%)	2 (3%)	2 (3%)	1 (1%)
Fulfilled	30 (73%)	30 (64%)	32 (57%)	33 (52%)	20 (32%)	8 (12%)	3 (3%)
Total <sup>4</sup>	41	47	56	63	62	67	91

<sup>1</sup> The establishment date is the date of the formal FDA communication to the applicant that included the final FDA required (PMR) or requested (PMC) postmarketing study or clinical trial.

<sup>2</sup> The table shows data for PMCs that were closed (fulfilled or released) as of FY2018. Therefore, data for PMCs that were closed in prior fiscal years are included.

<sup>3</sup> Percentages may not total 100 due to rounding.

<sup>4</sup> The total number of PMRs/PMCs established in FY2012 through FY2018 reflects the data in FDA's databases as of September 30, 2018. Because of data corrections, as well as improvements in ascertainment of the PMR/PMC establishment date, some of the total numbers of PMRs/PMCs established in each fiscal year are different from those reported in the prior fiscal year's (FY2017) *Federal Register* report.