Planned Review Timelines Assessment
Evaluations and Studies of New Drug Review Programs Under PDUFA IV for the Food and Drug Administration, Task Order 1, Order Number: HHSF223201010017B

Final Report

April 29, 2011
Booz | Allen | Hamilton
# TABLE OF CONTENTS

1. EXECUTIVE SUMMARY ................................................................................................................. 1

2. TASK BACKGROUND AND OBJECTIVES .............................................................................. 4

3. METHODOLOGY.......................................................................................................................... 5

4. ANALYSIS OF PLANNED REVIEW TIMELINES ....................................................................... 6
   4.1. Communication of Timelines in Filing Communication Letter ............................................ 6
   4.2. Adherence to Communicated Timelines ........................................................................... 9

5. DISCUSSION AND RECOMMENDATIONS ............................................................................. 12
   5.1. Communication of Timelines in Filing Communication Letter ........................................... 12
   5.2. Adherence to Communicated Timelines ........................................................................... 13

APPENDICES

   Appendix A: Study Cohort ........................................................................................................... 15
   Appendix B: Updated FY09 Planned Review Timelines DataFDA Interview Guide .................. 16
   Appendix C: FDA Interview Guide ............................................................................................ 17
   Appendix D: Applicant Interview Guide .................................................................................... 18
TABLE OF EXHIBITS

Exhibit 1. Study Cohort Adherence to Planned Review Timelines Milestones ...............................5
Exhibit 2. Timelines Included/Omitted by Review Division/Office ..................................................7
Exhibit 3. Planned Review Timelines Formal Training by Center .........................................................8
Exhibit 4. Timelines Included/Omitted in Filing Communication by Month .........................................8
Exhibit 5. Applicant Awareness and Opinion of Planned Review Timelines Requirement ..................9
Exhibit 6. Adherence to PMR/PMC and Labeling Discussion Milestones ......................................10
Exhibit 7. Adherence to Timelines by Action Taken ........................................................................10
Exhibit 8. Target Date Compliance by Priority or Standard Review..................................................11
Exhibit 9. Adherence to Timelines by Advisory Committee Meeting Held .....................................11
Exhibit 10. Amendments Submitted by Target Date Compliance ......................................................12
1. EXECUTIVE SUMMARY

Background
In conjunction with the authorization of the Prescription Drug User Fee Amendments of 2007 (PDUFA IV), the Food and Drug Administration (FDA) agreed to meet specific performance goals, described in PDUFA Reauthorization Performance Goals and Procedures. Under Goal X of the PDUFA IV goals, First Cycle Review Performance Proposal, FDA agreed to notify applicants in the Filing Communication letter of a target date for communication of feedback from the review division regarding proposed labeling and postmarketing commitments (PMCs) that the Agency will be requesting. In fiscal year 2009 (FY09), the first year of the new requirement, only new molecular entity (NME) New Drug Applications (NDAs) and original Biologics License Applications (BLAs) were required to include the target date in the Filing Communication letter.

FDA developed policy manuals, revised existing letter templates, and provided training to introduce and implement the new requirements. The Center for Drug Evaluation and Research (CDER) released the Manual of Policies and Practices (MaPP) 6010.8 in June 2008, which established the procedures for communicating the planned review timelines for CDER staff. The Center for Biologics Evaluation and Research (CBER) established the policy with the release of Standard Operating Procedures and Policies 8401.3. In CDER, RPMs and review disciplines were provided training opportunities through the Office of Training and Communications, as well as videotaped versions of the class that could be viewed as needed. Both Centers facilitated implementation of the new requirement by creating filing communication letter templates that contained new language to communicate the planned review timelines to applicants.

As of September 30, 2009, performance data were available for 44 planned review timelines notifications for original NMEs and BLAs, and FDA met the commitment for 86% (38/44) of them. FDA committed under PDUFA IV to reporting its performance in meeting the planned review timelines for communication of labeling and PMR/PMC comments. As of September 30, 2009, data showed FDA had met the planned target date for 39% (7/18) of the applications that had reached the communicated date.

CBER’s Regulatory Information Management Staff and CDER’s Division of Business Analytics and Reporting provided Booz Allen with the identity of the applications in the cohort, as well as their success or failure in meeting the two planned review timelines milestones. Data on each application for the root cause analysis were gathered from FDA documents, RPM interviews and applicant interviews. FDA documents were the first source for basic information about

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1 Although PDUFA Goal X only mentions PMCs, PDUFA IV created an FDA authority to require postmarketing requirements (PMRs), which FDA includes in the planned review timelines notification.
2 In the event that deficiencies preclude the discussion of labeling or PMRs/PMCs, FDA can meet the requirement by communicating this to the applicant by the target date.
3 The data in this report are those published in the FY 2009 Performance Report to the President and Congress on the Prescription Drug User Fee Act. While this study report was in final preparation, the FY 2010 Performance Report was released, which included updated FY 2009 numbers, shown in Appendix B.
4 As of September 30, 2009, the date communicated in 18 of the 38 applications that included planned review timelines had passed. Among the remaining 20 applications, the communicated dates for 18 applications had not yet passed, and a major amendment extended the review clock for two applications.
Planned Review Timelines Assessment
Final Report

product and review characteristics (e.g., priority/standard review designation, Advisory Committee (AC) meeting, number of amendments submitted, and approval or complete response action). These data were analyzed and hypotheses were developed regarding the explanation for failure to meet the planned review timelines milestones. Interviews with RPMs of cohort applications were subsequently conducted to identify root causes for non-adherence.

Inclusion of Planned Review Timelines in Filing Communication Letter
The six applications for which the planned review timelines were omitted from the filing communication letter were distributed across five review divisions, indicating that there was not any office- or division-specific practice or policy that led to the omission. Rather, five of the six non-compliant letters were issued for the first applications received by that division after the requirement for including planned review timelines was instituted, suggesting that failure to include the planned review timelines may have been due to slow adoption of a new policy. While 67% (12/18) of RPMs interviewed indicated that they did not recall participating in formal training about the planned review timelines requirement, most said that they learned of the policy through informal channels such as mentoring or team meetings.

Adherence to Communicated Review Timelines
FDA did not adhere to the communicated planned review timelines for 61% (11/18) of the applications that reached the communicated date. The two factors that seemed to explain the failure to meet the communicated target dates were an anticipated issuance of a complete response letter for an application (seven applications) and the need for an AC meeting (nine applications). For five of the seven applications that did not meet the target date and received a complete response, FDA did not initiate labeling communications with the applicant at all. Interviews with RPMs indicated that labeling discussions were not initiated because the previous policy was that they were unnecessary for an application that was going to receive a complete response. AC meetings were held during the review cycle for half of the applications in the study cohort. Two-thirds (6/9) of the applications in the cohort that did not have an AC meeting met the planned review timelines milestone date, while only 11% (1/9) of the applications that had an AC meeting were able to meet the target date. RPMs interviewed said that the additional time spent in preparation for the AC meeting caused delays for reviewers to work on labeling, and that FDA could not initiate labeling or PMR/PMC discussions until comments from the AC meeting were received. Neither priority review designation nor the number of amendments submitted during the review cycle appeared to impact the ability of FDA to meet the communicated target dates.

Recommendations
FDA compliance with including the planned review timelines in the Filing Communication letter was relatively high (86%) in the first year of implementation. Compliance was even higher (~97%) after the first three months, suggesting that adoption of the new policy was initially slow but has since been nearly universal. RPM interviews confirmed this, and suggest that FDA may not need to take additional action on this requirement.

By contrast, only 39% of the communicated planned review timelines were met. The primary drivers appeared to be a continuation of the prior policy of not communicating with the applicant on labeling or PMRs/PMCs for complete response applications, and the additional work and waiting time required from an advisory committee for an application. These challenges can be overcome by different measures. First, training on the planned review timelines should emphasize that the new policy is to communicate with the applicant about labeling and PMRs/PMCs by the target date in the Filing Communication letter, even if a complete response
is anticipated. Second, FDA should provide target dates that are as close to the end of the review cycle as possible while still adhering to the GRMPs, for applications that will require an AC meeting, which will give a more realistic goal and allow for better FDA compliance.
2. TASK BACKGROUND AND OBJECTIVES

On September 27, 2007, the Food and Drug Administration Amendments Act of 2007 (FDAAA) was signed into law, which reauthorized the Prescription Drug User Fee Act of 1992 (PDUFA) in Title I, Prescription Drug User Fee Amendments of 2007 (PDUFA IV). In conjunction with the reauthorization of PDUFA, the Food and Drug Administration (FDA) agreed to meet specific performance goals, described in PDUFA Reauthorization Performance Goals and Procedures. Under Goal X of the PDUFA IV goals, First Cycle Review Performance Proposal, FDA agreed to further enhancements, including notifying applicants in the Filing Communication letter of a target date for communication of feedback from the review division regarding proposed labeling and postmarketing commitments (PMCs)¹ the Agency will be requesting.⁶ In FY09, the first year of the new requirement, only NME NDAs and original BLAs were required to include the target date in the Filing Communication letter.

The Center for Drug Evaluation and Research (CDER) Manual of Policies and Practices (MaPP) 6010.8 was finalized in June 2008 and established the procedures for communicating the planned review timelines for CDER staff. According to the MaPP, the planned review timelines for communication of labeling comments and PMR/PMC requests:

- Will be consistent with the GRMPs for NDAs and BLAs, taking into consideration the specific circumstances surrounding the individual application.
- Will be based on the original PDUFA goal date.
- Will set forth the target date for communication of proposed labeling comments and PMR/PMC requirements and requests.

Major amendments to the application may change the timeline or in certain circumstances, cause the timeline to be withdrawn and not reissued.

CBER’s policy for communicating the planned review timelines is contained in Standard Operating Procedures and Policies 8401.3. In CDER, RPMs and review disciplines were provided training opportunities through the Office of Training and Communications, as well as videotaped versions of the class that could be viewed as needed. Both Centers facilitated implementation of the new requirement by creating filing communication letter templates that contained new language to communicate the planned review timelines to applicants.

As of September 30, 2009,⁷ performance data were available for 44 of 55 (80%) of the planned review timelines notifications for original NMEs and BLAs, and FDA met the commitment for 86% (38/44) of them. FDA committed under PDUFA IV to report its performance in meeting the planned review timelines for communication of labeling comments and PMR/PMC requirements.

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¹ Although PDUFA Goal X only mentions PMCs, PDUFA IV created an FDA authority to require postmarketing requirements (PMRs), which FDA includes in the planned review timelines notification.

⁶ In the event that deficiencies preclude the discussion of labeling or PMRs/PMCs, FDA can meet the requirement by communicating this to the applicant by the target date.

⁷ The data in this report are those published in the FY 2009 Performance Report to the President and Congress on the Prescription Drug User Fee Act. While this study report was in final preparation, the FY 2010 Performance Report was released, which included updated FY 2009 numbers, shown in Appendix B.
Planned Review Timelines Assessment
Final Report

and requests. This includes reporting on the number and percentage of applications for which the planned target dates for communication on labeling comments and PMR/PMC requirements and requests were met. As of September 30, 2009, data showed FDA had met the planned target date for 39% (7/18) of the applications.

The key objective of this task is to assess the progress of CDER and CBER in adhering to the planned review timelines. To accomplish this assessment, this task focuses on the following activities:

- Conduct a root-cause analysis to identify the main obstacles and enablers impacting adherence to planned review timelines
- Recommend actions that would improve the effectiveness of the adherence to planned review timelines.

3. METHODOLOGY

The study cohort for the planned review timelines analysis consisted of all 44 original applications (26 NME NDAs and 18 BLAs) that were received in FY09 (October 1, 2008 – September 30, 2009) and had reached the milestone date for sending the filing communication. The cohort was defined by FDA in its annual performance report for PDUFA, and included applications submitted to and reviewed by both CDER (33 applications) and CBER (11 applications). CBER’s Regulatory Information Management Staff and CDER’s Division of Business Analytics and Reporting provided Booz Allen with the identity of the applications in the cohort, as well as their success or failure in meeting the two planned review timelines milestones, summarized in Exhibit 1.

Exhibit 1. Study Cohort Adherence to Planned Review Timelines Milestones

<table>
<thead>
<tr>
<th>Planned Review Timelines</th>
<th>Compliance With Meeting Communicated Planned Review Timelines</th>
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<tbody>
<tr>
<td>Notification in Filing Communication</td>
<td>44 Applications</td>
</tr>
<tr>
<td>Yes</td>
<td>38, 88%</td>
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<tr>
<td>No</td>
<td>6, 14%</td>
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<table>
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<tr>
<th>Not Assessed: 20 Applications*</th>
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<tbody>
<tr>
<td>18 Pending*</td>
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<td>2 Major Amendments*</td>
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<table>
<thead>
<tr>
<th>Assessed: 18 Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>11, 61%</td>
</tr>
<tr>
<td>7, 39%</td>
</tr>
</tbody>
</table>

* 18 “Pending” applications included planned review timelines in the filing communication, but had not reached the communicated dates by the end of FY09; the review cycle was extended by three months due to major amendments for two applications.

Sources: FY 2009 Performance Report to Congress and the President on the Prescription Drug User Fee Act; FDA-provided data from CBER and CDER.

8 According to the GRMPs guidance, the filing communication should be sent to the applicant by day 74 after NDA/BLA receipt.
9 FY 2009 Performance Report to the President and Congress for the Prescription Drug User Fee Act
Of the applications in the cohort, 86% (38/44) included the Planned Review Timelines in the filing communication to the applicant. The remaining 14% (6/44) were the subject of further analysis, described below, to determine the explanation for the failure to include the milestone dates in the filing communication. Among the 38 applications in the cohort that included the planned review timelines in the filing communication, 20 could not be assessed for compliance in meeting those milestone dates, either because the dates were not reached prior to the end of FY09 (“pending”) or because the communicated dates were no longer applicable due to the submission of a major amendment. The remaining 18 applications were assessed for compliance with the communicated timelines, and 61% (11/18) did not meet this milestone date and were the subject of additional analysis to determine the root cause of non-compliance.10

Data on each application for the root cause analysis were gathered from FDA documents, RPM interviews and applicant interviews. FDA documents were the first source for basic information about product and review characteristics (e.g., priority/standard review designation, AC meeting, number of amendments submitted, and approval or complete response action). These data were analyzed and hypotheses were developed regarding the explanation for failure to adhere to the planned review timelines milestones. Interviews were conducted with RPMs for 4 of the 6 applications that did not include the planned review timelines in the filing communication, and 16 of the 18 applications for which adherence to the communicated timelines was evaluated. Standard questions were asked of each RPM using a brief interview guide, shown in Appendix C, to collect additional information to test the hypotheses. A structured interview guide was also employed for interviews of 13 applicants, and is included in Appendix D.

4. ANALYSIS OF PLANNED REVIEW TIMELINES

This section consists of analyses Booz Allen conducted to determine the factors that influenced the success or failure in adhering to the planned review timelines requirements.

4.1. Communication of Timelines in Filing Communication Letter

The applications in the study cohort were broadly distributed across most review divisions and offices, including 13 of 17 CDER review divisions and all three CBER review offices. Applications for which the planned review timelines were omitted from the filing communication letter were also distributed, as shown in Exhibit 2. Only one review division (Division of Drug Oncology Products (DDOP)) had more than one case of excluding the timelines from the filing communication, and that division also had the most cohort applications of any review division or office. Five of the six non-compliant letters were issued for the first application received by that division after the requirement for including planned review timelines was instituted (including DDOP, which omitted them in the first two applications received).

10 In accordance with the PDUFA IV performance goals, a 7-day grace period was allowed from the target date for initiating communications with the applicant.
Formal training was offered in both CDER and CBER prior to rolling out the planned review timelines requirement. Although all cases of omitting planned review times from the Filling Communication letters were for applications in CDER, the proportion of RPMs interviewed who recalled receiving formal training on the new requirement was lower in CBER than in CDER. Of the RPMs interviewed, only 14% (1/6) of CBER RPMs indicated that they recalled receiving training, while 45% (5/11) of CDER RPMs received the training. Most reviewers who did not recall participating in training said that they learned of the requirement through informal processes such as mentoring, RPM meetings and team meetings.
The overall timing of applications received by month and compliance with including the planned review timelines in the filing communication reveals a clear pattern, shown in Exhibit 4. Planned review timelines were rarely omitted after the first three months of the new requirement: 5 of the first 11 applications (45%) failed to include the timelines, but only 1 of the remaining 33 applications (3%) failed to include the timelines in subsequent months. Three of the four RPMs interviewed about the non-compliance of their application with this activity indicated that they did not remember to include the dates because the letter template for the filing communication had not been updated to include the new language at the time they drafted the letter.\textsuperscript{11} According to the CDER Standard Templates committee, the planned review timelines language in the CDER template was included as of January 23, 2009. The filing communication letter template for CBER, in which all FY09 applications included the planned review timelines in the filing communication, was updated to include the planned review timelines as of February 1, 2008. In addition, CDER data systems were updated in July 2009 to prompt RPMs to enter the target dates.

\textsuperscript{11} All three RPMs noted that they communicated the review timeline to the applicant through an e-mail, phone call or subsequent letter.
Among the applicants interviewed about the planned review timelines, 54% (7/13) were aware of the new requirement for FDA to include the target dates in the filing communication letter and to meet those targets (Exhibit 5). Among those applicants interviewed who were aware of the requirements, half (3/6) indicated that communicating the date in the filing communication letter was helpful. Specifically, these applicants noted that the timelines allowed them to plan and prepare for the labeling and PMR/PMC discussions, and to follow up with FDA if the date passes without hearing from the review team.

![Exhibit 5. Applicant Awareness and Opinion of Planned Review Timelines Requirement](image)

Note: *One applicant who was aware of the dates did not respond to the question of whether they were helpful or not.
Source: Interviews with applicants who were part of the planned review timelines cohort

### 4.2. Adherence to Communicated Timelines

The Planned Review Timelines Manual of Policies and Procedures indicates that the “timeline for communication of labeling comments and PMR/PMC requests will be consistent with the GRMPs for NDAs and BLAs, taking into consideration the specific circumstances surrounding the individual application.” The GRMPs guideline is to initiate discussions three weeks before division sign-off, which would typically be six weeks before the PDUFA goal date. The range of timeframes for the planned review timelines that were included in the filing communication was between 14 and 44 days prior to the PDUFA goal date for CDER applications, and 28-30 days before the PDUFA goal date for the CBER applications.

Among the applications that were evaluated for compliance with adhering to these communicated planned timelines, 61% (11/18) failed to meet the date established to initiate communications regarding labeling and/or PMRs/PMCs. More than half of the applications (56%; 10/18) missed the target date for initiating labeling discussions, as shown in Exhibit 6. While 22% (4/18) of the applications failed to initiate PMR/PMC discussions on time, nine of the applications did not have any PMRs/PMCs in their action letter, so the proportion of applications with PMRs/PMCs that missed the communicated target date was 44% (4/9). Three of the applications that missed the labeling target date initiated communications within 15 days of the communicated deadline; however, no labeling discussions were initiated by FDA with the

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12 One applicant who was aware of the dates did not respond to the question of whether they were helpful or not.
13 MaPP 6010.8: NDAs and BLAs: Communication to Applicants of Planned Review Timelines. 6/23/2008
applicant for five applications. There was a wide range of time by which the PMR/PMC discussion target date was missed, and three of the four applications that missed this target date also missed the PDUFA goal date. The only exception was an application that received a major amendment that extended the goal date by three months.

Exhibit 6. Adherence to PMR/PMC and Labeling Discussion Milestones

Exhibit 7. Adherence to Timelines by Action Taken

The action taken on applications in the study cohort was 50% (9/18) approval and 50% (9/18) complete response. As shown in Exhibit 7, 56% (5/9) of the applications that were approved met the planned review timelines milestone, while only 22% (2/9) of the applications that received a complete response met the target date. For five of the seven applications that received a complete response, FDA did not initiate labeling communications with the applicant at all. The RPMs of four of these five applications were interviewed for this study, and they all indicated that labeling discussions were not initiated because they were unnecessary for an application that was going to receive a complete response.

Exhibit 7. Adherence to Timelines by Action Taken

A priority review designation may be granted to NDAs or BLAs that provide a major advance in treatment over currently approved products, and this designation provides for a shorter review cycle (6 months) than for a standard review (10 months). In spite of this compressed review timeframe, there was very little difference in the proportion of applications that met and missed
the planned review timelines target dates between standard and priority review applications. As shown in Exhibit 8, the priority review applications met the target dates 38% (3/8) of the time, while standard review applications met the target date in 40% (4/10) of cases.

AC meetings were held during the review cycle for half of the applications in the study cohort. These meetings require a significant amount of review team preparation and are often difficult to schedule, which can lead to timeframe compression for the downstream activities. As shown in Exhibit 9, 67% (6/9) of the applications in the cohort that did not have an AC meeting met the planned review timelines milestone date, while only 11% (1/9) of the applications that had an AC meeting were able to meet the target date. Five RPMs of products that had an AC meeting and missed the target dates were interviewed, and three of them indicated that the advisory committee was a factor that led to missing the planned review timeline. More specifically, interviewees said that the additional time spent in preparation for the AC meeting caused delays for reviewers to work on labeling, and that FDA could not initiate labeling or PMR/PMC discussions until comments from the AC meeting were received.

Applicants frequently submit amendments to the application throughout the review cycle, many times requiring additional review by discipline reviewers. This can potentially delay the completion of the primary review and impact the initiation of labeling and PMR/PMC discussions with the applicant. The number of amendments submitted, as well as the proportion that were
submitted within the last 90 days prior to action, are shown for the cohort applications in Exhibit 10. There was no discernible pattern correlating the volume of amendment submissions to adherence with planned review timelines, as both the number of amendments submitted and the proportion submitted near the end of the review were similar for applications that met and did not meet the planned review timeline target date.

![Exhibit 10. Amendments Submitted by Target Date Compliance](image)

*Note: Data on amendments submitted were unavailable for 4 products (2 that met target dates and 2 that did not)*

### 5. DISCUSSION AND RECOMMENDATIONS

This section consists of a discussion of the findings from the analyses of the planned review timelines requirements, as well as Booz Allen’s recommendations to improve compliance.

#### 5.1. Communication of Timelines in Filing Communication Letter

In the first year following the implementation of the planned review timelines requirement, the vast majority (86%) of applicable filing communication letters were compliant with including the target dates for initiating discussions of labeling and PMRs/PMCs with the applicant. There did not appear to be any division-specific practices or policies that influenced compliance with this requirement, as the six non-compliant applications were distributed across five different divisions. The most significant factor influencing non-compliance with this requirement appears to be the close proximity in time of receipt of the application with the rollout of the requirement. Among the first 11 applications received after the requirement went into effect, 5 (45%) failed to include the timeline in the filing communication, while only 1 of the remaining 33 (3%) was non-compliant. Further evidence that the recent implementation of the requirement was the primary cause of non-compliance is that 5 of 6 non-compliant applications were the first application(s) received by the review division after the requirement went into effect. Interviews with RPMs provided additional evidence that this is the main cause. In addition to noting that they did not remember the new requirement, three out of four RPMs of non-compliant applications interviewed indicated that they did not include the timelines because the standard letter template had not been updated with the new language by the time the filing communication was drafted and sent to the applicant. Once the new template was developed and made available in January 2009, nearly all applications included the timelines in the filing communication letter.
Another possible contributing factor for failing to meet this new requirement is training. Relatively few RPMs interviewed (6/18, 33%) said that they remembered receiving formal training about this new requirement and the processes involved. Most indicated that they learned in team meetings, from mentors, or from seeing the new language in the updated standard letter template. However, the fact that the timelines were included in most of the letters, particularly those sent after the standard letter template was updated and more than three months after the new requirement went into effect, suggests that lack of training may have been a contributing but not primary cause. Additionally, while the proportion of RPMs that received training in CBER was lower than that in CDER, all the CBER Filing Communication letters were compliant with the new requirement. The high rate of compliance after the initial period suggests that no further action may be necessary by FDA for this requirement.

5.2. Adherence to Communicated Timelines

While compliance with including the planned review timelines in the filing communication letter was high, compliance with meeting the established dates was relatively low, with only 39% (7/18) of applications meeting the target date. A similar proportion of relevant applications missed the target date for labeling (9/18; 50%) and PMR/PMC (4/9; 44%) discussions. While compression of the review cycle with a priority review designation would appear to be a potential factor in the failure to meet any late-cycle milestone, in the study cohort there was virtually no difference in compliance between standard (40%) and priority (38%) review applications. Similarly, there did not appear to be any correlation with non-compliance and a large number of applicant-submitted amendments, nor the late-cycle submission of the amendments.

There were two factors in the analysis that appeared to impact compliance with adhering to the planned review timeline, and they were both affirmed during interviews with the application RPMs. The first is related to the action taken. For applications that received a complete response, 78% (7/9) failed to meet the communicated target dates, while only 44% (4/9) missed the target dates for approved applications. More specifically, among the seven missed target dates for complete response applications, five were non-compliant for not initiating labeling discussions at all. Typically FDA does not negotiate labeling with the applicant for applications receiving a complete response, so the data seemed to indicate that FDA may have continued to operate under this practice in spite of the new requirement. Indeed, four of the five RPMs of these applications indicated that labeling discussions were not initiated because a complete response action was imminent. According to CDER’s MaPP 6010.8, review divisions are to “communicate to the applicant no later than the target date, generally through the issuance of a discipline review letter, the deficiencies and its determination that the deficiencies preclude discussion of labeling or PMRs/PMCs.” However, there was only one instance in the study cohort of a discipline review letter issued notifying the sponsor that deficiencies would preclude these discussions.

The second factor revealed in the data analysis was the need for an AC meeting. Applications that had AC meetings had a lower compliance (11%) in meeting planned review timelines than those that did not have an AC meeting (67%). This finding seemed rational because AC meetings require a significant amount of preparation and can easily disrupt and delay the remainder of the milestones in the review cycle. Once again, interview responses from RPMs validated the finding in the data. Three of five RPMs interviewed that had missed this milestone for an application with an AC meeting indicated that the AC meeting played a role in the missed target date.
The failure to notify applicants that significant deficiencies preclude the discussion of labeling or PMRs/PMCs by the target date identified in the timeline could be addressed through training. Rather than continuing the former policy of not informing applicants that labeling reviews were not going to occur, compliance may improve if RPMs and discipline reviewers are trained on the correct policy to notify an applicant that significant deficiencies preclude the discussion of labeling or PMRs/PMCs by the target date identified in the timeline.\textsuperscript{14} For applications that will require an AC meeting, RPMs should take advantage of the flexibility in the policy allowing them to take into consideration special circumstances with an application, and provide planned review timeline dates closer to the PDUFA goal date. This would provide applicants with more reliable expectations for when they will hear from FDA regarding labeling and PMRs/PMCs, and would enable the review team to plan their activities against a more realistic schedule, which would improve compliance with meeting the communicated dates.

\textsuperscript{14}This notification should generally occur through the use of a discipline review letter.
## Appendix A: Planned Review Timelines Cohort Applications

<table>
<thead>
<tr>
<th>NDA/BLA #</th>
<th>Application Received Date</th>
<th>Action Taken</th>
<th>Center</th>
<th>Office</th>
<th>Division/Office</th>
<th>Standard/Priority</th>
<th>PMRs/PMCs</th>
<th>AC Meeting</th>
<th>Included Timelines in Filing Communication</th>
<th>Met Target Date</th>
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<tr>
<td>22288</td>
<td>11/12/08</td>
<td>Approval</td>
<td>CDER</td>
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*Information was redacted from the applications below to protect confidentiality.

| CR | P | N | ** | Y | Pending |
| CR | S | N | N  | Y | Did Not Meet |
| CR | S | N | ** | N | N/A |
| CR | S | N | N  | Y | Met Timeline |
| CR | S | N | N  | Y | Met Timeline |
| CR | S | N | ** | Y | Pending |
| CR | S | N | ** | Y | Pending |
| CR | P | N | N  | Y | Met Timeline |
| CR | P | N | ** | Y | Unsolicited Amendments |

Notes: * NDA22-465 and NDA 22-562 were deemed to have not included the timelines in the filing communication in the FY09 report, but were counted among those that did include the timelines in the revised data released with the FY10 performance report. **The presence of an Advisory Committee meeting was only determined for applications that included planned review timelines in the Filing Communication letter and had reached the communicated dates by the end of FY09. ***Application has since been approved.
Appendix B: Updated FY09 Planned Review Timelines Data

In Appendix C of the FY 2010 Performance Report to Congress and the President on the Prescription Drug User Fee Act, FDA provided updated data from FY09. These data were updated based on two factors:

- Applications that had previously been classified as “pending” because they had not reached the communicated target date by the end of FY09 were evaluated
- FDA considered the requirement to include the target date in the filing communication letter fulfilled if the date was included in a filing review letter.

The updated FY09 data are shown below.

* Four applications were not included in the assessment of FDA’s compliance in meeting the timelines communicated to the sponsor. One application was withdrawn prior to reaching the communicated date. The review cycles for three applications were extended by three months due to major amendments.

Source: FY 2010 Performance Report to Congress and the President on the Prescription Drug User Fee Act
Appendix C:  FDA Interview Guide

Assessment of Planned Review Timelines: Root Cause Analysis
Interview Guide for FDA RPMs

1) Did you participate in training on implementation of planned review timelines processes?

2) Why were planned review timelines for labeling and PMR/PMC discussions not included in the filing communication letter? (If applicable)

3) In your case, why were labeling discussions not initiated by the target date specified in the filing communication? (If applicable)

4) What could be improved in the process or tools available that would help to meet the target dates for initiating these discussions with the sponsor?
Appendix D: Applicant Interview Guide

Assessment of Planned Review Timelines: Root Cause Analysis
Interview Guide for FDA RPMs

1) Is your company aware of the new planned review timeline requirements as mandated by FDAAA which requires FDA to
   a. notify sponsors via the 74-day letter of the timeframe by which labeling and/or PMR/PMC discussions will be initiated?
      b. begin labeling and/or PMR/PMC discussions by the indicated timeframe?

2) Has implementation of the planned review timelines impacted your company’s processes for preparing submissions to FDA?
   a. If so, how?

3) Do discussions with FDA regarding labeling, PMR/PMCs, and/or REMS begin during the timeframe indicated to your company by FDA in the 74-day filing communication letter?

4) Do you ensure that your company’s labeling submissions are complete or finalized for FDA review by these dates?
   a. What actions are taken by your company to ensure timely completion/finalization of labeling submissions?
      b. What actions are taken by your company when preparing labeling submissions to minimize further FDA information requests and need for data?

5) What factors prevent your company from being able to finalize/complete labeling by the date when discussions are supposed to begin with FDA?

6) How do you decide what data to include in or exclude from your application?

7) Are there any processes that your company takes to ensure that FDA has adequate time to review and finalize labeling and PMR/PMCs? If so, please describe?