
# FY 2016

## *PERFORMANCE REPORT TO CONGRESS*

*for the*

# *Biosimilar User Fee Act*

# *Commissioner's Report*

I am pleased to present to the President and Congress the Food and Drug Administration's (FDA) Fiscal Year (FY) 2016 Performance Report to Congress for the Biosimilar User Fee Act (BsUFA). On July 9, 2012, the President signed into law the Food and Drug Administration Safety and Innovation Act (FDASIA), which included the first authorization of BsUFA. BsUFA provides FDA with user fee revenue to expedite the process for the review of biosimilar biological product submissions, including applications, supplements, notifications, responses, and meeting management.

This report details FDA's preliminary performance for FY 2016, and finalizes performance results for FY 2015. I can report that FDA met or exceeded 12 of the 18 FY 2015 performance goals and has the potential to meet or exceed 13 of 20 performance goals that apply to the biosimilar submissions for the FY 2016 cohort.

FDA is committed to meeting all BsUFA performance goals. We will continue to strengthen efforts to improve performance while, as always, maintaining a focus on ensuring that all biosimilar biological product submissions are reviewed for safety and effectiveness in an efficient and predictable time frame.

FDA is dedicated to improving the efficiency, quality, and predictability of the biosimilar biological product review process. We are committed to exploring new approaches and technologies that offer high-quality, cost-effective improvements in FDA's review of biosimilar biological product submissions.

We look forward to continued success and improvements in the biosimilar biological product review process, made possible by BsUFA, in the coming years.

Robert M. Califf, M.D.
Commissioner of Food and Drugs

# *Acronyms*

**BPCIA** – Biologics Price Competition and Innovation Act of 2009

**BPD** – Biosimilar Biological Product Development

**BsUFA** – Biosimilar User Fee Act

**CBER** – Center for Biologics Evaluation and Research

**CDER** – Center for Drug Evaluation and Research

**ETASU** – Elements to Assure Safe Use

**FDA** – Food and Drug Administration

**FDASIA** – Food and Drug Administration Safety and Innovation Act

**FY** – Fiscal Year (October 1 to September 30)

**PHS Act** – Public Health Service Act

**REMS** – Risk Evaluation and Mitigation Strategy

# *Executive Summary*

The BsUFA program provides funding for the review of biosimilar biologics authorized under the Biologics Price Competition and Innovation Act of 2009 (BPCIA), enacted in March 2010. On July 9, 2012, the President signed into law FDASIA, which included the authorization of BsUFA. BsUFA provides FDA with user fee revenue to expedite the process for the review of biosimilar biological product submissions, including applications, supplements, notifications, responses, and meeting management.

### Information Included in this Report

This report marks the fourth year of the BsUFA program. The report presents FDA's final performance in meeting BsUFA goals and commitments for FY 2015 and preliminary performance for FY 2016.

### Program Performance

FDA continues to work towards improving its performance in meeting or exceeding expectations in the implementation and completion of the performance goals established under BsUFA. Key highlights for this program during FY 2016 include the following:

- Of the 24 BsUFA goal categories, 18 applied to FY 2015 biosimilar submissions. FDA met or exceeded 12 of these 18 goals.

- FDA has the potential to meet or exceed 13 of the 20 goals that apply to the FY 2016 cohort once these actions are completed.

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# *Introduction*

On July 9, 2012, the President signed into law FDASIA, which included the authorization of BsUFA. The Federal Food, Drug, and Cosmetic Act, as amended by BsUFA, authorizes FDA to assess and collect fees for biosimilar biological products from October 2012 through September 2017. FDA dedicates these fees to the efficient review of biosimilar biological product (also referred to as biosimilar) submissions and to facilitate the development of safe and effective biosimilar biological products for the American public.

## Performance Presented in This Report

This report presents FDA's final performance in meeting BsUFA goals and commitments for FY 2015 and preliminary performance for FY 2016. These data represent FDA's performance on submissions received and actions taken as of September 30, 2016. Final FDA performance for FY 2016 submissions will be presented in the FY 2017 BsUFA Performance Report and will include final actions for submissions still pending within the BsUFA goal date as of September 30, 2016. More detailed information on submissions and performance calculations, as well as definitions of key terms used in this report, are presented in the appendices. The following information refers to performance presented in this report.

- The following terminology is used throughout this document:
    - *Application* means a new, original application
    - *Supplement* means a supplement to an approved application
    - *Resubmission* means a resubmitted application or supplement in response to a complete response or tentative approval letter
    - *Submission* applies to all of the above
- Performance goal results are reported for each fiscal year receipt cohort (defined as submissions filed from October 1 to September 30 of the following year). Submissions that are received too late to be reviewed by the end of the fiscal year in which they are received are reported on in the subsequent fiscal year report after FDA takes an action, or when the review goal period expires.
- Unless otherwise noted, all performance data are as of September 30, 2016.
- Preliminary performance data for FY 2016 submissions are reported as the current percentage of submissions that have been reviewed within the review goal. The highest possible performance column shows the percent of reviews that will be completed on time if all non-overdue pending reviews are completed within goal.
- Appendix A includes the detailed final performance calculations for FY 2015 and preliminary performance calculations for FY 2016, including the number of submissions reviewed or acted on by the goal date and the number of overdue goals (acted on after the goal due date or currently pending past the goal due date). Performance is presented as percent on time. Preliminary performance excludes actions pending within the BsUFA goal date.

### Biosimilar Application and Supplement Types

- **Original Biosimilar Product Application** – A new application for licensure of a biological product under section 351(k) of the Public Health Service Act (PHS Act).
- **Resubmitted Original Biosimilar Product Application** – A complete response to an action letter for an original application addressing all identified deficiencies.
- **Original Supplement with Clinical Data** – A request for FDA to approve a change in a biosimilar product application that has been approved, including a supplement requesting that FDA determine that the approved biosimilar meets the standards for interchangeability described in section 351(k)(4) of the PHS Act.
- **Resubmitted Supplement with Clinical Data** – A complete response to an action letter for an original supplement with clinical data addressing all identified deficiencies.
- **Manufacturing Supplement** – A request to FDA to approve a change in the manufacturing of an approved biosimilar.

Additional definitions are included in Appendix C and in the BsUFA statutory language: www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/UCM287749.pdf

# *BsUFA Performance Goals and Commitments*

The table below presents the goal timelines and the percentage of submissions that FDA committed to review within those goal timelines for FY 2013 through FY 2017. Additional information on BsUFA performance metrics and definitions for Biosimilar Biological Product Development (BPD) meeting types can be found in Appendix B.

**FDA Performance Goal Targets**

| BsUFA Submission Type | Review Goal* | FY 13 | FY 14 | FY 15 | FY 16 | FY 17 |
|---|---|---|---|---|---|---|
| **Biosimilar Applications and Supplements** | | | | | | |
| Original Biosimilar Product Applications | 10 months | 70% | 70% | 80% | 85% | 90% |
| Resubmitted Original Biosimilar Applications | 6 months | 70% | 70% | 80% | 85% | 90% |
| Original Supplements with Clinical Data | 10 months | 90% | 90% | 90% | 90% | 90% |
| Resubmitted Supplements with Clinical Data | 6 months | 90% | 90% | 90% | 90% | 90% |
| Manufacturing Supplements | 6 months | 90% | 90% | 90% | 90% | 90% |
| **Procedural Notifications** | | | | | | |
| Notification of Issues Identified During Review | 74 days | 90% | 90% | 90% | 90% | 90% |
| Notification of Planned Review Timeline | 74 days | 90% | 90% | 90% | 90% | 90% |
| Review of Proprietary Biosimilar Product Names (During BPD Phase) | 180 days | 90% | 90% | 90% | 90% | 90% |
| Review of Proprietary Biosimilar Product Names (with Application) | 90 days | 90% | 90% | 90% | 90% | 90% |
| Review of Proprietary Biosimilar Product Names (Resubmitted or Requests for Reconsideration) | 60 days | 90% | 90% | 90% | 90% | 90% |
| **Procedural Responses** | | | | | | |
| Major Dispute Resolution | 30 days | 90% | 90% | 90% | 90% | 90% |
| Responses to Clinical Holds | 30 days | 90% | 90% | 90% | 90% | 90% |
| Special Protocol Assessments | 45 days | 70% | 70% | 80% | 85% | 90% |
| **Meeting Management** | | | | | | |
| Meeting Requests: Initial Advisory Meeting | 21 days | 90% | 90% | 90% | 90% | 90% |
| Meeting Requests: BPD Type 1 | 14 days | 90% | 90% | 90% | 90% | 90% |
| Meeting Requests: BPD Type 2 | 21 days | 90% | 90% | 90% | 90% | 90% |
| Meeting Requests: BPD Type 3 | 21 days | 90% | 90% | 90% | 90% | 90% |
| Meeting Requests: BPD Type 4 | 21 days | 90% | 90% | 90% | 90% | 90% |
| Scheduling Meetings: Initial Advisory Meeting | 90 days | 70% | 70% | 80% | 85% | 90% |
| Scheduling Meetings: BPD Type 1 | 30 days | 70% | 70% | 80% | 85% | 90% |
| Scheduling Meetings: BPD Type 2 | 75 days | 70% | 70% | 80% | 85% | 90% |
| Scheduling Meetings: BPD Type 3 | 120 days | 70% | 70% | 80% | 85% | 90% |
| Scheduling Meetings: BPD Type 4 | 60 days | 70% | 70% | 80% | 85% | 90% |
| Provide Meeting Minutes: All Meeting Types | 30 days | 90% | 90% | 90% | 90% | 90% |

* Review goal was formerly reported as “review-time goal.”

# *FY 2015 Final BsUFA Performance Summary*

FY 2015 final BsUFA performance is summarized below. As nearly all FY 2015 submissions have been acted on as of September 30, 2016, the table below represents the final performance for that year. The details of the calculations can be found in Appendix A.

Of the 24 BsUFA goal categories, 18 applied to FY 2015 biosimilar submissions. FDA met or exceeded 12 of these 18 goals.

**FY 2015 Final Performance**

| BsUFA Submission Type | Review Goal | On Time | Performance Goal | Percent on Time | Goal Met |
|---|---|---|---|---|---|
| **Biosimilar Application Review Goals** | | | | | |
| Original Biosimilar Product Applications | 10 months | 5 of 5 | 80% | 100% | Yes |
| Resubmitted Original Biosimilar Applications | 6 months | 0 of 0 | 80% | NA* | NA |
| Original Supplements with Clinical Data | 10 months | 0 of 0 | 90% | NA | NA |
| Resubmitted Supplements with Clinical Data | 6 months | 0 of 0 | 90% | NA | NA |
| Manufacturing Supplements | 6 months | 0 of 0 | 90% | NA | NA |
| **Procedural Notifications** | | | | | |
| Notification of Issues Identified during Review | 74 days | 5 of 5 | 90% | 100% | Yes |
| Notification of Planned Review Timeline | 74 days | 5 of 5 | 90% | 100% | Yes |
| Review of Proprietary Biosimilar Product Names (During BPD Phase) | 180 days | 4 of 5 | 90% | 80% | No |
| Review of Proprietary Biosimilar Product Names (with Application) | 90 days | 7 of 7 | 90% | 100% | Yes |
| Review of Proprietary Biosimilar Product Names (Resubmitted or Requests for Reconsideration) | 60 days | 0 of 0 | 90% | NA | NA |
| **Procedural Responses** | | | | | |
| Major Dispute Resolution | 30 days | 0 of 0 | 90% | NA | NA |
| Responses to Clinical Holds | 30 days | 2 of 2 | 90% | 100% | Yes |
| Special Protocol Assessments | 45 days | 1 of 1 | 80% | 100% | Yes |
| **Meeting Management** | | | | | |
| Meeting Requests: Initial Advisory Meeting | 21 days | 3 of 3 | 90% | 100% | Yes |
| Meeting Requests: BPD Type 1 | 14 days | 3 of 3 | 90% | 100% | Yes |
| Meeting Requests: BPD Type 2 | 21 days | 47 of 48 | 90% | 98% | Yes |
| Meeting Requests: BPD Type 3 | 21 days | 1 of 1 | 90% | 100% | Yes |
| Meeting Requests: BPD Type 4 | 21 days | 3 of 3 | 90% | 100% | Yes |
| Scheduling Meetings: Initial Advisory Meeting | 90 days | 1 of 2 | 80% | 50% | No |
| Scheduling Meetings: BPD Type 1 | 30 days | 2 of 3 | 80% | 67% | No |
| Scheduling Meetings: BPD Type 2 | 75 days | 20 of 41 | 80% | 49% | No |
| Scheduling Meetings: BPD Type 3 | 120 days | 1 of 1 | 80% | 100% | Yes |
| Scheduling Meetings: BPD Type 4 | 60 days | 0 of 3 | 80% | 0% | No |
| Provide Meeting Minutes: All Meeting Types | 30 days | 36 of 47 | 90% | 77% | No |

* In all submission types marked not applicable (NA), performance goals do not apply because no submissions were received.

# *FY 2016 Preliminary BsUFA Performance Summary*

The tables below present preliminary FY 2016 BsUFA performance.

- The *Actions Completed* column shows how much of the cohort has been acted on so far by presenting the number of submissions that had actions taken in FY 2016 or were overdue as of September 30, 2016, out of all submissions received. This shows the share of the cohort that has had an action taken, whether or not it met the review goal.
- The *Percent On Time* column presents the percentage of actions completed that were within the review goal as of September 30, 2016. Actions that were pending and not yet past the goal date as of September 30, 2016, are excluded from this calculation. Please see Appendix A for the details of these percentages.
- The *Highest Possible Performance* column presents the scenario where all remaining non-overdue pending submissions are reviewed on time (by the BsUFA goal date).

FDA has the potential to meet or exceed 13 of the 20 goals that apply to the FY 2016 cohort once these actions are completed.

**FY 2016 Preliminary Performance**

| BsUFA Submission Type | Actions Completed | Review Goal | Performance Goal | Percent on Time | Highest Possible Performance |
|---|---|---|---|---|---|
| **Biosimilar Applications and Supplements** | | | | | |
| Original Biosimilar Product Applications | 1 of 5 Complete | 10 months | 85% | 100% | 100% |
| Resubmitted Original Biosimilar Applications | 1 of 1 Complete | 6 months | 85% | 100% | 100% |
| Original Supplements with Clinical Data | 0 of 0 Complete | 10 months | 90% | NA | NA |
| Resubmitted Supplements with Clinical Data | 0 of 0 Complete | 6 months | 90% | NA | NA |
| Manufacturing Supplements | 1 of 8 Complete | 6 months | 90% | 100% | 100% |
| **Procedural Notifications** | | | | | |
| Notification of Issues Identified During Review | 2 of 5 Complete | 74 days | 90% | 100% | 100% |
| Notification of Planned Review Timeline | 2 of 5 Complete | 74 days | 90% | 100% | 100% |
| Review of Proprietary Biosimilar Product Names (During BPD Phase) | 8 of 13 Complete | 180 days | 90% | 100% | 100% |
| Review of Proprietary Biosimilar Product Names (with Application) | 7 of 10 Complete | 90 days | 90% | 86% | 90% |
| Review of Proprietary Biosimilar Product Names (Resubmitted or Requests for Reconsideration) | 0 of 0 Complete | 60 days | 90% | NA | NA |
| **Procedural Responses** | | | | | |
| Major Dispute Resolution | 0 of 0 Complete | 30 days | 90% | NA | NA |
| Responses to Clinical Holds | 2 of 3 Complete | 30 days | 90% | 100% | 100% |
| Special Protocol Assessments | 2 of 2 Complete | 45 days | 85% | 100% | 100% |

## FY 2016 Preliminary Performance (continued)

| BsUFA Submission Type | Actions Completed | Review Goal | Performance Goal | Percent on Time | Highest Possible Performance |
|---|---|---|---|---|---|
| **Meeting Management** | | | | | |
| Meeting Requests: Initial Advisory Meeting | 10 of 10 Complete | 21 days | 90% | 70% | 70% |
| Meeting Requests: BPD Type 1 | 9 of 9 Complete | 14 days | 90% | 100% | 100% |
| Meeting Requests: BPD Type 2 | 44 of 46 Complete | 21 days | 90% | 91% | 91% |
| Meeting Requests: BPD Type 3 | 4 of 5 Complete | 21 days | 90% | 75% | 80% |
| Meeting Requests: BPD Type 4 | 9 of 11 Complete | 21 days | 90% | 89% | 91% |
| Scheduling Meetings: Initial Advisory Meeting | 8 of 8 Complete | 90 days | 85% | 75% | 75% |
| Scheduling Meetings: BPD Type 1 | 8 of 8 Complete | 30 days | 85% | 75% | 75% |
| Scheduling Meetings: BPD Type 2 | 41 of 42 Complete | 75 days | 85% | 73% | 74% |
| Scheduling Meetings: BPD Type 3 | 4 of 5 Complete | 120 days | 85% | 100% | 100% |
| Scheduling Meetings: BPD Type 4 | 8 of 10 Complete | 60 days | 85% | 63% | 70% |
| Provide Meeting Minutes: All Meeting Types | 44 of 63 Complete | 30 days | 90% | 73% | 81% |

# *BsUFA Workload*

## Review Workload: FY 2013 to FY 2016

The table below presents the review workload numbers from FY 2013 to FY 2016.

**Review Workload for Applications and Submissions**

| BsUFA Workload | FY 2013 | FY 2014 | FY 2015 | FY 2016 |
|---|---|---|---|---|
| **Biosimilar Application Review Goals** | | | | |
| Original Biosimilar Product Applications | 0 | 2 | 5 | 5 |
| Resubmitted Original Biosimilar Applications | 0 | 0 | 0 | 1 |
| Original Supplements with Clinical Data | 0 | 0 | 0 | 0 |
| Resubmitted Supplements with Clinical Data | 0 | 0 | 0 | 0 |
| Manufacturing Supplements | 0 | 0 | 0 | 8 |
| **Procedural Notifications** | | | | |
| Notification of Issues Identified during Review | 0 | 2 | 5 | 5 |
| Notification of Planned Review Timeline | 0 | 2 | 5 | 5 |
| Review of Proprietary Biosimilar Product Names (During BPD Phase) | 3 | 3 | 5 | 13 |
| Review of Proprietary Biosimilar Product Names (with Application) | 0 | 1 | 7* | 10 |
| Review of Proprietary Biosimilar Product Names (Resubmitted or Requests for Reconsideration) | 0 | 0 | 0 | 0 |
| **Procedural Responses** | | | | |
| Major Dispute Resolution | 0 | 0 | 0 | 0 |
| Responses to Clinical Holds | 1 | 1 | 2 | 3 |
| Special Protocol Assessments | 0 | 2 | 1 | 2 |
| **Meeting Management** | | | | |
| Meeting Requests: Initial Advisory Meeting | 4 | 11 | 3 | 10 |
| Meeting Requests: BPD Type 1 | 0 | 1 | 3 | 9 |
| Meeting Requests: BPD Type 2 | 21 | 30 | 48 | 46 |
| Meeting Requests: BPD Type 3 | 6 | 9 | 1 | 5 |
| Meeting Requests: BPD Type 4 | 1 | 3 | 3 | 11 |
| Scheduling Meetings: Initial Advisory Meeting | 3 | 9 | 2 | 8 |
| Scheduling Meetings: BPD Type 1 | 0 | 1 | 3 | 8 |
| Scheduling Meetings: BPD Type 2 | 20 | 25 | 41 | 42 |
| Scheduling Meetings: BPD Type 3 | 6 | 9 | 1 | 5 |
| Scheduling Meetings: BPD Type 4 | 1 | 3 | 3 | 10 |
| Provide Meeting Minutes: All Meeting Types | 29 | 44 | 47† | 63 |

* Number modified from preliminary data reported in FY 2015 from 8 to 7.
† Number modified from preliminary data reported in FY 2015 from 46 to 47.

## *Additional Reporting Requirements*

Section 408 of FDASIA requires that, beginning in FY 2014, FDA report the following:

- The number of applications for approval filed under section 351(k) of the PHS Act;
- The percentage of applications described in subparagraph (A) that were approved by the Secretary; and
- An explanation of how FDA is managing the biological product review program to ensure that the user fees collected under part 2 are not used to review an application under section 351(k) of the PHS Act.

As of September 30, 2016, nine 351(k) applications were accepted for filing by FDA.

As of September 30, 2016, 44 percent of the 351(k) applications that have been filed by FDA have been approved.

In reference to the third bullet above, FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER) are managing the biosimilar review program to ensure user fees collected under the Prescription Drug User Fee Act, the Medical Device User Fee Act, or the Generic Drug User Fee Act are not used to review applications under section 351(k) of the PHS Act. Both Centers track employee workload activities through periodic time reporting to ensure that labor costs related to the process for the review of biosimilars (versus those for the review of other human drugs, medical devices, or other activities) are recorded as BsUFA work and funded from appropriate accounts.

# *Appendices*

## Appendix A: Performance Calculations

The following tables detail the final performance for FY 2015 and preliminary performance for the FY 2016 cohort of submissions. These data include the number of submissions reviewed *on-time* (acted on by the BsUFA goal date) or *overdue* (acted on past goal or pending past the goal date) and the final *percent on time* (final performance with no actions pending within the BsUFA goal date). The FY 2015 performance data presented here have been updated from the preliminary performance information reported in the FY 2015 BsUFA Performance Report.

### Biosimilar Applications and Supplements

#### Original Biosimilar Product Applications

**Goal:** Review and act on 85 percent of submissions within 10 months by FY 2016

| Original Biosimilar Product Applications | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **5** | **5** |
| Pending | 0 | 4 |
| On-Time | 5 | 1 |
| Overdue | 0 | 0 |
| **Performance: % On-time** | **100%** | **100%** |
| Highest Possible Performance: | **100%** | **100%** |
| ***BsUFA Goal: On-time Target %*** | **80%** | **85%** |
| **Goal Met Status:** | **Goal Met** | **Currently Meeting, Pending** |

#### Resubmitted Original Biosimilar Applications

**Goal:** Review and act on 85 percent of submissions within 6 months by FY 2016

| Resubmitted Original Biosimilar Applications | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **0** | **1** |
| Pending | 0 | 0 |
| On-Time | 0 | 1 |
| Overdue | 0 | 0 |
| **Performance: % On-time** | **NA** | **100%** |
| Highest Possible Performance: | **NA** | **100%** |
| ***BsUFA Goal: On-time Target %*** | **80%** | **85%** |
| **Goal Met Status:** | **NA** | **Goal Met** |

### Manufacturing Supplements

**Goal:** Review and act on 90 percent of submissions within 6 months by FY 2016

| Manufacturing Supplements | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **0** | **8** |
| Pending | 0 | 7 |
| On-Time | 0 | 1 |
| Overdue | 0 | 0 |
| **Performance: % On-time** | **NA** | **100%** |
| Highest Possible Performance: | **NA** | **100%** |
| ***BsUFA Goal: On-time Target %*** | **90%** | **90%** |
| **Goal Met Status:** | **NA** | **Currently Meeting, Pending** |

## Procedural Notifications

### Notification of Issues Identified during Review

**Goal:** Review and act on 90 percent of submissions within 74 days

| Notification of Issues Identified During Review | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **5** | **5** |
| Pending | 0 | 3 |
| On-Time | 5 | 2 |
| Overdue | 0 | 0 |
| **Performance: % On-time** | **100%** | **100%** |
| Highest Possible Performance: | **100%** | **100%** |
| ***BsUFA Goal: On-time Target %*** | **90%** | **90%** |
| **Goal Met Status:** | **Goal Met** | **Currently Meeting, Pending** |

### Notification of Planned Review Timeline

**Goal:** Planned review timelines are in 90 percent of the 74-day filing review notification letters

| Notification of Planned Review Timeline | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **5** | **5** |
| Pending | 0 | 3 |
| In 74-Day Letter | 5 | 2 |
| Not in 74-Day Letter | 0 | 0 |
| **Performance:** | **100%** | **100%** |
| Highest Possible Performance: | **100%** | **100%** |
| ***BsUFA Goal:*** | **90%** | **90%** |
| **Goal Met Status:** | **Goal Met** | **Currently Meeting, Pending** |

### Review of Proprietary Biosimilar Product Names (During BPD Phase)

**Goal:** Review and act on 90 percent of submissions within 180 days

| Review of Proprietary Biosimilar Product Names (During BPD Phase) | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **5** | **13** |
| Pending | 0 | 5 |
| On Time | 4 | 8 |
| Overdue | 1* | 0 |
| **Current Performance: % On Time** | **80%** | **100%** |
| Highest Possible Performance: | **80%** | **100%** |
| **BsUFA Goal: On Time Target %** | **90%** | **90%** |
| **Goal Met Status:** | **Goal Not Met** | **Currently Meeting, Pending** |

* Submission is pending overdue.

### Review of Proprietary Biosimilar Product Names (With Application)

**Goal:** Review and act on 90 percent of submissions within 90 days

| Review of Proprietary Biosimilar Product Names (With Application) | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **7** | **10** |
| Pending | 0 | 3 |
| On-Time | 7 | 6 |
| Overdue | 0 | 1* |
| **Performance: % On-time** | **100%** | **86%** |
| Highest Possible Performance: | **100%** | **90%** |
| ***BsUFA Goal: On-time Target %*** | **90%** | **90%** |
| **Goal Met Status:** | **Goal Met** | **Currently Not Meeting, Pending** |

* Submission is pending overdue.

## Procedural Responses

### Responses to Clinical Holds

**Goal:** Review and act on 90 percent of submissions within 30 days

| Responses to Clinical Holds | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **2** | **3** |
| Pending | 0 | 1 |
| On Time | 2 | 2 |
| Overdue | 0 | 0 |
| **Current Performance: % On Time** | **100%** | **100%** |
| Highest Possible Performance: | **100%** | **100%** |
| **BsUFA Goal: On Time Target %** | **90%** | **90%** |
| **Goal Met Status:** | **Goal Met** | **Currently Meeting, Pending** |

### Special Protocol Assessments

**Goal:** Review and act on 85 percent of submissions within 45 days by FY 2016

| Special Protocol Assessments | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **1** | **2** |
| Pending | 0 | 0 |
| On-Time | 1 | 2 |
| Overdue | 0 | 0 |
| **Performance: % On-time** | **100%** | **100%** |
| Highest Possible Performance: | **100%** | **100%** |
| ***BsUFA Goal: On-time Target %*** | **80%** | **85%** |
| **Goal Met Status:** | **Goal Met** | **Goal Met** |

## Meeting Management[1]

### Responses to Meeting Requests: Initial Advisory Meetings

**Goal:** Review and act on 90 percent of submissions within 21 days

| Responses to Meeting Requests: Initial Advisory Meetings | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **3** | **10** |
| Pending | 0 | 0 |
| On-Time | 3 | 7 |
| Overdue | 0 | 3 |
| **Performance: % On-time** | **100%** | **70%** |
| Highest Possible Performance: | **100%** | **70%** |
| ***BsUFA Goal: On-time Target %*** | **90%** | **90%** |
| **Goal Met Status:** | **Goal Met** | **Goal Not Met** |

### Responses to Meeting Requests: BPD Type 1

**Goal:** Review and act on 90 percent of submissions within 14 days

| Responses to Meeting Requests: BPD Type 1 | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **3** | **9** |
| Pending | 0 | 0 |
| On-Time | 3 | 9 |
| Overdue | 0 | 0 |
| **Performance: % On-time** | **100%** | **100%** |
| Highest Possible Performance: | **100%** | **100%** |
| ***BsUFA Goal: On-time Target %*** | **90%** | **90%** |
| **Goal Met Status:** | **Goal Met** | **Goal Met** |

[1] Not all meeting requests are granted; therefore, the number of meetings scheduled may differ from the number of meeting requests received. Not all scheduled meetings are held; therefore, the number of meeting minutes may differ from the number of meetings scheduled.

### Responses to Meeting Requests: BPD Type 2

**Goal:** Review and act on 90 percent of submissions within 21 days

| Responses to Meeting Requests: BPD Type 2 | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **48** | **46** |
| Pending | 0 | 2 |
| On-Time | 47 | 40 |
| Overdue | 1 | 4 |
| **Performance: % On-time** | **98%** | **91%** |
| Highest Possible Performance: | **98%** | **91%** |
| ***BsUFA Goal: On-time Target %*** | **90%** | **90%** |
| **Goal Met Status:** | **Goal Met** | **Currently Meeting, Pending** |

### Responses to Meeting Requests: BPD Type 3

**Goal:** Review and act on 90 percent of submissions within 21 days

| Responses to Meeting Requests: BPD Type 3 | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **1** | **5** |
| Pending | 0 | 1 |
| On-Time | 1 | 3 |
| Overdue | 0 | 1 |
| **Performance: % On-time** | **100%** | **75%** |
| Highest Possible Performance: | **100%** | **80%** |
| ***BsUFA Goal: On-time Target %*** | **90%** | **90%** |
| **Goal Met Status:** | **Goal Met** | **Will Not Meet Goal** |

### Responses to Meeting Requests: BPD Type 4

**Goal:** Review and act on 90 percent of submissions within 21 days

| Responses to Meeting Requests: BPD Type 4 | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **3** | **11** |
| Pending | 0 | 2 |
| On-Time | 3 | 8 |
| Overdue | 0 | 1 |
| **Performance: % On-time** | **100%** | **89%** |
| Highest Possible Performance: | **100%** | **91%** |
| ***BsUFA Goal: On-time Target %*** | **90%** | **90%** |
| **Goal Met Status:** | **Goal Met** | **Currently Not Meeting, Pending** |

### Scheduling Meetings: Initial Advisory Meeting

**Goal:** Review and act on 85 percent of submissions within 90 days by FY 2016

| Scheduling Meetings: Initial Advisory Meeting | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **2** | **8** |
| Pending | 0 | 0 |
| On-Time | 1 | 6 |
| Overdue | 1 | 2 |
| **Performance: % On-time** | **50%** | **75%** |
| Highest Possible Performance: | **50%** | **75%** |
| ***BsUFA Goal: On-time Target %*** | **80%** | **85%** |
| **Goal Met Status:** | **Goal Not Met** | **Goal Not Met** |

### Scheduling Meetings: BPD Type 1

**Goal:** Review and act on 85 percent of submissions within 30 days by FY 2016

| Scheduling Meetings: BPD Type 1 | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **3** | **8** |
| Pending | 0 | 0 |
| On-Time | 2 | 6 |
| Overdue | 1 | 2 |
| **Performance: % On-time** | **67%** | **75%** |
| Highest Possible Performance: | **67%** | **75%** |
| ***BsUFA Goal: On-time Target %*** | **80%** | **85%** |
| **Goal Met Status:** | **Goal Not Met** | **Goal Not Met** |

### Scheduling Meetings: BPD Type 2

**Goal:** Review and act on 85 percent of submissions within 75 days by FY 2016

| Scheduling Meetings: BPD Type 2 | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **41** | **42** |
| Pending | 0 | 1 |
| On-Time | 20 | 30 |
| Overdue | 21 | 11 |
| **Performance: % On-time** | **49%** | **73%** |
| Highest Possible Performance: | **49%** | **74%** |
| ***BsUFA Goal: On-time Target %*** | **80%** | **85%** |
| **Goal Met Status:** | **Goal Not Met** | **Will Not Meet Goal** |

### Scheduling Meetings: BPD Type 3

**Goal:** Review and act on 85 percent of submissions within 120 days by FY 2016

| Scheduling Meetings: BPD Type 3 | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **1** | **5** |
| Pending | 0 | 1 |
| On-Time | 1 | 4 |
| Overdue | 0 | 0 |
| **Performance: % On-time** | **100%** | **100%** |
| Highest Possible Performance: | **100%** | **100%** |
| ***BsUFA Goal: On-time Target %*** | **80%** | **85%** |
| **Goal Met Status:** | **Goal Met** | **Currently Meeting, Pending** |

### Scheduling Meetings: BPD Type 4

**Goal:** Review and act on 85 percent of submissions within 60 days by FY 2016

| Scheduling Meetings: BPD Type 4 | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **3** | **10** |
| Pending | 0 | 2 |
| On-Time | 0 | 5 |
| Overdue | 3 | 3 |
| **Performance: % On-time** | **0%** | **63%** |
| Highest Possible Performance: | **0%** | **70%** |
| ***BsUFA Goal: On-time Target %*** | **80%** | **85%** |
| **Goal Met Status:** | **Goal Not Met** | **Will Not Meet Goal** |

### Provide Meeting Minutes: All Meeting Types

**Goal:** Review and act on 90 percent of submissions within 30 days

| Provide Meeting Minutes: All Meeting Types | FY 2015 | FY 2016 |
|---|---|---|
| **Total Submissions (Workload)** | **47** | **63** |
| Pending | 0 | 19 |
| On-Time | 36 | 32 |
| Overdue | 11 | 12* |
| **Performance: % On-time** | **77%** | **73%** |
| Highest Possible Performance: | **77%** | **81%** |
| ***BsUFA Goal: On-time Target %*** | **90%** | **90%** |
| **Goal Met Status:** | **Goal Not Met** | **Will Not Meet Goal** |

* Eleven submissions are overdue and one submission is pending overdue.

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# Appendix B: FY 2015-2016 Regulatory Science Progress Report Summary

FDA is charged with determining the safety, quality, and efficacy of new drugs, biologics, and medical devices[1] of increasing diversity and complexity. This responsibility shapes our scientific research portfolio, which seeks to develop the methods, tools, and standards needed to support evaluation of these products throughout their life cycle. Through guidance to industry, scientific publications, and open discussions at FDA-sponsored workshops and other forums, these methods, tools, and standards become valuable scientific resources in the public domain and furnish medical product developers with clear pathways and expectations as they generate the evidence to support their products. FDA is also responsible for the oversight of manufacturing quality throughout the lifecycle of medical products. In addition, the Agency plays a critical role in protecting the United States from emerging public health threats. These additional regulatory responsibilities are also important drivers of our research agenda. To address them, in fiscal years 2015 and 2016 we made significant progress in a number of areas:

***Refining non-clinical predictive models to support the evaluation of medical products***

FDA researchers developed and/or refined a wide variety of computational tools that now support nonclinical evaluation of medical products. These tools included sophisticated models to predict the carcinogenic effects of certain drug ingredients based on their structural attributes, computational phantoms[2] to evaluate medical imaging devices, and mechanistically informed pharmacokinetic models to help predict drug exposures in populations where clinical data is difficult to obtain. Genetic and transplantation approaches were used to create animal models that may more closely predict human response to medical products, and novel physical methods and procedures were developed to support the evaluation of bioequivalence[3] of generic versions of locally acting drugs, like those acting in the skin or airways.

***Improving clinical evaluation***

To support clinical evaluation of medical products, our statisticians helped design master protocols to efficiently evaluate therapies for treating defined subsets of cancer patients. Through a carefully designed pathway to foster biomarker development and adoption,[4] we have qualified new biomarkers to guide treatment decisions and to predict disease progression. A long-term research effort to improve prediction of cardiovascular risks contributed to the

[1] These products include generic drugs and, increasingly, combination products.
[2] Computational phantoms are mathematical representations of the human body that can be used to predict the effects of medical devices, such as exposure to radiation.
[3] Bioequivalence is the absence of a significant difference in the rate and extent to which the active ingredient or active moeity in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study. 21 CFR 314.3(b). One of the requirements for approval of a generic drug is that the generic drug must be bioequivalent to the innovator drug.
[4] The Biomarker Qualification Program.

recommendation by the International Conference on Harmonization[5] that the costly "thorough QT" clinical study (used to evaluate most drug candidates) could be replaced with electrocardiogram-based measurements performed during early-phase clinical studies.

***Ensuring product quality***

Our medical product centers continued to address scientific issues related to new technologies critical for product manufacturing, characterization of complex products, quality standards, post-approval monitoring of product quality, and understanding the complex interactions of regulated products with biological systems. We collaborated with the Biomedical Advanced Research and Development Authority to leverage continuous manufacturing to minimize domestic vulnerability to chemical, biologic, and radiologic threats, and we spearheaded creation of a 3-D printing facility to understand factors contributing to the quality and performance of implantable medical devices, drugs, and combination products made with this new technology. We developed automated approaches for predicting critical properties of human stem cell preparations, such as their ability to contribute to bone growth.

***Advancing capabilities for the post-marketing surveillance of medical products***

Exceeding our commitments to develop a national electronic system for active medical product surveillance, we expanded the Sentinel[6] system to include data from Medicare patients, and we developed new systems and tools for safety signal detection and interpretation. We worked with diverse stakeholders in the medical device ecosystem to further the development of a National Evaluation System for Health Technology (NEST) that will increase access to, and use of, real-world evidence to support regulatory decisions.

***Guidance to industry and promoting scientific collaboration***

We shared our research with the medical product industry by publishing guidance documents[7] on a number of scientific topics—for example, how to test for Zika virus in blood and biologic products, how to formulate and validate reprocessing instructions for reusable medical devices, and how to evaluate abuse-deterrent properties of opioids. Our research contributed to the development of consensus standards, providing medical product developers with clearer pathways to developing evidence for product approval. We sponsored public workshops to foster scientific exchanges[8] with stakeholders representing industry, government, the academic community, and the public, and conducted or participated in numerous training activities, professional and scientific meetings, and workshops to help our staff integrate new scientific knowledge into review and regulatory practice. We expanded the number of our public-private partnerships to advance drug development—for example, by inaugurating the International Neonatal Consortium, whose purpose is to forge a predictable regulatory path for evaluating therapies for neonates.

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[5] The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) was established to allow FDA and its counterparts in the European Union and Japan to achieve greater harmonization in the regulation of medical products.

[6] Launched as part of FDA's implementation of the Food and Drug Administration Amendments Act of 2007 (FDAAA), Sentinel is the FDA's national electronic system for monitoring of the safety of FDA-regulated medical products.

[7] www.fda.gov/RegulatoryInformation/Guidances/default.htm

[8] www.fda.gov/newsevents/meetingsconferencesworkshops/default.htm

***Improving our readiness to respond to health crises***

The medical product centers supported the regulatory public health response to the threats of Ebola virus and Zika virus through development of tools, reference materials, and publication of science-based guidance to support the rapid development of new medical products to diagnose, treat, or prevent diseases caused by these pathogens. Research efforts on other threats, such as pandemic influenza virus, continued to advance.

***Enhancing scientific infrastructure and coordination***

In the past 2 years, we enhanced information technology tools that support scientific review of regulatory applications. Following the success of the award-winning JumpStart service that allows reviewers to organize, manage, and verify the quality of the clinical data in product applications, FDA initiated Kickstart, a service that delivers individual training and user-driven support and analysis for non-clinical data. To make possible the secure deposition, retrieval, and analysis of the vast next-generation sequencing data that will support personalized medicine, we continued to enhance our high-performance scientific computing environments, enabling storage of regulatory data. We extended our laboratory capabilities and facilities for mission-critical areas, including advanced manufacturing, analytical methodology, and emerging infectious diseases.

Through organizational and programmatic changes, we have enhanced our ability to identify regulatory science issues and provide critical information for decision making. Within the Center for Drug Evaluation and Research, we created the Office of Pharmaceutical Quality to better align product quality research with review and inspection. Our Center for Biologics Evaluation and Research established a regulatory science council to oversee research activities and revamped its peer review process. The Center for Devices and Radiologic Health (CDRH) piloted a Regulatory Science Research Program Review to facilitate a feedback loop between CDRH reviewers and bench scientists. New programs to enhance scientific interactions with stakeholders, such as the Critical Path Information meetings, saw a surge of interest from stakeholders.

The medical product centers also worked collaboratively to bring new efficiencies to research efforts by creating a unified program for animal research on the White Oak campus. A new shared resources program provided for multi-center funding and governance of large shared equipment and computing resources, [9] and our Challenge Grant programs continued to support innovative projects to advance regulatory science.

A full report, "Regulatory Science Progress Report for FY 2015 and FY 2016," was completed in fulfillment of requirements under FDASIA Section 1124 and summarizes how FDA has advanced regulatory science to support medical product development in this time frame. The full

[9] One of the first shared resources under this initiative was a 3-D printing facility, jointly funded and managed by the medical product centers, which will allow researchers to better understand the application of this technology to new products and to more effectively develop standards and guidance to facilitate product development.

report is available on the FDA website at: www.fda.gov/RegulatoryInformation/Legislation/SignificantAmendmentstotheFDCAct/FDASIA/ucm356316.htm.

# Appendix C: Definitions of Key Terms

A. The phrase *review and act on* means the issuance of a complete action letter after the complete review of a filed complete application. The action letter, if it is not an approval, will set forth in detail the specific deficiencies and, where appropriate, the actions necessary to place the application in condition for approval.

B. Goal Date Extensions for Major Amendments

   1. A major amendment to an original application, supplement with clinical data, or resubmission of any of these applications, submitted at any time during the review cycle, may extend the goal date by 3 months.
   2. A major amendment may include, for example, a major new clinical safety/efficacy study report; major re-analysis of previously submitted study(ies); submission of a risk evaluation and mitigation strategy (REMS) with elements to assure safe use (ETASU) not included in the original application; or a significant amendment to a previously submitted REMS with ETASU. Generally, changes to REMS that do not include ETASU and minor changes to REMS with ETASU will not be considered major amendments.
   3. A major amendment to a manufacturing supplement submitted at any time during the review cycle may extend the goal date by 2 months.
   4. Only one extension can be given per review cycle.
   5. Consistent with the underlying principles articulated in the good review management principles guidance[1], FDA's decision to extend the review clock should, except in rare circumstances, be limited to occasions where review of the new information could address outstanding deficiencies in the application and lead to approval in the current review cycle.

C. A resubmitted original application is a complete response to an action letter addressing all identified deficiencies.

D. A Biosimilar Initial Advisory Meeting is an initial assessment limited to a general discussion regarding whether licensure under section 351(k) of the PHS Act may be feasible for a particular product, and, if so, general advice on the expected content of the development program. Such term does not include any meeting that involves substantive review of summary data or full study reports.

E. A BPD Type 1 Meeting is a meeting which is necessary for an otherwise stalled drug development program to proceed (e.g., meeting to discuss clinical holds, dispute resolution meeting), a special protocol assessment meeting, or a meeting to address an important safety issue.

F. A BPD Type 2 Meeting is a meeting to discuss a specific issue (e.g., proposed study design or endpoints) or questions where FDA will provide targeted advice regarding an ongoing biosimilar biological product development program. Such term includes substantive review of summary data, but does not include review of full study reports.

G. A BPD Type 3 Meeting is an in depth data review and advice meeting regarding an ongoing biosimilar biological product development program. Such term includes substantive review of full study reports, FDA advice regarding the similarity between the

[1] http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm079748.pdf

proposed biosimilar biological product and the reference product, and FDA advice regarding additional studies, including design and analysis.

H. A BPD Type 4 Meeting is a meeting to discuss the format and content of a biosimilar biological product application or supplement submitted under section 351(k) of the PHS Act.

Additional terms related to BsUFA are defined in the BsUFA statutory language: www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/UCM287749.pdf


**Department of Health and Human Services**
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