Review of Biosimilar Biologic Product Applications

Study of Workload Volume and Full Costs

Interim Results

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EXECUTIVE SUMMARY

Background

The Biologics Price Competition and Innovation Act of 2009 (BCPI Act)[1] amended the Public Health Service (PHS) Act and other statutes to create an abbreviated approval pathway for biological products that can be demonstrated to be "biosimilar" to or "interchangeable" with currently approved biological products. The BPCI Act also directed the Food and Drug Administration (FDA) to develop recommendations for a user fee program for the review of biosimilar and interchangeable products for fiscal years 2013 through 2017. Following consultation with stakeholders and holding a series of public meetings, FDA developed recommendations for a user fee program and submitted those recommendations to Congress on January 13, 2012. Congress enacted the Biosimilar User Fee Act (BsUFA) on July 9, 2012.[2] Section 7441(d) of the Food, Drug, and Cosmetic Act (FD&C Act), as amended by BsUFA, instructed FDA to contract with an independent consulting firm to develop an estimate of the workload volume and full costs associated with the process for the review of biosimilar biological product applications (hereafter referred to as biosimilar applications); Eastern Research Group, Inc. (ERG) of Lexington, MA was selected by FDA to develop these estimates. This Interim Report contains estimates from the beginning of Fiscal Year 2013 (FY13) through March 31, 2015, covering the first 2.5 fiscal years of FDA's biosimilars review program. FDA must also publish a Final Report that expands on and updates this Interim Report by September of 2016.

ERG's estimates of the workload cost under this project focus on the workload and cost associated with activities that FDA is allowed to expend fee-related revenue on under BsUFA. Appendix D of the FY13 BsUFA Financial Report[3] provides details on the set of allowable activities and costs that can be covered by BsUFA fees. The activities include:[4]

- *The activities necessary for the review of submissions in connection with biosimilar biological product development, biosimilar biological product applications, and supplements.*
- *Actions related to submissions in connection with biosimilar biological product development, the issuance of action letters which approve biosimilar biological product applications or which set forth in detail the specific deficiencies in such applications, and where appropriate, the actions necessary to place such applications in condition for approval.*
- *The inspection of biosimilar biological product establishments and other facilities undertaken as part of FDA's review of pending biosimilar biological product applications and supplements.*

[1] The BCPI Act was contained as a subtitle within the Patient Protection and Affordable Care Act (Affordable Care Act or ACA), which was signed into law on March 23, 2010 by President Obama.

[2] *http://www.gpo.gov/fdsys/pkg/BILLS-112s3187enr/pdf/BILLS-112s3187enr.pdf*.

[3] *http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/BsUFA/UCM395875.pdf*.

[4] The following list was taken directly from the FY13 BsUFA Financial Report; see footnote 3.

- *Activities necessary for the release of lots of biosimilar biological products under section 351(k) of the Public Health Service Act.*
- *Monitoring of research conducted in connection with the review of biosimilar biological product applications.*
- *Postmarket safety activities with respect to biologics approved under biosimilar biological product applications or supplements, including the following activities:*
    - *Collecting, developing, and reviewing safety information on biosimilar biological products, including adverse-event reports.*
    - *Developing and using improved adverse-event data-collection systems, including information technology systems.*
    - *Developing and using improved analytical tools to assess potential safety problems, including access to external data bases.*
    - *Implementing and enforcing section 505(o) of the FD&C Act (relating to post-approval studies and clinical trials and labeling changes) and section 505(p) of the FD&C Act (relating to risk evaluation and mitigation strategies).*
    - *Carrying out section 505(k)(5) of the FD&C Act (relating to adverse-event reports and postmarket safety activities).*

This is a broad set of activities and ERG collected data on activities that can be categorized under these requirements.

ERG was originally contracted to estimate the volume and full cost associated with FDA review of biosimilar applications through the end of FY14. FDA expanded ERG's scope to add the first half of FY15. The expansion in scope was deemed necessary because FDA received only two Biologic Licensing Applications (BLAs) submitted under 351(k) of the Public Health Service Act (hereafter, referred to as "351(k) BLAs") for proposed biosimilars by the end of FY14, and only one of these 351(k) BLAs was at its mid-way point at that time.[5] Furthermore, FDA received an additional three 351(k) BLAs in the first quarter of FY15, and FDA was scheduled to take action on the first 351(k) BLA in March of 2015 (approved on March 6, 2015). Based on the increased level of work at FDA and the ability to include the costs from receipt to approval associated with one 351(k) BLA, FDA and ERG agreed to extend ERG's work into the spring of 2015 to allow ERG to better capture the workload associated with reviewing 351(k) BLAs.

Estimates Included in Current Document

ERG's estimates cover the first 2.5 fiscal years of the FDA biosimilars review program, from the beginning of FY13 through the second quarter of FY15 (March 31, 2015). This report focuses primarily on work performed by FDA's Center for Drug Evaluation and Research (CDER). Nevertheless, the vast majority of the biosimilars work performed by FDA through March 31, 2015 has been performed by CDER. ERG has included FDA-provided estimates of biosimilars-related work performed by the Office of Regulatory Affairs (ORA), the FDA Office of the Commissioner, and the Center for Biologics Evaluation

[5] The second 351(k) BLA was received in September of 2014.

and Research (CBER). The Final Report on workload volume and cost (to be published in September of 2016) will expand the time frame for the estimates and fill in gaps identified in this report, including providing further details on costs incurred by ORA, FDA Office of the Commissioner, and CBER.

This document includes full-time equivalent (FTE) estimates for the following cost components:

- Investigational New Drug (IND) and pre-IND work including biosimilar product development (BPD) meetings – This includes the work associated with IND reviews, lifecycle costs for INDs, and participation in (preparation, attendance, and follow-up) BPD meetings.
- 351(k) BLA reviews – ERG's estimates cover 351(k) BLA review activities through March 31, 2015 for the first five 351(k) BLAs under the biosimilars review program. As of March 31, 2015, only one of the five 351(k) BLA had been approved and the other four were still within the review process.
- Regular biosimilar meetings within CDER – CDER holds a number of regular meetings to discuss specific applications and submissions and also to deal with policy issues.
- Policy-related work – FDA's work to interpret the BPCI Act, to develop policies related to the review and approval of biosimilar and interchangeable products, and to develop Guidance documents.
- Science and research – Science and research work at FDA related to biosimilars.
- Outreach – FDA's work on developing materials and conducting education and outreach related to biosimilars. This includes general outreach activities, but also the time and expense associated with biosimilar-related focus group testing and the time and expense associated with developing a continuing education course.
- FDA Office of the Chief Counsel (OCC) legal review and consultation – Legal work performed by OCC related to biosimilars. OCC is within the FDA Office of the Commissioner and FDA provided ERG with estimates to use for the Office of the Commissioner. Thus, we provide our OCC-specific estimates for informational purposes, but do not include them in our total since we have a separate estimate from FDA that encompasses the OCC numbers.
- CDER offices not otherwise covered by ERG's estimates – FDA provided ERG with estimates of the FTEs that can be allocated to the CDER offices for each fiscal year, including Office of the Center Director (OCD), Office of Executive Programs (OEP), Office of Management (OM), Office of Communications (OCOMM), and Office of Strategic Programs (OSP).
- Center for Biologics Evaluation and Research (CBER), FDA Office of the Commissioner, and Office of Regulatory Affairs (ORA) – ERG was provided with FTE estimates for CBER and ORA for FY13 and FY14 and a share of costs that was used to estimate FDA Office of the Commissioner work on biosimilars. It should be noted, however, that FDA's estimates indicate that ORA has performed no biosimilars work (i.e., zero FTEs) through the end of FY'14.

In our summary estimates we have also included data on operating and other indirect costs allocated by FDA to the biosimilars program.

Overall Approach and Data Collected Efforts

ERG collected data from multiple sources under this project.

- In the fall of 2014, ERG interviewed 43 individuals on a variety of biosimilar program-related subjects. These interviews covered IND and BLA review workload, including meetings, policy work, preparation for post-market activities, and outreach. Interviews that covered the IND and BLA review process involved refinement of an initial process map that ERG developed.
- In the spring of 2015, ERG interviewed 61 individuals,[6] 55 of whom were interviewed about their role in reviewing the five 351(k) BLAs received as of March 31, 2015. The interviews related to the five 351(k) BLAs provided ERG with estimates of the time it took specific individuals to perform their review functions for each BLA.
- ERG implemented a survey of individuals who were involved in the review of the five 351(k) BLAs who were not interviewed in person. A total of 88 surveys requests were sent out across the five 351(k) BLAs.[7] ERG received 46 surveys from the 88 requests (a 52 percent response rate).[8]
- In some cases, ERG sent email requests to FDA staff asking for time spent on certain biosimilar-related activities (e.g., developing a continuing education course). ERG limited these requests to areas where only specific information was being asked (e.g., time spent on a well-defined task/activity) and the question being asked could be answered more efficiently via email rather than in an interview setting.
- ERG was provided with CDER time reporting data for staff who had performed biosimilar-related work. ERG developed a method to use those data to develop quarterly-level projections of biosimilar-related hours for specific types of work (IND, pre-IND, and BPD meetings; policy-related work; and science and research) and 95 percent confidence intervals around those projections.
- ERG was provided with the 2013 and 2014 FDA BsUFA financial reports and the associated process cost spreadsheets. ERG was also provided with the 2013 and 2014 BsUFA performance reports.
- ERG was provided with volume numbers for BPD meetings, IND and pre-IND submissions, meeting requests, and other aspects that FDA tracks as program "volume" for biosimilars work.

[6] Some of the same individuals were interviews in both the fall of 2014 and spring of 2015.

[7] Some individuals received more than one survey request because they had worked on more than one 351(k) BLA; the 88 survey requests represented 74 individuals.

[8] ERG did not make an attempt to estimate the time of those who did not respond.

Limitations

The estimates that ERG developed have a number of limitations that should be kept in mind when reviewing the information in this report. These include:

- Interviewee recall – ERG has built a number of estimates from information collected through interviews with FDA staff. In these interviews we have asked respondents to recall the time spent on certain activities. Accurate recall of the time spent on certain activities is most likely an issue in the interviews we conducted, especially for work that was performed a year or more before the interview took place. For the most part, however, ERG did not ask interviewees to provide the time spent on work a year or more in the past. Rather, we asked respondents to provide an estimate of the "average" or "usual" time spent on an activity. Nevertheless, if the interviewee had not performed that work in a long time, the interviewee would have to recall from events in the past. The bulk of our interviews, however, were related to the 351(k) BLA reviews and, at most, respondents were recalling information from 10-12 months prior.[9]
- Average unit hours – ERG's estimates for IND and pre-IND work (including BPD meetings) are based on interviews in which we asked for the "average" or "usual" time it took to perform certain activities. From that information, we developed an estimate of the "average unit hours" for aspects of INDs, pre-IND work, and BPD meetings (e.g., average time the different types of BPD meetings). These average unit hours are then applied to the volume of activities in *each fiscal year* to develop an estimate of labor hours for the different aspects of IND and pre-IND work and BPD meetings.
- Limited response to survey – As noted above, ERG implemented a survey of FDA staff working on 351(k) BLA reviews who were not interviewed in person; 52 percent of the surveys were returned. Those who did not return the survey performed work on the 351(k) reviews; thus, our estimates do not include data from those individuals and ERG did not make an attempt to estimate their time.
- Misclassification of hours in time reporting data – Time reporting data are used in several areas of this report and most likely contain some misclassification of labor hours. Specifically, some staff may have inadvertently classified their labor hours as being under another program area (e.g., Prescription Drug User Fee Act (PDUFA) instead of a biosimilar-related category) or in an incorrect category (e.g., as being for 351(k) BLA review rather than being for pre-IND or IND review).
- Time reporting data represent a sample – The time reporting data are a sample of work performed based on a two-week period each quarter. This implies that any data from the time reporting system are subject to sampling error. ERG has attempted to account for that sampling error by calculating 95 percent confidence intervals. Additionally, the data are collected during two consecutive weeks in a quarter which may also introduce some error. For example, if some

[9] The first 351(k) BLA was received in May of 2014 and ERG performed the interviews for the 351(k) BLA reviews in late March through May of 2015.

key staff on biosimilars work are either on leave or performing other types of work during those two weeks, their time will be undercounted.

- Remaining gaps – As will be discussed in the section to follow, there are still some remaining gaps.

Remaining Gaps

The amount of biosimilars work being conducted at FDA is broad. ERG has been able to compile data on the primary areas where FDA has performed biosimilars program work, namely in IND and pre-IND reviews/lifecycle tasks (including BPD meetings), 351(k) BLA reviews (since mid FY14), policy-related work, and science and research. There are, however, a number of known gaps in our estimates:

- CDER clinical site inspections performed during 351(k) BLA reviews – ERG has compiled data on facility inspections conducted by CDER during 351(k) BLA reviews, but we have less information on clinical site inspections during those reviews. We did, however, ask for clinical site inspection data through the survey of review team staff and we specifically followed up with clinical inspection staff to obtain responses to the survey. For the most part, the FDA clinical inspection staff appeared to have provided data. Nevertheless, our expectation is that information on time spent for clinical inspections during 351(k) BLA review is still lacking. This is an important gap because clinical site inspections can be time-consuming, especially if the inspection occurs outside the United States. This gap will be addressed in the Final Report to be published in September 2016.
- Senior Management in 351(k) BLA Reviews – The lists obtained by ERG of 351(k) BLA review teams did not include senior managers in some disciplines. Most likely these senior staff performed some review functions. Time for these staff to perform review functions will be included in the Final Report.
- Postmarket-related work – At the time of this report, FDA has conducted little postmarket work. ERG has not included any time for postmarket work, which will be addressed in the Final Report.
- Independent estimates developed by ERG of the time spent by CBER, FDA Office of the Commissioner, and ORA – As mentioned before, this report focuses on work performed by CDER and we have included FDA-provided estimates of biosimilar program work for CBER, FDA Office of the Commissioner, and ORA. The Final Report will include estimates developed by ERG for these offices.
- Increased workload for Office of Chief Counsel (OCC) since the start of FY15 – ERG obtained data for OCC prior to the start of FY15. However, we understand that the increase in the number of 351(k) BLAs since the start of FY15 has led to an increased workload for OCC. This increased workload will be reflected in the Final Report.

Summary of Estimates and Comparison to FDA Financial Reporting Data

This section summarizes ERG's estimates for biosimilars review program workload at FDA from FY13 to second quarter of FY15 (the first 2.5 fiscal years of the program). The details of our approach to developing the estimates for each category appear in the main body of the report.

Table ES-1 provides a summary of the volume of biosimilars-related work at FDA between the start of FY13 and March 31, 2015. As of March 31, 2015, FDA has received a total of 52 INDs and pre-INDs, participated in 102 BPD meetings of all types (BIA meetings and the Type 1 – 4 BPD meetings), and received 5 351(k) BLAs for biosimilar products.

Table ES-1 - Volume of Biosimilar Program Submissions and Applications

Category	FY13	FY14	FY15 (first 2 quarters)	Total
Number of sponsors in the program (cumulative totals)	33	48	52	52
Biosimilar Application Review				
Original Biosimilar Product Applications	0	2	3	5
Resubmitted Original Biosimilar Product Applications	0	0	0	0
Original Supplements with Clinical Data	0	0	0	0
Resubmitted Supplements with Clinical Data	0	0	0	0
Manufacturing Supplements	0	0	0	0
Procedural Notifications				
Notification of Issues Identified during Review	0	2	3	5
Notification of Planned Review Timeline	0	2	3	5
Review of Proprietary Biosimilar Product Names (during BPD Phase)	3	3	3	9
Review of Proprietary Biosimilar Product Names (with Application)	0	1	4	5
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	4
Special Protocol Assessments	0	2	1	3
Meeting Requests				
Biosimilar Initial Advisory (BIA)	4	11	2	17
BPD Type 1	0	1	2	3
BPD Type 2	21	30	21	72
BPD Type 3	6	9	1	16
BPD Type 4	1	3	1	5
Scheduled Meetings				
Biosimilar Initial Advisory (BIA)	3	9	2	14
BPD Type 1	0	1	2	3
BPD Type 2	20	25	19	64
BPD Type 3	6	9	1	16
BPD Type 4	1	3	1	5
Provided Meeting Minutes (all meeting types)	29	42	17	88

Table ES-2 summarizes ERG's estimates of the FTEs spent on biosimilars-related work and Figure ES-1 provides a pie chart for the total FTEs by category over the first 2.5 fiscal years of the biosimilars review program. The data in Table ES-2 includes estimates that ERG developed in the course of this project plus FTEs values for other offices provided by FDA. ERG estimates that the biosimilars review program required 210.8 FTEs over the first 2.5 fiscal years of the program. Additionally, 34 percent of that number has been incurred in the first two months of FY15 alone. The largest category of work for FDA has been in performing IND and pre-IND work, including BPD meetings (55.8 FTEs). Policy work (23.7 FTEs) and then science and research work (21.0 FTEs) were the second and third largest categories of work.[10] Although 351(k) BLA reviews accounted for only 12.8 FTEs (7.4 percent) over the first 2.5 fiscal years, FDA has been performing 351(k) BLA reviews only since the middle of FY14. In FY15, 351(k) BLA review work was the largest single category of biosimilars work at FDA.

Table ES-2 - Summary of ERG Estimated Hours and FTEs by Cost Category, by Fiscal Year

Category	FY13	FY14	FY15 (first 2 quarters only)	Totals
FTEs Estimated by ERG for Biosimilars-Related Work				
IND, pre-IND, and BPD Meetings	21.73	23.28	10.79	55.80
351(k) BLA Review	0.00	0.95	11.79	12.75
Regular Biosimilars-Related Meetings	3.56	2.90	2.15	8.62
Policy	8.96	8.42	6.31	23.69
Science and Research	9.42	7.44	4.13	21.00
Outreach	0.00	0.00	1.29	1.29
CDER offices not covered by ERG estimates above (provided by FDA)	10.95	11.02	21.40	43.37
FDA Office of Commissioner [a]	12.98	13.43	11.41	37.82
ORA (provided by FDA)	0.00	0.00	-	0.00
CBER (provided by FDA)	3.89	1.33	-	5.22
Total FTEs	**70.99**	**68.90**	**70.93**	**210.83**

[a] FTEs for FY13 and FY14 for the FDA Office of the Commissioner were estimated based on the share of total FDA salary that the Office of the Commissioner represents. These percentages were 21.34 percent for FY13 and 21.18 percent in FY14. ERG used the FY14 percentage for FY15 since an estimate of the percentage for FY15 is not yet available. These percentages were then applied to the sum of all CDER, CBER, and ORA FTEs in this table.

[10] The categories in the table "CDER offices not covered by ERG estimates" and "FDA Office of the Commissioner" encompass a variety of different types of work.

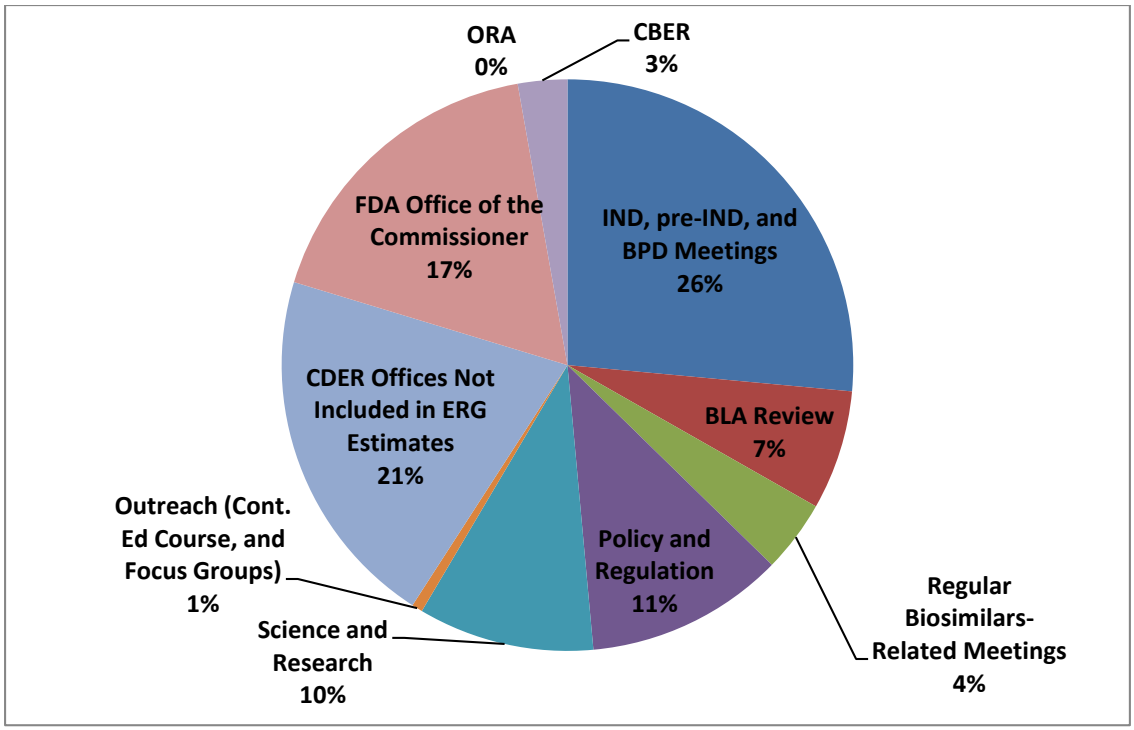

Figure ES-1 – Breakdown of FTEs by Category

Table ES-3 estimates the total cost associated with biosimilars work by first converting FTEs to costs (for salary and benefits),[11] then adding operating costs and costs for FDA centrally managed accounts. For FY13 and FY14 we took values from the BsUFA process cost worksheets. For FY15, we generated a projected amount for each category based on growth in the biosimilar-related hours between FY13/FY14 and FY15; the approach is described in a note to Table ES-3. ERG estimates that FDA spent $23.6 million in FY13, $21.4 million in FY14, and $20.9 million in the first two quarters of FY15. In total, ERG estimates that FDA has spent a total of $65.9 million on biosimilars-related work over the first 2.5 fiscal years of the program.

[11] This is described in Section 2.3, Estimating Labor Costs.

Table ES-3 - Summary of ERG Estimates: FTEs, Labor Costs, and Indirect Costs, by Fiscal Year

Category	FY13	FY14	FY15 (first 2 quarters only)	Total
Total Biosimilars FTEs	70.99	68.90	70.93	**210.83**
Labor Costs (salary and benefits) ($1,000s)	$11,105.3	$10,998.1	$11,488.7	**$33,592.2**
Operating Costs ($1,000s)	$7,663.9	$6,216.7	$5,734.5 [a]	**$19,615.1**
Centrally Managed Accounts Costs ($1,000s)				
FDA Central	$1,861.5	$1,560.7	$1,413.8 [a]	**$4,836.0**
GSA Rent	$964.3	$867.3	$756.7 [a]	**$2,588.2**
Other Rent Related	$403.6	$628.8	$426.5 [a]	**$1,458.9**
White Oak Relocation	$697.5	$456.3	$476.7 [a]	**$1,630.4**
HR	$166.4	$116.7	$117.0 [a]	**$400.1**
Shared Services	$699.0	$544.1	$513.6 [a]	**$1,756.7**
Total Costs ($1,000s)	**$23,561.5**	**$21,388.7**	**$20,927.5**	**$65,877.6**

[a] These are projected values. ERG estimated these values by applying a projected increase to the average of the FY13 and FY14 amounts. The projected increase was calculated by using the time reporting data for all biosimilars-related hours. ERG totaled the hours logged to biosimilars-related tasks in FY13 and FY14 and averaged the two amounts. We then totaled the amount of hours logged to biosimilars-related tasks in the first two quarters of FY15 and doubled that amount to get an FY15 annual value. We then divided the FY15 annual value by the average of the FY13 and FY14 amounts. This resulted in a projected mark-up factor (projected increase) of 1.653, which was applied to the average of the FY13 and FY14 costs in this table and divided by two (reflecting only half a fiscal year). For example, the average of the FY13 and FY14 operating costs multiplied by 1.653 and then divided by two equals the estimated FY15 operating cost value.

Table ES-4 compares ERG's estimates to the values reported by FDA in its annual BsUFA financial reporting.[12] We compared our estimates to FDA financial reporting values in three ways:

- ERG totals to FDA totals.
- ERG CDER-only totals to FDA CDER-only values – This comparison is done because much of our data centers on CDER sources (time reporting and also interviewees).
- ERG labor-related estimates to FDA labor-related values – This comparison is done because the ERG values share the same non-labor values (operating costs, FDA centrally managed accounts, overhead) as the FDA financial reports.

ERG's total cost estimates represent 84 to 91 percent of the values that are reported by FDA in its BsUFA financial reporting. The labor costs represent 83 to 98 percent of the FDA-reported values. ERG's FTE estimates are between 72 and 88 percent of the FDA reported FTEs. ERG's understanding is that the FDA estimate of FTEs in its financial report is calculated by multiplying the number of total FTEs for each CDER office by a percentage reflecting biosimilars-related work for that office. ERG's estimates, on the

[12] *http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/BsUFA/default.htm*.

other hand, are built from projections based on the time reporting data and interviews with FDA staff on time spent performing biosimilars-related work. As noted, there are some limitations related to ERG's estimates. First, ERG's estimates rely on interviews and interviewees may not fully remember all work performed. Second, FDA's time reporting data is based on only a two-week sample each quarter and is thus subject to sampling error. Additionally, FDA expects that some staff may have reported time as being PDUFA-related rather than being related to biosimilars review program work. Finally, our survey of FDA staff resulted in a 52 percent response rate and those who did not respond are not included in these estimates.

Table ES-4 – Comparison of ERG Estimate for FDA Financial Reporting Estimates

Category	FTEs		Costs	
	FY13	FY14	FY13	FY14
ERG Estimates				
Totals	70	69	$23,561.5	$21,388.7
CDER Only	54	56	$21,034.2	$19,262.7
Labor Only	70	69	$11,019.3	$11,054.0
FDA Financial Reporting				
Totals	98	78	$28,040.5	$23,391.6
CDER Only	87	70	$24,759.3	$21,087.7
Labor Only	98	78	$13,400.5	$11,187.4
ERG Value Relative to FDA Value				
FDA Total	72%	88%	84%	91%
FDA CDER Only	63%	79%	85%	91%
Labor Only	72%	88%	83%	98%

1. INTRODUCTION

The Biosimilar User Fee Act (BsUFA) was created as part of the Affordable Care Act (ACA) signed into law in 2010. The ACA contains a subtitle called the Biologics Price Competition and Innovation Act of 2009 (BPCI Act) that amends the Public Health Service (PHS) Act and other statutes to create an abbreviated approval pathway for biosimilar and interchangeable biological products. Section 351(k) of the PHS Act, added by the BPCI Act, allows a company to submit an application for licensure of a biosimilar biological product (hereafter referred to as a "biosimilar"). The BPCI Act directed the Food and Drug Administration (FDA) to develop recommendations for a user fee program for 351(k) applications for fiscal years (FYs) 2013 through 2017. The FDA consulted with regulated industry and public stakeholders to develop recommendations for the user fee program, published the recommendations in the Federal Register, and held a public meeting to review the recommendations. The recommendations were provided to Congress on January 13, 2012, and the Biosimilar User Fee Act of 2012 (BsUFA) was enacted on July 9, 2012.

FDA did not receive any biosimilar applications or supplements in FY13 but devoted considerable resources and effort in reviewing submissions for biosimilars in development, meeting with sponsors to discuss their development programs, and developing other non-application review portions of the program (e.g., guidance documents, staff training).[13] As of March 31, 2015, 52 programs were participating in the biosimilar product development program (BPD program), and FDA had received a total of 5 Biologic Licensing Applications (BLAs) submitted under 351(k) of the PHS Act (hereafter, referred to as "351(k) BLAs") for proposed biosimilars (with one being approved in March of 2015).

This document presents the interim findings of a study of the workload volume and full cost associated with the process for the review of biosimilar applications (hereafter referred to as the "biosimilars review program"). This Interim Report contains ERG's estimate of the workload volume and full cost associated with FDA biosimilar-related work from the beginning of FY13 through March 31, 2015, covering the first 2.5 fiscal years of biosimilars review program work at FDA. FDA must also publish a Final Report that expands on and updates this Interim Report by September of 2016.

1.1 Project Purpose and Scope

The purpose of this project is to provide an independent study of the workload volume and full cost associated with the biosimilars review program as required by Section 7441(d) of the Food, Drug, and Cosmetic Act (FD&C Act), as amended by BsUFA.[14] The study, performed by Eastern Research Group, Inc. (ERG), estimates the volume of biosimilars review program work components and estimates the workload and full costs (direct and indirect) of these work components.

[13] FY 2014 Performance Report to the President and Congress for the Biosimilar User Fee Act. FDA Department of Health and Human Services.

[14] The Biosimilar User Fee Act of 2012, *http://www.gpo.gov/fdsys/pkg/BILLS-112s3187enr/pdf/BILLS-112s3187enr.pdf*

Appendix D of the FY13 BsUFA Financial Report[15] provides details on the set of activities that comprise FDA's biosimilars review program and includes:

- *The activities necessary for the review of submissions in connection with biosimilar product development, applications, and supplements.*
- *Actions related to submissions in connection with biosimilar product development, the issuance of action letters which approve biosimilar product applications or which set forth in detail the specific deficiencies in such applications, and where appropriate, the actions necessary to place such applications in condition for approval.*
- *Development of policy and guidance related to the biosimilars program.*
- *The inspection of biosimilar product establishments and other facilities undertaken as part of the Secretary's review of pending biosimilar product applications and supplements.*
- *Activities necessary for the release of lots of biosimilar products under section 351(k) of the Public Health Service Act.*
- *Monitoring of research conducted in connection with the review of biosimilar product applications.*
- *Postmarket safety activities with respect to biologics approved under biosimilar product applications or supplements.*[16]

This interim report will focus on the workload volume and costs of the biosimilars review program from FY13 through March 31, 2015.

This report focuses primarily on work performed by FDA's Center for Drug Evaluation and Research (CDER). Nevertheless, the vast majority of the biosimilars work performed by FDA through March 31, 2015 has been performed by CDER. ERG has included FDA-provided estimates of biosimilars-related work performed by Office of Regulatory Affairs (ORA), the FDA Office of the Commissioner, and the Center for Biologics Evaluation and Research (CBER). The Final Report on workload volume and cost (to be published in September of 2016) will expand the time frame for the estimates and fill in gaps identified in this report, including providing further details on costs incurred by ORA, FDA Office of Commissioner, and CBER.

ERG was originally contracted to estimate the volume and full cost associated with FDA review of biosimilar applications through the end of FY14. FDA expanded ERG's scope to add the first half of FY15. The expansion in scope was deemed necessary because FDA received only two 351(k) BLAs for proposed biosimilars by the end of FY14, with only one of these 351(k) BLAs at its mid-way point at that time.[17] Furthermore, FDA received an additional three 351(k) BLAs in the first quarter of FY15 and FDA was

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[15] *http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/FinancialReports/BsUFA/UCM395875.pdf*.

[16] At the time of this report, only one 351(k) BLA had been approved. The final report scheduled for September of 2016 will include additional details on post-market safety work.

[17] The second 351(k) BLA was received in September of 2014.

scheduled to take action on the first 351(k) BLA in March of 2015 (approved on March 6, 2015). Based on the increased level of work at FDA and the ability to include the costs from receipt to approval associated with one 351(k) BLA, FDA and ERG agreed to extend ERG's work into the spring of 2015 to allow ERG to better capture the workload associated with reviewing 351(k) BLAs. Thus, although this report is being published after the June 1, 2015 deadline, the report contains a detailed set of estimates on the workload associated with biosimilars work at FDA from the beginning of FY13 through March 31, 2015.

1.2 Scope of the Data Collection and Analysis

FDA asked ERG to develop estimates for work performed from the start of FY13 (October 1, 2012) through March 31, 2015. This time frame allowed ERG to include one full 351(k) BLA review and significant portions of the other four 351(k) BLAs received by FDA as of March 31, 2015.

This report provides estimates of the labor hours, full-time equivalents (FTEs), and costs incurred by FDA for biosimilars review program-related activities. Included in this report are estimates for the following activity areas:

- Investigational New Drug (IND) and pre-IND work and BPD meetings
- 351(k) BLA review
- Regular biosimilars-related meetings held by CDER
- Policy-related work
- Science and research work
- Outreach work
- OCC legal review and consultation work
- FDA-provided estimates for CDER offices not included in ERG's estimates, including Office of the Center Director (OCD) , Office of Executive Programs (OEP), Office of Management (OM), Office of Communications (OCOMM), and Office of Strategic Programs (OSP).
- FDA-provided estimates for CBER, FDA Office of the Commissioner, and ORA for FY13 and FY14.[18]

1.3 Limitations

The estimates that ERG developed have a number of limitations that should be kept in mind when reviewing the information in this report. These include:

- Interviewee recall – ERG has built a number of estimates from information collected through interviews with FDA staff. In these interviews we have asked respondents to recall the time spent on certain activities. Accurate recall of the time spent on certain activities is most likely an issue in the interviews we conducted, especially for work that was performed a year or more

[18] The FDA-provided estimates indicate no time was spent by ORA in FY13 or FY14.

before the interview took place. For the most part, however, ERG did not ask interviewees to provide the time spent on work a year or more in the past. Rather, we asked respondents to provide an estimate of the "average" or "usual" time spent on an activity. Nevertheless, if the interviewee had not performed that work in a long time, the interviewee would have to recall from events in the past. The bulk of our interviews, however, were related to the 351(k) BLA reviews and, at most, respondents were recalling information from 10-12 months prior.[19]

- Average unit hours – ERG's estimates for IND and pre-IND work (including BPD meetings) are based on interviews in which we asked for the "average" or "usual" time it took to perform certain activities. From that information, we developed an estimate of the "average unit hours" for aspects of INDs, pre-IND work, and BPD meetings (e.g., average time the different types of BPD meetings). These average unit hours are then applied to the volume of activities in *each fiscal year* to develop an estimate of labor hours for the different aspects of IND and pre-IND work and BPD meetings.
- Limited response to survey – As noted above, ERG implemented a survey of FDA staff working on 351(k) BLA reviews who were not interviewed in person; 52 percent of the surveys were returned. Those who did not return the survey performed work on the 351(k) reviews; thus, our estimates do not include data from those individuals and ERG did not make an attempt to estimate their time.
- Misclassification of hours in time reporting data – Time reporting data are used in several areas of this report and most likely contain some misclassification of labor hours. Specifically, some staff may have inadvertently classified their labor hours as being under another program area (e.g., Prescription Drug User Fee Act (PDUFA) instead of a biosimilar-related category) or in an incorrect category (e.g., as being for 351(k) BLA review rather than being for pre-IND or IND review).
- Time reporting data represent a sample – The time reporting data are a sample of work performed based on a two-week period each quarter. This implies that any data from the time reporting system are subject to sampling error. ERG has attempted to account for that sampling error by calculating 95 percent confidence intervals. Additionally, the data are collected during two consecutive weeks in a quarter which may also introduce some error. For example, if some key staff on biosimilars work are either on leave or performing other types of work during those two weeks, their time will be undercounted.
- Remaining gaps – As will be discussed in the section to follow, there are still some remaining gaps.

1.4 Remaining Gaps

The amount of biosimilars work being conducted at FDA is broad. ERG has been able to compile data on the primary areas where FDA has performed biosimilars program work, namely in IND and pre-IND

[19] The first 351(k) BLA was received in May of 2014 and ERG performed the interviews for the 351(k) BLA reviews in late March through May of 2015.

reviews/lifecycle tasks (including BPD meetings), 351(k) BLA reviews (since mid FY14), policy-related work, and science and research. There are, however, a number of known gaps in our estimates:

- CDER clinical site inspections performed during 351(k) BLA reviews – ERG has compiled data on facility inspections conducted by CDER during 351(k) BLA reviews, but we have less information on clinical site inspections during those reviews. We did, however, ask for clinical site inspection data through the survey of review team staff and we specifically followed up with clinical inspection staff to obtain responses to the survey. For the most part, the FDA clinical inspection staff appeared to have provided data. Nevertheless, our expectation is that information on time spent for clinical inspections during 351(k) BLA review is still lacking. This is an important gap because clinical site inspections can be time-consuming, especially if the inspection occurs outside the United States. This gap will be addressed in the Final Report to be published in September 2016.
- Senior Management in 351(k) BLA Reviews – The lists obtained by ERG of 351(k) BLA review teams did not include senior managers in some disciplines. Most likely these senior staff performed some review functions. Time for these staff to perform review functions will be included in the Final Report.
- Postmarket-related work – At the time of this report, FDA has conducted little postmarket work. ERG has not included any time for postmarket work, which will be addressed in the Final Report.
- Independent estimates developed by ERG of the time spent by CBER, FDA Office of the Commissioner, and ORA – As mentioned before, this report focuses on work performed by CDER and we have included FDA-provided estimates of biosimilar program work for CBER, FDA Office of the Commissioner, and ORA. The Final Report will include estimates developed by ERG for these offices.
- Increased workload for Office of Chief Counsel (OCC) since the start of FY15 – ERG obtained data for OCC prior to the start of FY15. However, we understand that the increase in the number of 351(k) BLAs since the start of FY15 has led to an increased workload for OCC. This increased workload will be reflected in the Final Report.

1.5 Volume of Biosimilar Program Applications and Submissions

Table 1 provides a summary of the volume of biosimilars-related work at FDA from the start of FY13 through March 31, 2015. As of March 31, 2015, FDA has received a total of 52 INDs and pre-INDs, participated in 102 BPD meetings of all types (BIA meetings and the Type 1 – 4 BPD meetings), and received 5 351(k) BLAs for biosimilar products.

Table 1 - Volume of Biosimilar Program Submissions and Applications

Category	FY13	FY14	FY15 (first 2 quarters only)	Total
Number of sponsors in the program (cumulative totals)	33	48	52	52
Biosimilar Application Review				
Original Biosimilar Product Applications	0	2	3	5
Resubmitted Original Biosimilar Product Applications	0	0	0	0
Original Supplements with Clinical Data	0	0	0	0
Resubmitted Supplements with Clinical Data	0	0	0	0
Manufacturing Supplements	0	0	0	0
Procedural Notifications				
Notification of Issues Identified during Review	0	2	3	5
Notification of Planned Review Timeline	0	2	3	5
Review of Proprietary Biosimilar Product Names (during BPD Phase)	3	3	3	9
Review of Proprietary Biosimilar Product Names (with Application)	0	1	4	5
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	4
Special Protocol Assessments	0	2	1	3
Meeting Requests				
Biosimilar Initial Advisory (BIA)	4	11	2	17
BPD Type 1	0	1	2	3
BPD Type 2	21	30	21	72
BPD Type 3	6	9	1	16
BPD Type 4	1	3	1	5
Scheduled Meetings				
Biosimilar Initial Advisory (BIA)	3	9	2	14
BPD Type 1	0	1	2	3
BPD Type 2	20	25	19	64
BPD Type 3	6	9	1	16
BPD Type 4	1	3	1	5
Provided Meeting Minutes (all meeting types)	29	42	17	88

1.6 Organization of the Report

The remainder of this report is organized as follows:

- Section 2 discusses the methods and data sources that ERG used to develop our estimates.
- Section 3 provides estimates for IND, pre-IND, and BPD meeting work.
- Section 4 provides estimates for 351(k) BLA reviews.
- Section 5 provides estimates for CDER's regular biosimilars meetings.

- Section 6 provides estimates for policy-related work.
- Section 7 provides estimate for science and research work.
- Section 8 provides estimates for a set of work that ERG categorized as “miscellaneous”.
- Section 9 summarizes the FTE estimates from Sections 3 through 8, converts the FTE estimates to costs (for salary and benefits), and adds costs from CDER offices not included in ERG’s estimates, CBER, FDA Office of the Commissioner, and ORA. Section 9 also compares the resulting estimates to data reported in FDA’s BsUFA financial reports.

2. APPROACH AND DATA

This section provides an overview of the data and methods that ERG used to develop estimates of workload and full costs associated with the FDA biosimilars review program. Details that are specific to the cost categories (e.g., 351(k) BLA review) are discussed within the section for each category.

2.1 Process Maps

ERG developed process maps reflecting biosimilars development work (pre-IND and IND reviews), BPD meetings, and the 351(k) BLA review process for biosimilars. The initial process maps were developed based on FDA background documents, biosimilars-related reports, and related established review programs such as PDUFA. Key resources included:

- FY13 BsUFA Financial Report.
- FY13 Performance Report to the President and Congress for the Biosimilar User Fee Act.
- Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products.
- CDER 21st Century Review Process Desk Reference Guide.

The process maps were revised iteratively based on feedback from FDA and during interviews with FDA staff that ERG performed in the fall of 2014 and spring of 2015. The primary purpose of developing these process maps was to provide interviewees with prompts to remember the time spent on different review tasks.

2.2 Data Sources and Data Processing

ERG used a number of data sources to develop the estimates summarized in this report. The two main sources of data for this report are in-person interviews conducted in the fall of 2014 and the spring of 2015 and CDER's time reporting data. ERG also performed a survey of staff not interviewed in person for the 351(k) BLA reviews and sent a limited number of email requests on specific subjects. FDA also provided ERG with a number of data items to use in our analyses.

2.2.1 In-Person Interviews

ERG performed a series of in-person interviews with FDA staff involved in biosimilars review program work at the Agency in the fall of 2014 and then again in the spring of 2015. In the fall of 2014, ERG interviewed 43 individuals on a variety of biosimilars-related subjects. These interviews covered IND and 351(k) BLA review workload, policy work, preparation for post-market activities, and outreach. Interviews that covered the IND and 351(k) BLA review process involved refinement of an initial process map ERG developed. In the spring of 2015, ERG interviewed 61 individuals,[20] 55 of whom were interviewed about their role in reviewing the 5 351(k) BLAs received as of March 31, 2015. The

[20] Some of the same individuals were interviews in both the fall of 2014 and spring of 2015.

interviews related to the 351(k) BLAs provided ERG with estimates of the time it took specific individuals to perform their review functions for each BLA.

The interviews usually involved one or more individuals to allow the interviewees to prompt one another; for example, when interviewing staff regarding 351(k) BLA reviews, ERG tried to interview both primary reviewers and their team leads at the same time. This allowed the primary reviewers to remind the team leads of the work performed or vice versa. Most interviews lasted between 30 and 60 minutes, with some taking 20 minutes or less.[21]

For both the 351(k) BLA review-related interviews and the interviews related to IND-related work and participation in BPD meetings, ERG used the process maps we developed at the outset of the project. As noted, the fall 2014 interviews assisted us in refining the map early on. The process maps break the 351(k) BLA review process, the IND review process, and BPD meetings down into discrete work areas (e.g., for 351(k) reviews; filing meeting, primary review, mid-cycle meeting). During these interviews, ERG went step by step through the process map and asked interviewees to provide estimates of the labor time they spent on each step. This step-by-step process allowed the interviewees to think through the time they spent on specific tasks to build a "bottom-up" estimate of their workload. We expect this to be a more comprehensive approach to estimating workload compared to asking for a total time. After we completed reviewing the process map with the interviewees, we asked if there was any additional work performed on the 351(k) BLA or IND/BPD activity that had not been discussed.

In many cases interviewees provided ERG with ranges for some estimates (e.g., 10-20 hours) for steps in the process. ERG dealt with the ranges in three ways:

- For ranges that were large in magnitude (e.g., 100-200 hours), ERG asked follow-up questions to discern whether the mid-point of the range was a reasonable point estimate or whether the upper or lower end of the range was more likely. This follow-on discussion worked to clarify a representative value for the time spent and to reduce the breadth of the range.
- For ranges that involved small values (e.g., 1-2 hours), ERG used the upper end-point of the range.
- For all other ranges, ERG used the mid-point value (rounded up to the nearest whole integer value).

Most ranges that were provided by interviewees fell into the third category; i.e., they were neither large in magnitude nor involved small values.

2.2.2 Survey of 351(k) BLA Review Teams

ERG used a survey approach to collect data from individuals involved in the 351(k) BLA reviews whom we did not interview in person. As noted, the interviews in the spring of 2015 focused on the review of the five 351(k) BLAs received prior to March 31, 2015. At the start of the interview process, ERG contacted the Regulatory Project Managers (RPMs) for each 305(k) BLA and requested a list of FDA staff who were involved in each. The list contained 207 names (145 distinct names; some individuals were involved in multiple 351(k) BLAs). FDA and ERG agreed that interviewing all individuals would not be

[21] Interviews that took 20 minutes or less tended to be focused on a specific activity that was easily explained/discussed or involved discussion of review time for one of the four 351(k) BLAs awaiting action as of March 31, 2015.

possible in the time frame of this project. ERG met with each RPM and asked them to identify the "key" staff on each 351(k) BLA review; ERG then scheduled interviews with these key staff (see Section 2.2.1 above).[22] Any individual who ERG did not interview was asked to take a survey to record their time. A total of five surveys were developed, one for each 351(k) BLA.

The surveys were implemented as web-based surveys and used the refined version of the process map to guide respondents through a series of tables where they could record their time. Respondents were also provided text boxes where they could record additional notes and comments. FDA staff who were involved in more than one 351(k) BLA received one survey request for each 351(k) BLA.

ERG implemented the surveys using our online account with Qualtrics, Inc. After sending out the initial request, ERG sent three reminders to staff to complete the surveys. A total of 88 surveys were sent and ERG received a total of 46 in return (52 percent response rate). ERG did not attempt to include hours for those who did not respond to the survey.

2.2.3 CDER Time Reporting Data

FDA provided ERG with CDER time reporting data for FY13 through the second quarter of FY15. CDER staff report time for two weeks each quarter. The time reporting system has CDER staff put their time into both "projects" and "tasks." The set of tasks can be used to identify which hours were associated with biosimilars review program-related work. FDA provided ERG with a list of task codes that can be considered biosimilars work. The set of task codes can be used to divide labor hours into types of work such as IND/pre-IND, 351(k) BLA review, policy-related work, etc. Based on the task codes, ERG was able to categorize labor hours reported by CDER staff into the following categories:

- IND and pre-IND review activities (including BPD meetings)
- Special Protocol Assessments (SPAs)
- Original 351(k) BLA reviews
- Supplement review activities, including industry meetings
- Post-marketing annual reports, safety activities, and surveillance
- Enforcement
- Policy and regulation
- Science and research
- Training
- Program management and administration
- Employee leave

ERG developed an approach for using these data for estimating time spent on certain activities. First, we assumed that the CDER time reporting data are a sample for all work performed in the Center. For some types of work, however, the work is too periodic to assume that the time reporting survey periods captured a representative time frame. To assess this, ERG reviewed the number of times different task

[22] During our interviews, some interviewees also added names to ERG's interview list from the original list provided by the RPMs.

codes were reported by FDA staff on a quarterly basis. ERG determined that three categories were reported at a high enough frequency each quarter to allow for extrapolation of the reported hours to the entire quarter for CDER:

- IND and pre-IND review activities (including BPD meetings)
- Policy and Regulation
- Science and Research

This decision was based on the fact that each category includes at least 100 entries per quarter for most of the quarters in our time period. The numbers of times each of these codes were reported each quarter appears in Table 2.

Table 2 – Number of CDER Time Reporting Entries by Quarter for Categories of Work Selected for Analysis

Category	FY13				FY14				FY15		Total
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	
IND and pre-IND review activities (including BPD meetings)	366	504	588	458	432	479	572	594	494	593	5,080
Policy and Regulation	159	275	283	259	201	268	377	249	371	362	2,804
Science and Research	80	130	213	145	94	73	141	158	143	108	1,285

To extrapolate to the quarter, ERG calculated the total number of hours for each category from the individual time sheet entries and multiplied by 6.5 (13 weeks per quarter divided by 2 weeks of time reporting). The resulting values reflect statistical estimates of the total number of hours in each quarter being spent on biosimilars review program-related work. An estimate of the total hours spent on work over the first 2.5 years of the program is calculated by summing over the estimates for each quarter.

Given that these estimates are derived from a sample, ERG developed 95 percent confidence intervals around each quarterly total hour estimate and around the estimate for the 2.5-year period. The upper and lower confidence limits were calculated by assuming the data reflect an exponential distribution.[23] The functional form of the exponential distribution has one shape parameter, λ, which can be approximated using the inverse of the sample mean value. A suitable approximation for the confidence interval of λ when there are more than 15 to 20 subjects is[24]

$$\lambda_{lower} = \hat{\lambda}\left(1 - \frac{1.96}{\sqrt{n}}\right)$$

$$\lambda_{upper} = \hat{\lambda}\left(1 + \frac{1.96}{\sqrt{n}}\right)$$

[23] An exponential distribution can be used to reflect the distribution of a non-negative variable where the probability density is a concave decreasing function.

[24] Guerriero, V. (2012). "Power Law Distribution: Method of Multi-scale Inferential Statistics". Journal of Modern Mathematics Frontier (JMMF) 1: 21–28.

where $\hat{\lambda}$ is the sample estimate of λ estimated as the inverse of the sample mean and *n* is the number of sample units (time sheet entries). Once we calculate both the lower and upper bounds for λ, we invert the values (to approximate upper and lower bounds on the sample mean), multiply each by *n* (to approximate the total hours), and then multiply each by 6.5 to extrapolate to the quarter. For the 2.5-year period, we follow the same process but use the total calculated for the 2.5-year period and the total number of timesheet entries over the 2.5-year period.

In summarizing our estimates in this report, we focus on the value for the 2.5-year period and not on the values for the individual quarters. For context, we provide the 95 percent confidence intervals in the text and details on the intervals in Appendix A.

2.2.4 Email Requests

In some cases, ERG sent email requests to FDA staff asking for time spent on certain biosimilars review program-related activities. ERG limited these requests to areas where only specific information was being asked for (e.g., time spent on a well-defined task/activity) and the question being asked could be answered more efficiently via email rather than in an interview setting. These requests covered:

- Developing a biosimilars continuing education course
- Developing and performing biosimilars focus group testing
- Outreach performed by the Office of Commissioner's Office of External Affairs

2.2.5 Other Data Provided to ERG

In addition to the data sources discussed above, ERG was provided with a number of other data items for use in this project:

- ERG received the 2013 and the draft 2014 FDA BsUFA financial reports and the associated process cost spreadsheets. ERG also received the 2013 and 2014 BsUFA performance reports. These reports were used in multiple ways in this report, including as a source for FTEs and costs associated with CBER, FDA Office of the Commissioner, and ORA.
- ERG received volume numbers, which were summarized in Section 1.5, Table 1.
- ERG received a summary estimate of the labor hours for CDER's Division of Advisory Committee and Consultant Management (DACCM) to organize and hold Advisory Committee meetings. However, ERG also received an FTE estimate for the CDER OEP, which encompasses DACCM; thus, ERG did not include the DACCM-specific estimates in our totals. ERG also removed DACCM staff from the list of people who would receive surveys under the project to avoid double-counting.
- Following an interview with the Office of Medical Policy (OMP), ERG received data on OMP's development of guidance documents and performing policy-related work.
- Following an interview with Division of Medication Error Prevention and Analysis (DMEPA) and Division of Risk Management (DRISK) staff, ERG received data for the time spent on Risk Evaluation and Mitigation Strategies (REMS)-related work for reviewing the five 351(k) BLAs. DMEPA and DRISK staff were also removed from the list of people receiving a survey.

- ERG received estimates of the FTEs that can be allocated to CDER offices not included in our other estimates for each fiscal year, including Office of the Center Director (OCD), OEP, OM, OCOMM, and OSP.
- ERG received operating costs and costs for FDA centrally managed accounts; these were added to the labor costs we estimated (see Section 2.3 below for discussion of calculation of labor costs).

2.3 Estimating Labor Costs

The data sources described above, for the most part, provided estimates of the labor hours associated with biosimilars review program work at FDA. To develop cost estimates associated with the labor time, ERG used an estimate of 1,600 productive labor hours (value provided by FDA) to define a full-time equivalent (FTE). ERG then converted FTEs into a cost per FTE for salary and benefits using data taken from the FY13 and (draft) FY14 BsUFA financial reports. A value for CDER in FY15 was provided by FDA for ERG to use as a place-holder value. These data appear in Table 3.

For CBER in FY13 and FY14, ERG used the CBER values for each fiscal year found in Table 3. We calculated a FY15 value by first calculating the percentage change from FY13 to FY14 in the cost per FTE value (a 3.7 percent increase) and then applying that percentage increase to the FY14 value to approximate a FY15 value.

For costs incurred by the FDA Office of the Commissioner, ERG used the percentages of total salary that the Office of the Commissioner represents to calculate values from the CDER and CBER totals. These percentages were 21.34 percent for FY13 and 21.18 percent in FY14.[25] ERG used the FY14 percentage for FY15 because an estimate of the percentage for FY15 is not yet available. These percentages were then applied to the sum of all CDER and CBER labor costs to generate an estimate of the FDA Office of the Commissioner labor costs.[26]

ERG also had to allocate some labor hours for the 351(k) BLA review between fiscal years. Specifically, FDA received the first two 351(k) BLAs in FY14 and continued to review those in FY15. ERG divided the 351(k) BLA review process into four stages: Receipt and Filing Review, Primary and Secondary Review (including mid-cycle meeting), Advisory Committee Meeting, and Finalizing the Review. For each 351(k) BLA we specified a percentage of hours for each stage that we assumed were incurred in FY15, with the remaining hours being incurred in FY14. These allocation percentages appear in Table 4.

[25] These percentages were taken from FDA biosimilars process cost woksheets.

[26] A similar process was used to estimate FTEs.

Table 3 – Calculation of Cost Per FTEs for Salary and Benefits

FY and Center	Salary and Benefits	FTEs	Salary and Benefit Cost Per FTE ($1,000s)
FY13			
CDER	$529,388,910	3,370.6	$157.1
CBER	$150,766,567	1,021.4	$147.6
Total	$680,155,477	4,391.9	$154.9
FY14			
CDER	$588,671,430	3,684.4	$159.8
CBER	$153,403,094	1,001.7	$153.1
Total	$742,074,524	4,686.1	$158.4
FY15			
CDER	NA	NA	$162.0
CBER	NA	NA	$158.9 [a]

Source: BsUFA financial reports for FY13 and FY14 and FDA-provided estimate for FY15.
[a] Estimated by calculating the percentage change from FY13 to FY14 for CBER (3.7 percent) and then applying that percentage change to the FY14 value for CBER.

Table 4 – Fiscal Year 2015 Allocation Percentages for Stages of Each 351(k) BLA

Stage	BLA 125553 - Sandoz/ filgrastim	BLA 125544 - Celltrion/ Infliximab	BLA 761026 - Apotex/ Peg-filgrastim	BLA 761027 - Apotex/ filgrastim	BLA 125545 - Hospira/ Epoetin
Receipt and Filing Review	0%	0%	100%	100%	100%
Primary and Secondary Review (including mid-cycle meeting)	70%	100%	100%	100%	100%
Advisory Committee Meeting	100%	100%	100%	100%	100%
Finalizing the Review	100%	100%	100%	100%	100%

2.4 Dealing with Overlapping Estimates

There are a number of areas where ERG's data collection activities led to collecting data on the same activity twice. For example, OMP provided ERG with an estimate of the time it spent on guidance documents and on policy work. OMP also reports in the CDER time reporting system and some, if not all, of these hours would also be captured in the time reporting data we processed. For the most part, overlaps occurred between time reporting data and other data sources; i.e., some of the hours estimates we collected from other sources might also be covered by the time reporting data. To avoid double-counting the hours in our estimates, ERG assessed each instance of potential overlap and made a decision based on our understanding of the data. We address these instances in the sections that follow.

3. Investigational New Drug (IND) Reviews and Biosimilar Product Development (BPD) Meetings

3.1 Approach and Data

Elements Included in the Workload Estimates

- *Review of IND and pre-IND submissions*
- *Preparation and participation in BPD meetings (BIA and BPD Type 1 – 4 meetings)*
- *IND lifecycle FTEs*

- During the fall of 2014, ERG interviewed staff working on biosimilar-related INDs. Data collected from those interviews were used to calculate the unit hours associated with IND/pre-IND review work and for preparation for and participation in BPD meetings.
- Volume numbers for pre-INDs, INDs, BPD meetings, and programs in the BPD program were either provided by FDA directly for this report or were taken from FDA reports.
- ERG used the time reporting data to estimate total quarterly hours for IND and pre-IND work. The method developed by ERG involves assuming the time reporting data (reported 2 weeks each quarter) are a sample of hours and then using the sample data to calculate a total for each quarter and then a total for the 2.5-year period. ERG then calculated 95 percent confidence intervals around the estimated totals for each quarter and for the 2.5-year period to provide context. This approach generated an estimate of the total hours and cost associated with IND, pre-IND, and BPD meeting work at FDA from FY13 to FY15Q2.
- ERG back-calculated "lifecycle" costs as the totals estimated from the time reporting data minus the values estimated for IND/pre-IND review and BPD meetings.

3.2 Estimated Hours and FTEs

Table 5 presents the estimated hours and FTEs associated with IND and pre-IND review work. Total hours for each fiscal year are estimated by multiplying the volume of IND and pre-INDs each year by the estimated number of hours to perform the reviews. Volume data were provided by CDER's OSP, Performance Analysis and Data Services Staff (PADSS). The number of hours to perform IND and pre-IND reviews was derived from interviews ERG performed in the fall of 2014.[27] ERG estimates that IND and pre-IND review work involved 17.2 FTEs over the first 2.5 fiscal years of the program.

[27] The unit hour estimates are the same for each FY and reflect an average for performing this type of work. There may be some learning curve-related costs associated with work performed in FY13. ERG has not made an attempt to capture any increased cost associated with work performed early in the program.

Table 5 - Estimated Hours, FTEs, and Costs Associated with IND and Pre-IND Reviews

FY	Number of IND and Pre-INDs	Unit Hours [a]	Total Hours	FTEs
2013	33	527.75	17,415.75	10.88
2014	15	527.75	7,916.25	4.95
2015 (first 2 quarters only)	4	527.75	2,111.00	1.32
Totals	**52**		**27,443.00**	**17.15**

[a] The unit hour estimates are the same for each FY and reflect an average for performing this type of work. There may be some learning curve-related costs associated with work performed in FY13. ERG has not made an attempt to capture any increased cost associated with work performed early in the program.

Table 6 provides estimates for the total hours and FTEs associated with participating in BPD meetings, including the time to prepare for, attend, and perform any follow-up related to the meetings. Total hours are estimated by multiplying the number of meetings by the labor hours associated with the Biosimilar Initial Advisory (BIA) meeting and BPD Type 1 to 4 meetings. The numbers of meetings were taken from PADSS tracking files and reflect the number of *scheduled* meetings in each fiscal year. Hours associated with each type of meeting were derived from interviews ERG conducted in the fall of 2014. ERG estimates that 25.5 FTEs were incurred by FDA to participate in BPD meetings over the first 2.5 years of the program.

Table 7 presents estimates of hours and FTEs associated with IND, pre-IND, and BPD meeting work derived from CDER's time reporting data. The estimates reflect all work in these categories, including the work covered in Table 5 and Table 6 above. The hour estimates in Table 7 reflect the hours reported in the time reporting data extrapolated to a whole quarter and the total in the table reflects the total number of hours and FTEs for the entire 2.5-year period. The method used by ERG to develop 95 percent confidence intervals for these estimates is described in Section 2.2.3. ERG estimates that CDER has used 55.8 FTEs in the first 2.5 years of FDA's biosimilars program implementation for IND, pre-IND, and BPD meeting-related work. Table A-1 in Appendix A provides the 95 percent confidence intervals for the data derived from the time reporting data. The 95 percent confidence interval around the estimated 2.5 year total of 55.8 FTEs is 52.8 FTEs to 59.1 FTEs.

Table 6 - Estimated Hours, FTEs, and Cost Associated with BPD Meetings

FY	Meeting Type	Number of Meetings	Unit Hours [a]	Total Hours	FTEs
2013	BIA	3	599.97	1,799.91	1.12
	Type 1	0	7.50	0.00	0.00
	Type 2	20	322.68	6,453.62	4.03
	Type 3	6	631.26	3,787.57	2.37
	Type 4	1	331.51	331.51	0.21
FY13 Totals				*12,372.61*	*7.73*
2014	BIA	9	599.97	5,399.72	3.37
	Type 1	1	7.50	7.50	0.00
	Type 2	25	322.68	8,067.02	5.04
	Type 3	9	631.26	5,681.36	3.55
	Type 4	3	331.51	994.53	0.62
FY14 Totals				*20,150.12*	*12.59*
2015 (first 2 quarters only)	BIA	2	599.97	1,199.94	0.75
	Type 1	2	7.50	14.99	0.01
	Type 2	19[b]	322.68	6,130.94	3.83
	Type 3	1	631.26	631.26	0.39
	Type 4	1	331.51	331.51	0.21
FY15 Totals (first 2 quarters only)				*8,308.64*	*5.19*
Totals				**40,831.37**	**25.52**

[a] The unit hour estimates for each meeting type are the same for each FY and reflect an average for performing this type of work.
[b] This includes one meeting that was classified as an "unknown" meeting type. ERG included it here because most meetings are Type 2 meetings.

Table 7 - Estimated Total Hours, FTEs, and Cost Associated with IND, Pre-IND, and BPD Meeting Activities Derived from Time Reporting Data

Quarter	Estimated Total Hours	FTEs
2013Q1	6,462.63	4.04
2013Q2	8,008.98	5.01
2013Q3	11,092.25	6.93
2013Q4	9,199.13	5.75
2014Q1	8,079.50	5.05
2014Q2	9,283.63	5.80
2014Q3	9,586.20	5.99
2014Q4	10,302.50	6.44
2015Q1	8,333.00	5.21
2015Q2	8,928.73	5.58
Totals	**89,276.53**	**55.80**

Table 8 provides a summary of the FTEs estimated in this section. ERG assumes that the difference between the totals in Table 7 and the estimates in Table 5 (IND and pre-IND review work) and Table 6 (BPD meetings) provides a reasonable estimate of all other costs associated with IND and pre-IND work (e.g., lifecycle costs). ERG estimates that non-review, non-BPD meeting lifecycle workload involved 13.1 FTEs over the first 2.5 years of the FDA biosimilars program.

Table 8 - Summary Estimates for FTEs and Cost by Type of IND-Related Activity

FY	IND Review	BPD Meetings	Other (Lifecycle Costs)	Total
FTEs				
2013	10.88	7.73	3.11	21.73
2014	4.95	12.59	5.74	23.28
2015(first 2 quarters only)	1.32	5.19	4.28	10.79
Totals	***17.15***	***25.52***	***13.13***	***55.80***

4. 351(k) Biologic Licensing Application (BLA) Review

4.1 Approach and Data

> ***Elements Included in the Workload Estimates***
> - *Time to perform reviews of the five 351(k) BLAs received prior to March 31, 2015. This includes time spent on the following stages of review:*
> - *Receipt and Filing Review*
> - *Primary and Secondary Review (including mid-cycle meeting)*
> - *Advisory Committee Meetings*
> - *Finalizing Review*

- During the fall of 2014, ERG interviewed staff who perform BLA and NDA reviews. The interviews focused on refining a process map for conducting reviews and on obtaining estimates for the time it took to perform different parts of the review process. Given the limited experience with 351(k) BLA reviews in the fall of 2014, however, ERG asked interviewees to extrapolate from similar work being performed under 351(a) BLA reviews.[28] ERG used the data from the fall interviews to (1) directly provide estimates of the time to review biosimilar BLAs for some steps in the process for individuals who had worked on biosimilar 351(k) BLAs at that time, (2) fill in gaps[29] from the interviews we conducted in the spring of 2015 (discussed below), and (3) provide a consistency check against the data we collected in spring 2015.
- ERG contacted the RPM for each 351(k) BLA and obtained a list of the FDA staff working on each. ERG then interviewed each RPM[30] to discuss the current status of each 351(k) BLA, identify issues involved in each BLA that would affect workload, and identify the FDA staff that ERG should interview to obtain information on workload.
- ERG interviewed a total of 55 staff (including the RPMs) working on the five 351(k) BLAs. Interviews were performed from March to May 2015. For each interview, ERG used a process map for 351(k) BLA review that started with the receipt of the application to final action.[31] For each step on the process map, ERG reviewed the labor time it took interviewees to perform each step.
- ERG also developed a short survey based on the interview protocol and sent the survey to all staff who were not interviewed and whose time in 351(k) BLA review was not being estimated through another source.[32] The survey presented the respondents with the stages and steps in the review process in graphical form and asked respondents the time it took to perform each

[28] A 351(a) BLA is an application for a new product.

[29] For example, one individual we interviewed in the spring of 2015 was unable to provide an estimate of the time to work on one aspect the 351(k) BLA she was involved in. Instead, she indicated it took 1.5 times the effort of a "normal" review. We used the time for her discipline to review a 351(a) NDA (obtained in the fall interviews) and multiplied by 1.5.

[30] There were 6 total RPMs for the 5 351(k) BLAs since one 351(k) BLA had a change in RPM partway through the review.

[31] Since only one 351(k) BLA had reached final action as of March 31, 2015, ERG focused only on the relevant parts of the process for each 351(k) BLA through March 31, 2015.

[32] DMEPA and DRISK agreed to provide estimates for its staff performing REMS-related work on the 351(k) BLAs.

step in the process. ERG used feedback from the 55 interviewees to refine the survey instrument and obtained feedback from OSP and the Therapeutic Biologics and Biosimilars Staff (TBBS) on the wording of items prior to sending out the survey. A total of 88 survey requests were sent and ERG received 46 survey responses.

4.2 Estimates of Hours and FTEs

Table 9 summarizes information on the five 351(k) BLAs covered under this analysis and the numbers of FDA staff identified by RPMs, interviewed in person, and surveyed under this project.

Table 9 - Summary Information for Five 351(k) BLAs Received by FDA as of March 31, 2015

351(k) BLA	Date Received	Status as of March 31, 2015	FDA Staff		
			Number of Staff Identified by RPM	Number of Staff Interviewed [a]	Number of Staff Receiving a Survey [b], [c]
BLA 125553 - Sandoz/ filgrastim	5/8/14	Approved by FDA on March 6, 2015	28	20	13 (11)
BLA 125544 - Celltrion/ Infliximab	8/8/14	Mid-cycle meeting was on 1/26/15, but review was still on-going as of 3/31/15. Some planning for Advisory Committee meeting had taken place.	37	18	14 (8)
BLA 761026 - Apotex/ Peg-filgrastim	10/16/14	Review was three weeks past the mid-cycle meeting (3/3/15)	51	16	22 (9)
BLA 761027 - Apotex/ filgrastim	12/15/14	Filing meeting had been held, but review had not reached mid-cycle meeting as of 3/31/15.	49	13	23 (11)
BLA 125545 - Hospira/ Epoetin	12/16/14	Filing meeting had been held, but review had not reached mid-cycle meeting as of 3/31/15.	42	17	16 (7)

[a] ERG interviewed a total of 55 individuals, some of whom had performed work on more than one 351(k) BLA. Thus, the total in this column does not add to 55.
[b] ERG removed a few names from the survey list. These removals included staff working for DACCM and working for DMEPA or DRISK on REMS issues (both covered under estimates from another source). ERG also removed staff who had left FDA. Thus, the number of staff who were interviewed and the number receiving a survey do not add to the total number identified by the RPMs.
[c] The number in parentheses reflects the number who replied to the survey as of June 24, 2015.

Table 10 provides a summary of the estimated labor hours and FTEs associated with reviewing the five 351(k) BLAs received as of March 31, 2015. In total, the interviewees ERG talked with provided estimates that totaled to 12.8 FTEs in reviewing the five 351(k) BLAs through March 31, 2015. The survey respondents indicated a total of 1.5 FTEs were incurred to review the 351(k) BLAs. Thus, ERG's total estimates for reviewing the five 351(k) BLAs is 14.3 FTEs. There are, however, a few caveats on this estimate:

- The interviews were conducted in March to May of 2015. This means that some interviewees were being asked to recall information on the time spent on tasks 10-12 months prior.
- The response rate for the survey we sent was 52 percent. ERG did not attempt to adjust for the missing data from those who did not respond to the survey.
- OSP and TBBS suggested we add in some senior management individuals not included in our lists from the RPMs. Time for these individuals was not included in these estimates, but will be added in the Final Report in September 2016.
- We expect that some time related to clinical inspections might still be missing from these estimates. This was discussed in greater detail in Section 1.4.
- As noted in Table 8, only one 351(k) BLA review was completed as of March 31, 2015. Thus, the data in Table 10 reflect one complete 351(k) BLA review and four partial reviews.

Table 10 - Summary of Estimated Labor Hours, FTEs, and Cost from Interviews and Survey Responses

351(k) BLA Stage	Labor Hours	FTEs
Interviews		
Receipt and Filing Review	1,635.6	1.02
Primary and Secondary Review (including mid-cycle)	16,352.5	10.22
Advisory Committee Meeting	2,282.5	1.43
Finalizing Review	124.0	0.08
Totals from Interviews	***20,394.6***	***12.75***
Survey Responses [a]		
Receipt and Filing Review	785.0	0.49
Primary and Secondary Review (including mid-cycle)	1,457.5	0.91
Advisory Committee Meeting	146.0	0.09
Finalizing Review	25.5	0.02
Totals from Survey Responses	***2,414.0***	***1.51***
Interviews and Survey Total		
Receipt and Filing Review	2,420.6	1.51
Primary and Secondary Review (including mid-cycle)	17,810.0	11.13
Advisory Committee Meeting	2,428.5	1.52
Finalizing Review	149.5	0.09
Totals	**22,808.6**	**14.26**

[a] The survey data reflect collection of 52 percent of the surveys sent out.

Table 11 re-summarizes the estimates of hours and FTEs by fiscal year.

Table 11 - Summary of 351(k) BLA Review Estimates by Fiscal Year

Fiscal Year	Hours	FTEs
FY13	NA	NA
FY14	3,937.1	2.46
FY15 (first 2 quarters only)	18,871.5	11.79
Totals	**22,808.6**	**14.26**

5. Regular Biosimilars-Related Meetings

This section provides estimates for CDER to hold regular biosimilars review program-related meetings. These meetings can involve a variety of topics, including policy-related topics and discussions that deal with specific applications or submissions. This section provides estimates for three regular meetings that relate to biosimilars within CDER:

- CDER's TBBS (a cross-functional team within CDER) holds the Biologics Review Committee (BRC) meetings on a frequent basis.
- CDER's Office of Clinical Pharmacology (OCP) holds weekly meetings.
- CDER's Office of Biotechnology Products (OBP) holds weekly meetings.

5.1 Approach and Data

- ERG interviewed (via phone) staff from OCP, OBP, and TBBS to develop estimates of the time FDA staff spend in regular meetings associated with biosimilars.
- Time spent in these meetings could potentially be covered under two separate areas of this report: (1) in the hours for IND and pre-IND work (Section 3) or in reviewing 351(k) BLAs (Section 4) because the meetings will often involve discussions related to specific applications and/or submissions or (2) in the policy-related hours under Section 6. We are including the estimates in this section as separate line items in our analysis for the following reasons:
    - *IND, pre-IND, or 351(k) BLA review.* Although some interviewees appeared to have included time for these meetings in the estimates provided during interviews, some might not have. Additionally, the magnitude of the estimates in this section seems to indicate that the interviewees did not capture this time in the estimates provided to ERG during the interviews related to IND, pre-IND, and 351(k) BLA review.
    - *Policy-related work.* ERG has assumed that attendance at and preparation for these meetings is not well captured in the time reporting data. There are a number of reasons for this. First, although attendance at these regular meetings might be captured in the time reporting data, preparation time might be missed because preparation time might fall outside of the two-week reporting periods, or vice versa. Second, we are not certain that staff would categorize their time as "policy and regulation" time in the CDER time reporting for these meetings; regular meetings are often categorized under the "Program Administration and Management" category in the time reporting data.
    - *Overall*. While including these hours in the totals might, in certain instances, result in some double-counting with the time reporting estimates, we expect the amount of double counting in this case would be minimal. On the other hand, not including them in the total will likely result in under-counting the hours spent on these regular meetings.

5.2 BRC Meetings

ERG discussed the number and frequency of BRC meetings with TBBS. In total, there were 46 BRC meetings held between FY13 and March 31, 2015 (20 in FY13, 13 in FY14, and 13 in FY15). All meetings

held before January of 2015 were scheduled for 1.5 hours, while those in January 2015 and after were 2 hours. Based on our discussion with TBBS, 39 BRC meetings in the time period for this report lasted 1.5 hours, with the remaining 7 lasting 2 hours.

There are approximately 45 members of the BRC and approximately 30 attend each meeting. Additionally, review team members from the disciplines also attend meetings to present and discuss information and proposals related to their review; this adds, on average, 12 people per meeting. Thus, ERG estimates that, on average, 42 people attend each BRC meeting. Based on this estimate for attendance, the time per meeting, and the number of meetings held, ERG estimates that a total of 3,045 labor hours have been spent on BRC meeting time (see Table 12).

In addition to meeting time, staff prepare for the meeting ahead of time. ERG estimates the following time is spent on meeting preparation:

- TBBS spends approximately 40 hours preparing an agenda, including questions for committee discussion.
- Each member of the BRC spends, on average, 30 minutes reviewing the agenda and other associated tasks. With 30 BRC members per meeting, this is a total of 15 hours per meeting for BRC members.
- Review team members prepare presentations and other materials. Based on our interviews in the fall of 2014, we estimate that approximately 4 people will spend 8 hours each for each BRC meeting from the review teams. This results in a total of 32 hours per BRC meeting for review team preparation.

The sum total of preparation time is 81 hours per BRC meeting. Applying this estimate to the number of BRC meetings results in a total of 4,002 hours of preparation time for BRC meetings between FY13 and March 31, 2015 (see Table 12).

The combined estimate for labor hours for meeting time and preparation time is 7,047 hours, or a total of 4.4 FTEs.

Table 12 – Data for Estimating BRC Meeting Workload

Fiscal Year/ Time Period	Meetings	Meeting Time			Preparation Time		Totals
		Attendees	Hours Per Meeting	Total Meeting Time Hours	Per Meeting	Hours	
FY13	20	42	1.5	1,260	81	1,740	**3,000**
FY14	13	42	1.5	819	81	1,131	**1,950**
FY15 (Oct-Dec)	6	42	1.5	378	81	522	**900**
FY15 (Jan-Mar)	7	42	2	588	81	609	**1,197**
Totals	**46**	-	-	**3,045**	-	**4,002**	**7,047**

5.3 OCP Regular Meetings

OCP has been holding weekly meetings since 2011 to discuss biosimilars-related issues.[33] OCP also estimates that about 8 to 10 of these are canceled each year for various reasons, resulting in an estimated 40 to 42 meetings each year; ERG used 42 meetings in our estimates. The meetings last 1.5 hours on average and have 8 to 10 attendees; ERG used 10 attendees in our estimates. Among the meetings attendees, approximately 3 will need to do preparation ahead of time. OCP assumed that one person would spend 1 to 2 days (ERG estimate: 12 hours on average) and the other 2 would spend half that time (ERG estimate: 6 hours each). These estimates of time spent result in a total of 630 meeting hours (42 meetings × 10 attendees per meeting × 1.5 hours per meeting) and a total of 1,008 preparation hours (42 meetings × [1 person × 12 hours preparation time + 2 people × 6 hours preparation time]) annually. Thus, each year OCP spends 1,638 hours in biosimilar meetings, or 1.02 FTEs. Over the first 2.5 fiscal years of the program, OCP has spent 4,095 hours (2.6 FTEs) on the regular OCP biosimilar meetings.

5.4 OBP Regular Meetings

OBP has been holding regular meetings at least once per week since 2010 and few of these are canceled each year. OBP indicated that they hold at least 42 meetings each year (ERG estimate: 46). The meetings run for one hour. The meetings involve a core group of 13 people and also include at least 2 more people each meeting to present on the current issues/submissions they are dealing with. Thus, at a minimum 15 people attend each meeting (ERG estimate: 16 people). Of those involved, 3-5 might need to prepare materials ahead of time. OBP estimated that a total of 7 hours would be spent on preparation for each meeting for the staff presenting. Thus, ERG estimates that OBP staff spent 736 hours in meetings (46 meetings × 16 people per meeting × 1 hour per meeting) and 322 hours in preparing for meetings (46 meetings × 7 hours per meeting for staff to prepare) each year. This is a total 1,058 labor hours each year for regular meetings, or 0.66 FTEs annually. Over the first 2.5 fiscal years of the program, OBP has spent 2,645 hours (1.7 FTEs) on regular biosimilar meetings.

5.5 Summary

Table 13 summarizes the estimates for regular biosimilars review program-related meetings by fiscal year. Overall, ERG estimates that FDA has spent 13,787 hours and 8.62 FTEs for these regular meetings between FY13 and March 31, 2015.

[33] ERG has only included hours from FY13 to March 31, 2015 in our estimates.

Table 13 – Summary of Estimates for Regular Biosimilar-Related Meetings

Office/Meetings	FY13	FY14	FY15 (first 2 quarters only)	Totals
Hours				
BRC	3,000	1,950	2,097	7,047
OCP	1,638	1,638	819	4,095
OBP	1,058	1,058	529	2,645
Totals	**5,696**	**4,646**	**3,445**	**13,787**
FTEs				
BRC	1.88	1.22	1.31	4.40
OCP	1.02	1.02	0.51	2.56
OBP	0.66	0.66	0.33	1.65
Totals	**3.56**	**2.90**	**2.15**	**8.62**

6. BIOSIMILARS-RELATED POLICY WORK

6.1 Approach and Data

Elements Included in the Workload Estimates
Policy-related work that can be categorized as "Policy and Regulation" in the time reporting data. This includes work such as developing policy and developing guidance documents.

- ERG used the time reporting data to estimate total quarterly hours for biosimilars policy-related work. The method developed by ERG involves assuming the time reporting data (reported 2 weeks each quarter) are a sample of hours and then using the sample data to calculate a total for each quarter and then a total for the 2.5-year period. ERG then calculated 95 percent confidence intervals around the estimated totals for each quarter and for the 2.5-year period to provide context. This approach generated an estimate of the total hours and cost associated with policy-related work at FDA from FY13 to FY15Q2.
- ERG interviewed staff in OMP regarding the time and effort spent on developing guidance documents.[34] OMP agreed to provide estimates for guidance documents development and other biosimilar policy work. ERG used the OMP data to develop independent estimates of OMP's role in policy development which could be compared to the estimates developed using the time reporting data.[35]

6.2 Estimates of Hour and FTEs

6.2.1 Time Reporting Data Estimates

Table 14 provides estimates for policy-related work derived from the CDER time reporting data. These estimates indicate that CDER has spent 23.7 FTEs on biosimilars policy-related work over the first 2.5 years of the program. Table A-2 in Appendix A provides the estimates and the associated confidence intervals for policy-related work derived from the time reporting data. The number of FTEs (23.69) over the first 2.5 fiscal years of the program has a 95 percent confidence interval that ranges from 22.05 to 25.60.

Table 14 - Estimated Total Hours and FTEs Associated with Policy-Related Work Derived from Time Reporting Data

Quarter	Estimated Total Hours	FTEs
2013Q1	2,665.0	1.67
2013Q2	4,134.0	2.58
2013Q3	3,861.0	2.41
2013Q4	3,670.2	2.29

[34] During project meetings with FDA, ERG was asked to ensure it had included OMP's work on guidance documents. Thus, ERG set up meetings with OMP to ensure we covered their work on guidance documents.

[35] The time reporting data include OMP staff and the Policy and Regulation category in the time reporting data should cover Guidance document development and OMP's policy other policy work.

Quarter	Estimated Total Hours	FTEs
2014Q1	3,009.5	1.88
2014Q2	3,188.3	1.99
2014Q3	4,365.1	2.73
2014Q4	2,910.4	1.82
2015Q1	4,819.8	3.01
2015Q2	5,282.9	3.30
Totals	**37,906.1**	**23.69**

6.2.2 OMP-Specific Estimates

The estimates provided in Table 14 include OMP staff. However, ERG was also asked to discuss guidance document development in particular with OMP to ensure it was included in our workload cost estimates. OMP agreed to develop a set of estimates on its own (not within an interview format) for ERG to use and ERG met with OMP to discuss the requirements. OMP provided those estimates to ERG through OSP. The OMP estimates, however, included all biosimilars policy-related work, and not just guidance document development. The OMP estimates can be summarized as follows:

- 3 Technical Leads have spent approximately 40 percent of their time on biosimilar policy work.
- 1 Senior Policy Analyst has spent approximately 40 percent of her time on biosimilar policy work.
- 1 Project Manager has spent approximately 30 percent of his/her time on biosimilar policy work.
- 3 Clearing Officials have spent approximately 10 percent of their time on biosimilar policy work.

This results in a total of 2.2 FTEs per year from OMP on biosimilar policy (3×0.4 + 1×0.4 + 1×0.3 + 3×0.1). The time reporting data indicate that OMP staff have spent considerable time on biosimilar policy work since the beginning of FY13.[36] Thus, a reasonable estimate of the time spent by OMP on policy-related work is 2.2 FTEs multiplied by 2.5 fiscal years, resulting in an estimated 5.5 FTEs since FY13.

ERG also broke out OMP staff in the time reporting data and calculated hours from the time reporting data for just OMP's performance of policy-related work.[37] From FY13Q1 to FY15Q2, OMP staff worked an estimated 6.96 FTEs worth of hours on biosimilar policy and regulatory work with a 95 percent confidence interval ranging from 5.95 to 8.38 FTEs. Thus, the OMP estimate is slightly lower than the lower bound of the 95 percent confidence interval calculated from the time reporting data. ERG expects that the time reporting data will provide a more comprehensive estimate because it includes hours from more than 6 OMP staff (see bulleted estimates from OMP above). Thus, we have assumed the OMP estimates are already subsumed in the CDER time reporting data we summarized above.

[36] OMP staff averaged approximately a total of 171 hours per time reporting collection period and accounted for one-fifth to one-third of all biosimilars policy-related hours each collection period (except in the first quarter of 2013 when they accounted for over half of the total policy hours).

[37] OMP incurred few hours outside of the "policy and regulation" category in the time reporting data.

6.2.3 Summary for Policy-Related Work

Table 15 summarizes ERG's estimates for policy-related work by fiscal year. Overall, ERG estimates that a total of 37,906 hours (23.7 FTEs) were spent on biosimilars-related policy work between FY13 and March 31, 2015.

Table 15 – Summary of Policy-Related Work Estimates by Fiscal Year

Fiscal Year	Hours	FTEs
FY13	14,330.2	8.96
FY14	13,473.2	8.42
FY15 (first 2 quarters only)	10,102.6	6.31
Totals	37,906.1	23.69

7. SCIENCE AND RESEARCH

7.1 Approach and Data

- ERG used the time reporting data to estimate total quarterly hours for science and research work. The method developed by ERG involves assuming the time reporting data (reported 2 weeks each quarter) are a sample of hours and then using the sample data to calculate a total for each quarter and then a total for the 2.5-year period. ERG then calculated 95 percent confidence intervals around the estimated totals for each quarter and for the 2.5-year period to provide context. This approach generated an estimate of the total hours and cost associated with science and research work at FDA from FY13 to FY15Q2.

Elements Included in the Workload Estimates

- Work that would be categorized as "Science and Research" in the time reporting data.
- Time spent on lab-related work.

- ERG obtained estimates from CDER to determine the number of hours that FDA has spent on lab-related research. These estimates provide a check on the estimates derived from the time reporting data.

7.2 Estimates of Hour and FTEs

Table 16 provides estimates for science and research work derived from the CDER time reporting data. These estimates indicate that CDER has spent 21.0 FTEs on biosimilar science and research-related work. Table A-3 in Appendix A provides the estimates and the associated confidence intervals for science and research work derived from the time reporting data. The number of FTEs (21.0) over the first 2.5 years of the program has a 95 percent confidence interval that ranges from 18.9 to 23.7.

Table 16 - Estimated Total Hours, FTEs, and Labor Cost Associated with Science and Research Work Derived from Time Reporting Data

Quarter	Estimated Total Hours	FTEs
2013Q1	1,748.50	1.09
2013Q2	3,885.70	2.43
2013Q3	5,736.25	3.59
2013Q4	3,705.00	2.32
2014Q1	2,590.25	1.62
2014Q2	1,850.88	1.16
2014Q3	3,446.63	2.15
2014Q4	4,020.25	2.51
2015Q1	3,872.38	2.42
2015Q2	2,736.50	1.71
Totals	**33,592.33**	**21.00**

CDER provided an alternative set of estimates for lab-related work at FDA on biosimilars. These estimates are summarized in Table 17. CDER developed the labor estimates by working back from its FY15 allocation. First, the labs at CDER had 45 FTEs in FY15 and CDER assumed 25 percent would be allocated to biosimilars work (11.25 FTEs), half of which would be incurred in the first half of the fiscal year (5.63 FTEs). CDER then assumed that FY14 would be two-thirds of the total FY15 biosimilar allocation (i.e., two-thirds of 11.25 FTEs) and FY13 would be one-tenth of the total FY15 biosimilar allocation (one-tenth of 11.25 FTEs). This results in an estimated 14.25 FTEs over the first 2.5 fiscal years of biosimilars work. CDER also added costs of supplies and contracts of $1.9 million.

Table 17 - FTEs and Costs for Biosimilar Labs Work

Fiscal Year	FTEs as a Percentage of FY15 FTEs	FTEs	Supplies and Contracts ($1,000s)
FY13	10%	1.13 [a]	$150
FY14	67%	7.50 [a]	$1,000
FY15 (first 2 quarters only)	-	5.63 [b]	$750 [c]
Totals	**-**	**14.25**	**$1,900**

[a] Calculated as 45 total FTEs for FY15 multiplied by 25 percent (biosimilar allocation in FY15) and then multiplied by the percentage in the preceding column.
[b] Calculated as 45 FTEs total in the labs, multiplied by 25 percent allocation to biosimilars, and then divided by half to reflect only a half a fiscal year for 2015.
[c] CDER indicated $1.5 million had been allocated for FY15 in this category. ERG assumed half could be allocated to the first two quarters of the fiscal year.

The lab work represents a subset of the science and research hours. Thus, the 14.25 FTEs for labs can assumed to part of the 21 FTEs estimated from the time reporting data. The difference, 6.75 FTEs, can be assumed to be non-lab science and research work. Furthermore, the amounts for supplies and contracts is included under operating costs (added in Section 9.2) and thus we do not add in the estimated values for supplies and contracts to avoid double-counting.

Table 18 summarizes the estimates for biosimilars science and research work. ERG estimates that biosimilars science and research work at FDA between FY12 and March 31, 2015 has involved 21.0 FTEs and $1.9 million in non-labor cost.

Table 18 - Summary Estimates by Fiscal Year for Science and Research Work

Fiscal Year	FTEs	Non-Labor Cost ($1,000s)
FY13	9.42	$150
FY14	7.44	$1,000
FY15 (first 2 quarters only)	4.13	$750
Totals	**21.00**	**$1,900.0**

8. MISCELLANEOUS COSTS

This section summarizes estimates for a set of offices and cost categories that were not covered under previous sections and that did not require a full report section to describe. Included in this section are:

- Time spent by FDA Office of the Commissioner's Office of External Affairs (OEA) on biosimilar-related outreach.
- Time spent by OMP and TBBS staff on developing and implementing a biosimilars continuing education course and on biosimilars-related focus group testing.
- Time spent by OCC staff to perform legal review and consultation on reviews and other biosimilar work.

8.1 Approach and Data

Data for these estimates were collected through a combination of interviews and email requests.

8.2 Estimates of Hours and FTEs

8.2.1 OEA Outreach

OEA provided ERG with estimates of time to work on biosimilar-related outreach over email. A total of 77 hours were incurred by OEA in FY15 on biosimilar outreach. Given the fact that ERG was provided with data to develop an FTE estimate for the FDA Office of the Commissioner, ERG has not included these hours in our totals to avoid double counting them.

8.2.2 Continuing Education Course

ERG obtained a list of names of FDA staff in OMP and TBBS who had worked on developing a biosimilar-related continuing education course. ERG collected information on the labor hours and other cost associated with development of this course through an email query of the staff involved. The estimates from OMP and TBBS totaled 1,538 labor hours and a contract worth $342,480 in FY15. ERG assumed that one half of the contract value would accrue in the first two quarters of FY15 ($171,240). The contract value, however, is already included in FDA operating costs (added in Section 9.2) and is not added to our costs in Section 9 to avoid double-counting.

8.2.3 Focus Groups

ERG also obtained a list of names of FDA staff in OMP and TBBS who had worked on developing and implementing biosimilars-related focus group testing. As with the continuing education course, ERG collected information on labor time and other costs through an email query of those staff. The estimates from OMP and TBBS totaled 525.5 labor hours and a contract worth $269.596 in FY15. ERG assumed that one half of the contract value would accrue in the first two quarters of FY15 ($134,798). The contract value, however, is already included in FDA operating costs (added in Section 9.2) and is not added to our costs in Section 9 to avoid double-counting.

8.2.4 OCC Legal Work

OCC provided an encompassing estimate of 1-2 days per week on biosimilar work for 2 attorneys. This translates to a range of 16-48 hours per week. This time encompassed time to consult on reviews (IND and 351(k) BLAs) and time to consult on other policy and legal issues. ERG used the mid-point of that estimate (32) hours and assumed this could applied over the 2.5 fiscal years. This suggests that OCC has spent 4,160 hours on biosimilars since FY13. As with the OEA estimate above, because ERG was provided with data to develop an FTE estimate for the FDA Office of the Commissioner, we have not included these hours in our totals to avoid double counting them.

8.2.5 Summary of Miscellaneous Costs Estimates

Table 19 provides a summary of the labor-related estimates for work we categorized as miscellaneous by fiscal year. Non-labor costs (contract costs) also appear in the table by fiscal year.

Table 19 - Summary of Hours, FTEs, and non-Labor Costs Categorized as Miscellaneous by Fiscal Year

Category	FY13	FY14	FY15 (first 2 quarters only)	Total
Labor Hours				
OEA Outreach [a]	-	-	77.0	77.0
Continuing Education Course	-	-	1,538.0	1,538.0
Focus Groups	-	-	525.5	525.5
OCC Legal Review [a]	1,664.0	1,664.0	832.0	4,160.0
Totals	***1,664.0***	***1,664.0***	***2,972.5***	***6,300.5***
FTEs				
OEA Outreach [a]	-	-	0.05	0.05
Continuing Education Course	-	-	0.96	0.96
Focus Groups	-	-	0.33	0.33
OCC Legal Review [a]	1.04	1.04	0.52	2.60
Totals	***1.04***	***1.04***	***1.86***	***3.94***
Contract Costs ($1,000s)				
Continuing Education Course [b]	-	-	$171.2	$171.2
Focus Groups [b]	-	-	$134.8	$134.8
Totals	***-***	***-***	***$306.0***	***$306.0***

[a] Although summarized here, these hours were not included in the report totals because ERG was provided with an estimate of the FTEs for the FDA Office of the Commissioner, which would include these hours.
[b] Not included in our totals because ERG was provided with an estimate of operating costs for CDER.

9. SUMMARY: BIOSIMILAR FTES, COSTS, AND COMPARISON TO FDA ESTIMATES

This section summarizes ERG's FTE estimates, estimates total costs, and compares our estimates to those developed by FDA in its BsUFA financial reports. The section begins by summarizing the estimated FTEs from the previous sections of the report. Next, we add FTEs (provided by FDA) for CDER offices not covered in our other estimates, and then we add estimates for CBER, FDA Office of the Commissioner, and ORA. The total FTEs are then translated into labor costs (salary and benefits). We then add operating costs and costs allocated to the biosimilars review program from FDA's centrally-managed accounts. Finally, we compare our FTE and cost estimates with the costs reported in FDA's financial reports.

9.1 Estimated Total FTEs for Biosimilars Work

Table 20 summarizes ERG's estimates for the total number of FTEs associated with biosimilars review program work at FDA for the first 2.5 fiscal years of the program. The data in the table combine the estimates detailed in Sections 3 through 8. FDA also provided ERG with FTE estimates for CDER offices not included in ERG's estimates; these are detailed in Table 21.

Table 20 - Estimated CDER FTEs for Biosimilars Program Work

Category	FY13	FY14	FY15 (first 2 quarters only)	Totals
FTEs Estimated by ERG for Biosimilars-Related Work				
IND, pre-IND, and BPD Meetings	21.73	23.28	10.79	55.80
351(k) BLA Review	0.00	2.46	11.79	14.26
Regular Biosimilars Meetings	3.56	2.90	2.15	8.62
Policy	8.96	8.42	6.31	23.69
Science and Research	9.42	7.44	4.13	21.00
Outreach	0.00	0.00	1.29	1.29
Total CDER FTEs	**43.67**	**44.51**	**36.47**	**124.65**

Table 21 – FTEs for CDER Offices Not Covered by ERG Estimates

CDER Office	FY13	FY14	FY15 (first 2 quarters only)
Office of the Center Director (OCD)	1.49	1.44	2.11
Division of Advisory Committee and Consultant Management (DACCM), part of Office of Executive Programs (OEP)	0.00	0.19	4.69
OEP, excluding DACCM	0.13	1.21	1.82
Office of Management (OM)	3.18	2.84	4.24
Office of Communications (OCOMM)	1.76	1.5	2.24
Office of Business Informatics (OBI), part of Office of Strategic Program (OSP)	2.04	1.75	2.38
OSP, excluding OBI	2.35	2.09	3.92
Total CDER FTEs for Office not covered by ERG estimates	**10.95**	**11.02**	**21.40**

Finally, FDA also provided ERG with the number of biosimilars review program-related FTEs for CBER and ORA in FY13 and FY14; these estimates are provided in Table 22. As noted before, ORA did not incurred labor time in FY13 and FY14 and we have not included labor time for ORA in FY15.[38] ERG assumes that one half of the FY14 value would be a reasonable estimate for the first half of FY15 for CBER. FDA Office of the Commissioner estimates for FY13 and FY14 were derived by assuming FDA Office of the Commissioner biosimilars FTEs represented a percentage of the total FTEs for CDER and CBER in each year.[39] For FY13 we used 21.34 percent and for FY14 the percentage was 21.18 percent.[40] To derive an estimate for the FDA Office of the Commissioner for the first two quarters of FY15, ERG used the FY14 percentage value.

Table 22 - Summary of Non-CDER FTEs

Office/Center	FY13	FY14	FY15 (first 2 quarters only)
CBER	3.89	1.33	0.67 [a]
FDA Office of the Commissioner	12.49	12.04	12.40
ORA	0.0	0.0	0.0
Total Non-CDER FTEs	**16.38**	**13.37**	**13.06**

[38] Labor time incurred by ORA in FY15 will be addressed in the Final Report in September 2016.

[39] The total number of CDER and CBER FTEs in each fiscal year is calculated by summing the total values for each fiscal year from Table 20 and Table 21 and then adding the CBER value in Table 22.

[40] These percentages reflect the percentage of total salary represented by FDA Office of the Commissioner staff and were taken from the FDA biosimilars process cost worksheets for each fiscal year.

9.2 Estimated Costs

Table 23 summarizes ERG's estimates for the total biosimilars review program costs. We begin with the FTEs (Section 9.1) and then calculate labor costs based on the method described in Section 2.3 using the cost of salary and benefits per FTE found in Table 3. ERG then added operating cost values and the amounts allocated to biosimilars review program work from FDA's centrally managed accounts made available to ERG by FDA from BsUFA financial reporting.[41] ERG estimates that FDA spent $23.6 million in FY13, $21.4 million in FY14, and $20.9 million in the first two quarters of FY15.

Table 23 - Summary of ERG Estimates: FTEs, Labor Costs, and Indirect Costs, by Fiscal Year

Category	FY13	FY14	FY15 (first 2 quarters only)	Total
Total Biosimilars FTEs	70.99	68.90	70.93	210.83
Labor Costs (salary and benefits) ($1,000s)	$11,105.3	$10,998.1	$11,488.7	$33,592.2
Operating Costs ($1,000s)	$7,663.9	$6,216.7	$5,734.53 [a]	$19,615.1
Centrally Managed Accounts Costs ($1,000s)				
FDA Central	$1,861.5	$1,560.7	$1,413.8 [a]	$4,836.0
GSA Rent	$964.3	$867.3	$756.7 [a]	$2,588.2
Other Rent Related	$403.6	$628.8	$426.5 [a]	$1,458.9
White Oak Relocation	$697.5	$456.3	$476.7 [a]	$1,630.4
HR	$166.4	$116.7	$117.0 [a]	$400.1
Shared Services	$699.0	$544.1	$513.6 [a]	$1,756.7
Total Costs ($1,000s)	**$23,561.5**	**$21,388.7**	**$20,927.5**	**$65,877.6**

[a] These are projected values. ERG estimated these values by applying a projected increase to the average of the FY13 and FY14 amounts. The projected increase was calculated by using the time reporting data for all biosimilars review program hours. ERG totaled the hours logged to biosimilar tasks in FY13 and FY14 and averaged the two amounts. We then totaled the amount of hours logged to biosimilar tasks in the first two quarters of FY15 and doubled that amount to get an FY15 annual value. We then divided the FY15 annual value by the average of the FY13 and FY14 amounts. This resulted in a projected mark-up factor (projected increase) of 1.653, which was applied to the average of the FY13 and FY14 costs in this table and divided by two (reflecting only half a fiscal year). For example, the average of the FY13 and FY14 operating costs multiplied by 1.653 and then divided by two equals the estimated FY15 operating cost value.

[41] For FY13 and FY14, ERG took values from the BsUFA process cost worksheets provided to ERG by OSP. For FY15, we generated a projected amount for each category based on changes in time reporting data and the FY13 and FY14 amounts for each category; the approach is described in a table footnote.

9.3 Comparison to FDA Financial Report Values

Table 24 compares ERG's estimates to the values reported by FDA in its annual BsUFA financial reporting. We compare our estimates to FDA financial reporting values in three ways:

- ERG total to FDA totals.
- ERG CDER-only values to CDER-only values – This comparison is done because much of our data centers on CDER sources (time reporting and also interviewees).
- ERG labor-related estimates to FDA labor-related values – This comparison is done because the ERG values share the same non-labor values (operating costs, FDA centrally managed accounts, overhead) as the FDA financial reports.

ERG's total cost estimates represent 84 to 91 percent of the values that are reported by FDA in its BsUFA financial reporting. The labor costs represent 83 to 98 percent of the FDA-reported values. ERG's FTE estimates are between 72 and 88 percent of the FDA reported FTEs. ERG's understanding is that the FDA estimate of FTEs in its financial report is calculated by multiplying the number of total FTEs for each CDER office by a percentage reflecting biosimilars work for that office. ERG's estimates, on the other hand, are built from projections based on the time reporting data and interviews with FDA staff on time spent performing biosimilars work. As noted, there are some limitations related to ERG's estimates. First, ERG's estimates rely on interviews and interviewees might not fully remember all work performed. Second, FDA's time reporting data is based on a two week sample each quarter and is thus subject to sampling error. Additionally, FDA expects that some staff might have reported time as being PDUFA-related rather than being related to biosimilars review program work. Finally, our survey of FDA staff resulted in a 52 percent response rate and those who did not respond are not included in these estimates.

Table 24 - Comparison of ERG Estimates to FDA BsUFA Financial Reporting

Category	FTEs		Costs	
	FY13	FY14	FY13	FY14
ERG Estimates				
Totals	71	69	$23,561.5	$21,388.7
CDER Only	55	56	$21,034.2	$19,262.7
Labor Only	71	69	$11,105.3	$10,998.1
FDA Financial Reporting				
Totals	98	78	$28,040.5	$23,391.6
CDER Only	87	70	$24,759.3	$21,087.7
Labor Only	98	78	$13,400.5	$11,187.4
ERG Value Relative to FDA Value				
FDA Total	72%	88%	84%	91%
FDA CDER Only	63%	79%	85%	91%
Labor Only	72%	88%	83%	98%

Appendix A: 95 Percent Confidence Intervals for Time Reporting Data Estimates

Table A-1 - Estimated Total Hours, FTEs, and Cost Associated with IND, Pre-IND, and BPD Meeting Work Derived from Time Reporting Data, Including 95 Percent Confidence Intervals

	Estimated Total Hours			FTEs			Cost		
Quarter	95 Percent CI Lower Bound	Mean	95 Percent CI Upper Bound	95 Percent CI Lower Bound	Mean	95 Percent CI Upper Bound	95 Percent CI Lower Bound	Mean	95 Percent CI Upper Bound
2013Q1	5,361.11	6,462.63	8,133.83	3.35	4.04	5.08	$921.4	$1,110.8	$1,398.0
2013Q2	6,834.16	8,008.98	9,671.55	4.27	5.01	6.04	$1,174.6	$1,376.5	$1,662.3
2013Q3	9,459.79	11,092.25	13,405.64	5.91	6.93	8.38	$1,625.9	$1,906.5	$2,304.1
2013Q4	7,822.30	9,199.13	11,164.17	4.89	5.75	6.98	$1,344.5	$1,581.1	$1,918.8
2014Q1	6,792.46	8,079.50	9,968.29	4.25	5.05	6.23	$1,167.5	$1,388.7	$1,713.3
2014Q2	7,854.29	9,283.63	11,348.92	4.91	5.80	7.09	$1,350.0	$1,595.6	$1,950.6
2014Q3	8,189.16	9,586.20	11,557.94	5.12	5.99	7.22	$1,407.5	$1,647.6	$1,986.5
2014Q4	8,810.69	10,302.50	12,402.46	5.51	6.44	7.75	$1,514.3	$1,770.7	$2,131.7
2015Q1	7,010.76	8,333.00	10,269.92	4.38	5.21	6.42	$1,248.8	$1,484.3	$1,829.3
2015Q2	7,619.00	8,928.73	10,782.23	4.76	5.58	6.74	$1,357.1	$1,590.4	$1,920.6
Totals	**84,497.63**	**89,276.53**	**94,628.42**	**52.81**	**55.80**	**59.14**	**$13,111.6**	**$15,452.3**	**$18,815.2**

Table A-2 - Estimated Total Hours, FTEs, and Cost Associated with Biosimilars Policy-Related Work Derived from Time Reporting Data, Including 95 Percent Confidence Intervals

	Estimated Total Hours			FTEs			Cost		
Quarter	95 Percent CI Lower Bound	Mean	95 Percent CI Upper Bound	95 Percent CI Lower Bound	Mean	95 Percent CI Upper Bound	95 Percent CI Lower Bound	Mean	95 Percent CI Upper Bound
2013Q1	2,077.32	2,665.00	3,716.37	1.30	1.67	2.32	$357.0	$458.0	$638.8
2013Q2	3,349.36	4,134.00	5,398.73	2.09	2.58	3.37	$575.7	$710.5	$927.9
2013Q3	3,115.09	3,861.00	5,076.60	1.95	2.41	3.17	$535.4	$663.6	$872.5
2013Q4	2,929.07	3,670.23	4,913.52	1.83	2.29	3.07	$503.4	$630.8	$844.5
2014Q1	2,366.33	3,009.50	4,132.81	1.48	1.88	2.58	$406.7	$517.3	$710.3
2014Q2	2,572.31	3,188.25	4,192.04	1.61	1.99	2.62	$442.1	$548.0	$720.5
2014Q3	3,646.72	4,365.08	5,435.87	2.28	2.73	3.40	$626.8	$750.2	$934.3
2014Q4	2,337.65	2,910.38	3,854.80	1.46	1.82	2.41	$401.8	$500.2	$662.5
2015Q1	3,970.62	4,819.75	6,130.86	2.48	3.01	3.83	$707.3	$858.5	$1,092.1
2015Q2	4,328.39	5,282.88	6,777.41	2.71	3.30	4.24	$771.0	$941.0	$1,207.2
Totals	**35,274.04**	**37,906.05**	**40,962.50**	**22.05**	**23.69**	**25.60**	**$6,062.7**	**$6,515.1**	**$7,040.4**

Table A-3 - Estimated Total Hours, FTEs, and Cost Associated with Biosimilars Science and Research-Related Work Derived from Time Reporting Data, Including 95 Percent Confidence Intervals

	Estimated Total Hours			FTEs			Cost		
Quarter	95 Percent CI Lower Bound	Mean	95 Percent CI Upper Bound	95 Percent CI Lower Bound	Mean	95 Percent CI Upper Bound	95 Percent CI Lower Bound	Mean	95 Percent CI Upper Bound
2013Q1	1,233.18	1,748.50	3,003.64	0.77	1.09	1.88	$212.0	$300.5	$516.3
2013Q2	2,721.64	3,885.70	6,789.71	1.70	2.43	4.24	$467.8	$667.9	$1,167.0
2013Q3	4,404.25	5,736.25	8,223.24	2.75	3.59	5.14	$757.0	$985.9	$1,413.4
2013Q4	2,836.69	3,705.00	5,339.39	1.77	2.32	3.34	$487.6	$636.8	$917.7
2014Q1	1,871.04	2,590.25	4,207.60	1.17	1.62	2.63	$321.6	$445.2	$723.2
2014Q2	1,305.39	1,850.88	3,179.51	0.82	1.16	1.99	$224.4	$318.1	$546.5
2014Q3	2,615.13	3,446.63	5,053.36	1.63	2.15	3.16	$449.5	$592.4	$868.5
2014Q4	2,960.76	4,020.25	6,260.57	1.85	2.51	3.91	$508.9	$691.0	$1,076.0
2015Q1	2,898.19	3,872.38	5,833.10	1.81	2.42	3.65	$516.2	$689.8	$1,039.0
2015Q2	1,965.88	2,736.50	4,500.82	1.23	1.71	2.81	$350.2	$487.4	$801.7
Totals	**30,182.53**	**33,592.33**	**37,870.67**	**18.86**	**21.00**	**23.67**	**$4,295.0**	**$5,815.0**	**$9,069.3**