February 24, 2014

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2013-N-1618: Draft Prescription Drug User Fee Act V Information Technology Plan; 78 Fed. Reg. 248 (December 26, 2013)

Dear Sir or Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) and Biotechnology Industry Organization (BIO) are pleased to submit these comments in response to the Food and Drug Administration's (FDA's) Draft Prescription Drug User Fee Act V (PDUFA V) Information Technology Plan (IT Plan). PhRMA is a voluntary, non-profit association that represents the country's leading innovative biopharmaceutical research and biotechnology companies, which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives. Since 2000, PhRMA member companies have invested approximately $550 billion in the search for new treatments and cures, including an estimated $48.5 billion in 2012 alone. BIO represents more than 1,100 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products, thereby expanding the boundaries of science to benefit humanity by providing better healthcare, enhanced agriculture, and a cleaner and safer environment.

The PDUFA V Performance Goals (Section XIV. B.)[1] commit the FDA to periodically updating and publishing a five-year plan for business process improvement enabled by IT investments. PhRMA and BIO remind the Agency that the last update to the PDUFA IV IT Plan was published on September 19, 2011 with information current as of May 2010.[2] PhRMA and BIO note that the 2011 update of the IT plan indicates that the information is valid through September 2012. Therefore, there has been a period of 15 months during which FDA was unable to provide a current IT plan to the Industry and

[1] Available at: http://www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm270412.pdf
[2] Available at: http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM272334.pdf

the public. With the publication of the proposed PDUFA V Goals Letter on September 1, 2011 and the reauthorization of PDUFA V on July 9, 2012, PhRMA and BIO expected that the Agency would be timelier in the publication of an IT plan that addressed the outstanding PDUFA IV IT initiatives and new PDUFA V IT initiatives (*e.g.,* having a draft IT plan available for public review in the first quarter of PDUFA V). PhRMA and BIO note that the Agency published the draft plan over one year into PDUFA V and only shortly before the publication of draft guidance[3] that, when final, will trigger new regulatory requirements for electronic submission and data standardization. Further, we believe that additional rounds of revision to draft guidance[4] intended to implement PDUFA V goals may have been avoidable had a PDUFA V IT plan been in place earlier (*e.g.,* at the start of PDUFA V). The delay in the release of this plan has a significant, negative impact on Industry's ability to budget for, adequately plan for, and prioritize internal investments that are necessary to meet new regulatory requirements and expectations. PhRMA and BIO appreciate the effort put forth by the Agency to develop this draft plan; however, we urge the FDA to publish the PDUFA IT plans in a timelier manner and without gaps in time during which no current plan is available.

General Comments

I. FDA's Strategy for Prioritizing IT-enabled Business Process Change and Tracking Pace and Progress

The PDUFA V Performance Goals Letter (Section XIV.B.1.a.) states that the plan will "frame the strategy for prioritizing IT-enabled business process change, enumerate the business process improvements expected from each IT investment, and convey a consistent series of milestones for each initiative to track pace and progress." PhRMA and BIO believe that the draft plan does not adequately address these issues. For example, the timelines presented in the plan are rarely more granular than milestones by fiscal year, and we believe that annual milestones are not sufficient to track pace and progress of initiatives. PhRMA and BIO urge the FDA to include an appropriate level of detail within the IT Plan to allow Industry to prepare for upcoming IT changes, and we remind the Agency that the budgeting process for a biopharmaceutical company typically occurs months before the start of the fiscal year. PhRMA and BIO ask that the FDA provide additional detail by quarter for all major milestones. In the absence of a detailed, clearly articulated plan for IT changes, it will be challenging for Industry and the FDA to work in a collaborative manner to reach the shared goal of a more efficient human drug review process through improvements of standardization of data and electronic submissions.

[3] Draft Guidance for Industry: Providing Regulatory Submissions in Electronic Format – Submissions Under Section 745A(a) of the Federal Food, Drug and Cosmetic Act. February 2014. Available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM384686.pdf

[4] Draft Guidance for Industry: Providing Regulatory Submissions in Electronic Format – Standardized Study Data. February 2014, Revision 1. Available at: http://www.fda.gov/downloads/Drugs/Guidances/UCM292334.pdf

The draft IT Plan is very broad and it is not explicit in detailing which projects map to a particular PDUFA V goal, the expected business process improvement from each IT initiative and investment, nor the series of milestones to track pace and progress against the goal. PhRMA and BIO strongly urge the Agency to release a comprehensive IT Plan that clearly identifies how IT initiatives and data standardization efforts map directly to PDUFA Goals; enumerates business process improvements and how these improvements will be measured; and provides a mechanism for stakeholders to track pace and progress of the initiative.

II. Annual Assessments of Progress Against the IT Plan

Section XIV.B.1.b. of the PDUFA V Performance Goals clearly states that annual assessments of progress against the IT plan will be released within three months after the close of each fiscal year (*e.g.*, the FY 2013 assessment by December 31, 2013). PhRMA and BIO note that the Agency has not yet published assessments for FY 2011 or FY 2012. With the delay in publication of previous assessments and the absence of a comprehensive assessment of progress against PDUFA IV Goals, PhRMA and BIO believe that it will be challenging for the Agency to accurately assess and communicate the state of implementation of PDUFA IV IT Goals and the potential impact on the Agency's ability to successfully implement PDUFA V IT Goals. PhRMA and BIO are concerned that IT goals from previous PDUFA commitments may not be met and that key technology enablers of PDUFA V Goals may be overlooked. PhRMA and BIO strongly urge the FDA to conduct a full analysis of the status of implementation of previous and current PDUFA IT goals and to make the results of this analysis publically available. In preparing a comprehensive assessment of IT improvements and investments, PhRMA and BIO urge the FDA to articulate the Agency's long-term vision for information technology and data standards in the final PDUFA V IT plan and to clearly articulate how projects and initiatives support progress towards those long-term goals.

III. Updates to the IT Plan

Section XIV.B.1.c. of the PDUFA V Performance Goals states that the FDA will publish updates to the plan as the Agency deems appropriate. PhRMA and BIO strongly recommend that the FDA ensures that updates to the IT Plan are frequent enough to be relevant and to allow Industry adequate time to budget for and put systems in place to meet the Agency's expectations and requirements. As discussed above, PhRMA and BIO believe it is important to have continuity in planning, prioritization, and investments such that PDUFA IT goals are supported seamlessly across fiscal years and PDUFA reauthorizations.

IV. Use of User Fee Funds to Support Center- and Agency-wide IT Priorities

With the authorization of new user fee programs in 2012 (*e.g.*, GDUFA, BsUFA, MDUFA), PhRMA and BIO ask that the Agency articulate in the respective IT plans how

the various user fee program funds will support shared IT systems and efforts. PhRMA and BIO encourage the FDA to develop integrated systems across the Agency to the greatest extent feasible, and ask that the FDA account for the relative IT and informatics needs of each user fee program when allocating specific user fee funds. PhRMA and BIO note that the PDUFA V IT Plan and the Generic Drug User Fee Act (GDUFA) IT Plan are nearly identical in content. We believe this is appropriate for initiatives that impact more than one user fee program, but we believe that it is important that the Agency be transparent about how it is assessing the relative IT and informatics needs of each user fee program and the determination of the relative contributions from each user fee fund to support shared systems and efforts.

V. Forecasting of IT Changes

Section XIV.C.2. of the PDUFA V Performance Goals Letter states that, on an annual basis, FDA will measure and report on the "number and significance of IT technical specifications or e-submission guidance implemented requiring Industry to change submission content that was not forecasted accurately in the five-year plan." PhRMA and BIO note that it will not be possible for the Agency to accurately report on this measure given the delay in publishing the PDUFA V IT Draft Plan. PhRMA and BIO remind the Agency that the successful implementation of PDUFA IT and informatics Goals relies on FDA's clear and timely articulation of requirements and expectations. FDA's accurate forecasting of the timeline for changes that require IT investment, training, and updates to process by Industry is essential. PhRMA and BIO encourage the FDA to give this provision of the PDUFA V Goals Letter higher priority given the importance of accurate forecasting of changes and clear communication about those changes.

VI. Governance Processes to Ensure Alignment of IT Investments with PDUFA Commitments

PhRMA and BIO believe that centralization of IT decision-making and alignment among stakeholders within FDA on priorities is paramount to the successful execution of the IT plan. PhRMA and BIO acknowledge the FDA's efforts to form an Information Technology Investment Review Board (ITIRB) within each Center but remain concerned about the adequacy of coordination across Centers and the robustness of the process for resolving differences in priorities between Centers. In particular, it is important that technology investments within each FDA center are balanced against those investments that are necessary to improve technology across the entire Agency and that there be adequate oversight of investments to ensure this balance. PhRMA and BIO strongly encourage the FDA to continue to implement governance processes that define decision-making authorities, assign accountability for executing decisions, recommend and prioritize IT investment decisions, and monitor performance and risks with each

investment. PhRMA and BIO strongly support the early and clear articulation of performance metrics, and regular review of these metrics, for each IT initiative.

VII. Supporting Regulatory Operations

PhRMA and BIO note that Section 2.0 of the draft PDUFA V IT Plan states that the Electronic Submission Gateway (ESG) is currently supporting seven centers, the Office of the Commissioner, and, in the near future, Health Canada. PhRMA and BIO strongly urge the FDA to accelerate the efforts to assess the stability and security of the ESG and ensure that it is able to meet current and projected future increases in submission loads. PhRMA and BIO commend the FDA for beginning this work in FY 2014, encourage the FDA to complete these efforts in a timely manner, and recommend that this be accomplished with support from third party auditors and security experts. As emphasized earlier, PhRMA and BIO believe that robust governance processes for these efforts are critical to the successful and timely completion of this important assessment.

As the Agency seeks to improve the stability of the ESG, PhRMA and BIO request that the Agency articulate a plan for continuity of operations in the event that the ESG fails or is unavailable. Further, we request that the Agency implement a robust disaster recovery plan for the ESG. PhRMA and BIO remind the Agency that the stable and reliable functioning of the ESG is essential for the efficient and timely submission of information to the Agency.

VIII. Relationship of FDA's PDUFA V IT Plan to Other FDA and HHS IT Plans

PhRMA and BIO commend the FDA on its publication of the Office of Information Management (OIM) Strategic Plan in 2012[5] and, we support FDA's progress against the goals articulated in the plan. As outlined in the plan, PhRMA and BIO agree that clear identification of start dates, end dates, success criteria, key personnel, dedicated budget, and collaborators for each major technology initiative is an important component of improving understanding and support for significant IT initiatives. However, the connections between the OIM Strategic Plan and the PDUFA V IT Plan are unclear, and we urge the Agency to articulate how various IT plans and initiatives intersect and complement each other.

PhRMA and BIO note that the FY 2014 Work Plan of the Department of Health and Human Services (HHS) Office of the Inspector General (OIG)[6] includes review of HHS' operating divisions' compliance with the Federal Information Security Management Act of 2002 (FISMA), a determination of the adequacy of information technology security of selected HHS systems, and network and web application penetration testing to determine whether these networks and applications are susceptible to hackers. PhRMA

[5] Available at: http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM325437.pdf
[6] Available at: http://oig.hhs.gov/reports-and-publications/archives/workplan/2014/Work-Plan-2014.pdf

and BIO believe that the efforts described above are relevant to systems and applications critical to the human drug review process. PhRMA and BIO request greater insight into how these issues will be addressed for systems and applications central to the human drug review process if they are not included in HHS' FY 2014 assessment.

Conclusion

In addition to the above general comments, we have attached specific technical comments by section of the draft IT Plan (Appendix I). PhRMA and BIO hope that these comments are helpful as the Agency seeks to publish a robust five-year IT Plan.

PhRMA and BIO strongly urge the Agency to articulate a clear, comprehensive, long-term strategy for achieving PDUFA IT Goals. PhRMA and BIO encourage FDA leadership to provide enhanced oversight of PDUFA IT investments and initiatives and to provide more timely, detailed and accurate updates to the public regarding the status of these investments and initiatives. PhRMA and BIO are committed to continue to work with the Agency and other stakeholders to improve the efficiency of the regulatory review process through strategic investments in efficient, standards-based information technology.

If you have any questions, please do not hesitate to contact us.

Respectfully submitted,

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Appendix I – Specific Comments by Section

SECTION 2: Supporting Regulatory Operations

- ESG Capacity
    - Due to the increasing size of data sets coupled with Patient Data Records (*i.e.*, eCRFs) and image files, submissions may be over 200 GB in size. We believe that the maximum submission size submitted via the ESG must be increased to accommodate the increase in the amount of data Sponsors are expected to provide. It is understood that applicants have the option to use media for larger submissions, but we believe that the ESG should be enhanced to accommodate larger submissions via the Gateway.
    - We have concerns about implementation of expectations that promotional material be submitted through the ESG prior to completion of efforts to enhance the ESG to support the volume and capacity needed for large submissions.
- ESG Security
    - With the addition of Health Canada as users of the ESG, it is critical that the ESG analysis include a review of their security model. The ESG must be secure, stable and flexible enough to meet both current future submission workloads.
- We encourage FDA to develop common eCTD validation capabilities to support regulatory operations. Currently, commercially available tools that perform the validation activity also provide a variety of other checks that do not relate to the specific validation of the eCTD criteria. Tools with differing interpretations of criteria yield mixed "validation" results, which lead to confusion on what content is compliant with eCTD specifications. A common capability that strictly focuses on validation criteria would promote greater understanding of and ability to generate compliant submissions.

SECTION 4: Data Standards

- What criteria will be used to assess the benefits and value proposition of standards being developed and implemented?

SECTION 4.1: Study Data Standards

- PhRMA and BIO agree that consistent application of study data standards is important to maximize efficiencies gained.
- As the Agency adopts data standards and the Industry is required to use data standards for submissions, it is critically important that there is consistent and robust use of data standards within the Agency. PhRMA and BIO encourage the FDA to implement policies that reduce the number of FDA requests for non-

standard data sets or analysis that Sponsors receive during the regulatory review process.

SECTION 4.3: Identification of Medicinal Products

- When does FDA intend to finalize the implementation guides? EMA has indicated they intend to implement EVMPD changes by 2016. If FDA is working with EMA to implement this standard, is the Agency targeting a similar timeframe?

SECTION 7: Next Steps

- Change Management
    - FY2014 introduces many changes - what change management strategy/training is the Agency currently planning within and across Centers and Divisions?