May 7, 2014

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

Re: Docket No. FDA-2012-D-0097: Revised Draft Guidance for Industry on Providing Regulatory Submissions in Electronic Format – Standardized Study Data; 79 Fed. Reg. 25 (February 6, 2014)

Dear Sir or Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) and the Biotechnology Industry Organization (BIO) filed comments in response to the Food and Drug Administration's (FDA's) Draft Guidance for Industry on Providing Regulatory Submissions in Electronic Format – Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act (Docket No. FDA-2014-D-0085).

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. PhRMA members have invested more than half a trillion dollars in the search for new treatments and cures, including an estimated $51 billion in 2013 alone.

BIO represents more than 1,000 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.

PhRMA and BIO believe that the comments filed to Docket No. FDA-2014-D-0085 are relevant to Docket No. FDA-2012-D-0097. Therefore, PhRMA and BIO respectfully request that these comments be considered in the FDA's review of comments on the Revised Draft Guidance for Industry on Providing Regulatory Submissions in Electronic Format – Standardized Study Data.

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

Respectfully Submitted,

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Scientific and Regulatory Affairs
PhRMA

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Director
Science and Regulatory Affairs
BIO

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Dear Sir or Madam:

The Pharmaceutical Research and Manufacturers of America (PhRMA) and the Biotechnology Industry Organization (BIO) submit these comments in response to the Food and Drug Administration's (FDA's) Draft Guidance for Industry on Providing Regulatory Submissions in Electronic Format – Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act.

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. PhRMA members have invested more than half a trillion dollars in the search for new treatments and cures, including an estimated $51 billion in 2013 alone.

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PhRMA and BIO appreciate the opportunity to comment on this draft guidance and welcome the Agency's efforts to clarify the process for implementing electronic submission requirements under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act (FDCA). In general, PhRMA and BIO agree with the FDA's interpretation of Section 745A(a) of the FDCA, but note there are some areas that require clarification prior to finalization of and implementation of this binding guidance. These areas requiring further clarification include (1) the process FDA intends to use to communicate and implement specific electronic submission requirements, specifically related to

revisions and updates to existing standards, and (2) the process for determining the timeline in which certain requirements will take effect.

To successfully implement Section 745A(a) of FDCA, it will be important that binding guidances and the standards and formats specified therein are clearly distinguishable from other non-binding guidances and documents. Therefore, in addition to the language included in the 745A(a) draft guidance that explains its binding nature, PhRMA and BIO recommend that the FDA include a comprehensive list of the guidances that are affected or delivered as a result of the binding provisions under Section 745A(a). If guidances are added or withdrawn from the list, PhRMA and BIO recommend that the Agency follow a formal process for public comment.

PhRMA and BIO remind the Agency of the importance of using the formal guidance process and public comment period before triggering requirements for use of any standard or format. While it is clear in Section D (lines 132 through 139) of the 745A(a) draft guidance that FDA intends to provide opportunity to comment on the first communication of a required electronic format requirement, FDA later indicates (lines 150 through 153) that revisions or updates to specified formats may be announced via the website and published in the *Federal Register*. Consistent with the spirit of the PDUFA V Goals Letter (Section XII), PhRMA and BIO believe that these revisions and updates are unlikely to have only minor impact on sponsors, and therefore should only be required after notice of availability of revised draft guidance and public comment period.

In Section F (lines 165 through 229) of the 745A(a) draft guidance, FDA states that it "does not interpret Section 745A(a) to impose a 24-month period before updates and corrections to an existing required electronic format can be implemented," and "subsequent revisions or updates to existing required format(s) may be implemented on a shorter timetable…" PhRMA and BIO are concerned that the Agency's interpretation of 745A(a)(2)(A), in the absence of clear definition of what constitutes a revision, update or correction and a transparent process by which to make this determination, presents a significant risk of confusion of requirements and timelines for implementation. The purpose of the formal guidance process specified in Section 1136 of FDASIA is to allow sponsors time to prepare for new requirements of a particular standard or format, including updated versions of existing standards. If FDA plans to implement a shorter timetable for certain revisions or updates, PhRMA and BIO urge the FDA define, in the 745A(a) draft guidance, the criteria by which revisions, updates, and corrections will be assessed for the ability to implement on an accelerated timeline. When defining these criteria, PhRMA and BIO strongly urge the FDA to consider the impact on sponsors, particularly as changes, even minor, in a standard may require the company's initiation of an impact assessment, development or purchase of new software (including validation of new systems and software), development of new processes, updates to data capture systems, additional training of personnel, re-work of components of submissions that had already been prepared, or all of the above. In general,

requirements should be implemented no earlier than 24 months after publication of a final guidance.

In the *Providing Regulatory Submissions in Electronic Format – Standardized Study Data* revised draft guidance, the FDA states that the *Federal Register* notice of availability will specify an effective date for all version updates that will correspond to a specific calendar month (lines 211 through 213). PhRMA and BIO appreciate the FDA's plan to align the effective dates of version updates, but PhRMA and BIO recommend that the FDA explicitly state in the Section 745A(a) draft guidance that all updates stemming from guidances subject to the binding provisions of Section 745A(a) will utilize the same effective date each year (*i.e.,* it is more appropriate to specify March in the Section 745A(a) draft guidance than in subsequent guidances such as Standardized Study Data).

PhRMA and BIO caution the FDA that there is a risk for confusion in the interpretation of when new requirements take effect after standards and formats are updated and/or corrected, or minor changes are made. The PDUFA V Goals Letter explicitly states that requirements to use a specified format shall be applied prospectively to studies starting 12 months or more after the publication of final guidance that specifies the standard or format. PhRMA and BIO request that the FDA clarify that the requirement for use of a particular standard or format at the time of submission is directly tied to the requirement that was in place at the time of study start. PhRMA and BIO remind the Agency that development programs often take 10 or more years, so there may be many years between the date of study start and submission. Therefore, FDA must be able to accept previously required standards for decades after the standard has been deprecated.

PhRMA and BIO remind the Agency of the provision in the PDUFA V Goals Letter that FDA must support previous versions of standards and formats for no less than 24 months after the effective date of a new standard or format and requests that the FDA make this explicit in the 745A(a) draft guidance. In certain examples within the draft guidance, such as Examples 3 and 4 on page 6 implementing minor changes, it is unclear that this provision is incorporated. In addition, it is unclear which party will be responsible for cataloguing standards and formats that were in place at the study start date. PhRMA and BIO request that the Agency clarify if they will take ownership of the catalogue, which sponsors can then reference in a submission; or if the current standards and formats at the study start date should be captured by sponsors.

The draft guidance (lines 177 through 180) states that "minor changes to a required format, such as corrections of typographical errors, may be implemented immediately or shortly after announcement of availability of the corrected format." While it may be appropriate to implement minor changes to standards on an accelerated timeline, the process by which a change to a standard is deemed a minor "update" or "correction" must be transparent and the timelines for implementation articulated in advance (*i.e.*, in the 745A(a) guidance). PhRMA and BIO note that in a regulated environment, even small changes will take time to implement. Sponsors will need

to conduct an impact assessment and will only implement changes to their systems and develop new processes after the assessment is completed. PhRMA and BIO caution the FDA that even changes that may seem minor, such as changes to a clinical trial data capture system, will have a significant impact on sponsors and may negatively impact the timely start of clinical trials. In addition to the conduct of an impact assessment, sponsors may have systems that require that a vendor implement the change, which adds additional time and resources.

In addition to clear criteria for evaluating the magnitude of a change and the timeline that it will follow for implementation, PhRMA and BIO urge the Agency to consider the maturity of the standard prior to implementation of requirements for use. PhRMA and BIO believe that a standard may not be sufficiently mature to warrant implementation of requirements if there is a need for frequent revisions, updates or corrections. PhRMA and BIO remind the Agency that much of the value of standardization is achieved through consistent, long-term use of a standard, and we request that the Agency use appropriate caution when considering adoption of versions of standards that are only minor improvements or corrections over an existing standard.

PhRMA and BIO appreciate the opportunity to submit these comments, and we hope that the Agency will find them helpful in the development of the final guidance to industry on providing regulatory submissions in an electronic format. As the Agency implements Section 745A(a) of the Food, Drug, and Cosmetic Act, PhRMA and BIO appreciate the FDA's efforts to adopt a predictable, clear, and consistent process that is used Agency-wide for communicating specific requirements for electronic submissions and data standards through use of the Federal Register, issuance of draft guidance for public comment, and issuance of final guidance.

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

Respectfully submitted,

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