Biotechnology Industry Organization

May 8th, 2013

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

Re: Docket No. FDA–2013-D-0349: Draft Guidance for Industry on Providing Postmarket Periodic Safety Reports in the International Conference on Harmonisation E2C(R2) Format (Periodic Benefit-Risk Evaluation Report)

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the "Draft Guidance for Industry on Providing Postmarket Periodic Safety Reports in the International Conference on Harmonisation E2C(R2) Format (Periodic Benefit-Risk Evaluation Report)." BIO commends FDA in releasing this Draft Guidance and taking steps toward international harmonization and efficiency in the safety reporting process.

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.

GENERAL COMMENTS:

In general, BIO finds this Draft Guidance on the PBRER to be very helpful to Sponsors who are already using, or transitioning to the PBRER in light of the International Conference on Harmonization (ICH) E2C(R2) step 4 guideline. The Draft Guidance answers many of the questions industry had regarding transitioning from the use of periodic adverse drug experience reports/ periodic adverse experience reports (PADERs/PAERs) to PBRERs. BIO seeks clarification on the following five issues:

1. Under the Draft Guidance a Sponsor that has a periodic safety update report (PSUR) waiver in place and wants to use a different data lock for the PBRER than was being used for the PSUR is given two options to ensure there are no gaps in reporting intervals. However, for Sponsors who do not have a PSUR waiver in place and are transitioning to the PBRER, if the data lock point is not the one aligned to the U.S. approval date, Sponsors are given an additional option: extending the reporting interval of the final PADER/PAER to close the gap. BIO requests that all three options are available in both instances.

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2. BIO suggests that FDA consider waivers for reporting intervals greater than one year (*i.e.* every 3 or 5 years). Doing so will allow Sponsors that do not have annual reporting requirements in the European Union (EU) to align and transition to the PBRER without reverting to the PADER/PAER in intervening years.

3. BIO encourages FDA to continue to accept Volume 9A PSUR and inter-PSUR Addendums in lieu of annual PADERs when there is an existing FDA-approved waiver in place if the Sponsor has not yet converted to using PBRERs. Additionally, BIO suggests FDA allowing such reports to follow the 70 and 90-day timelines to align with updated EU timelines.

4. In the past FDA has accepted non-expedited Individual Case Safety Reports (ICSRs) for PADER waivers via standard transmission procedures specified by the ICH Electronic Standards for the Transfer of Regulatory Information (ESTRI) Expert Working Group (M2), this Draft Guidance indicates that copies of these ICSRs would need to be included in the U.S. appendix to the PBRER. BIO requests that the Draft Guidance permits the continuation of submission of the ICSRs electronically with a statement only in the U.S. appendix to the PBRER indicating how the reports are being transmitted.

5. BIO suggests the page 3 Section C1 of the Draft Guidance be edited to read "A narrative that identifies any significant changes made to the approved U.S. labeling that occurred as a result of information obtained ~~based on new information~~ in the PSUR, as required under §§ 314.80(c)(2)(ii)(c) and 101 600.80(c)(2)(ii)(C), along with a copy of the most recent U.S. labeling." The ICH guideline states "such changes might include information relating to contraindications, warnings, precautions, ADRs, overdose, and interactions; important findings from ongoing or completed clinical trials and significant non-clinical findings (*e.g.* carcinogenicity studies)." BIO also suggests that this ICH definition of significant changes be incorporated into FDA's Draft Guidance for consistency and clarity across regulatory agencies.

CONCLUSION:

BIO appreciates this opportunity to comment on the "Draft Guidance for Industry on Providing Postmarket Periodic Safety Reports in the International Conference on Harmonisation E2C(R2) Format (Periodic Benefit-Risk Evaluation Report)." We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/

Andrew J. Emmett
Managing Director, Science & Regulatory Affairs
Biotechnology Industry Organization (BIO)