Biotechnology Industry Organization

July 22, 2014

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

Re: Docket No. FDA–2014-D-0363: Expedited Access for Premarket Approval Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Disease or Conditions; Draft Guidance for Industry and Food and Drug Administration Staff; Availability

Dear Sir/Madam:

The Biotechnology Industry Organization (BIO) thanks the Food and Drug Administration (FDA) for the opportunity to submit comments on the "Expedited Access for Premarket Approval Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Diseases or Conditions; Draft Guidance for Industry and Food and Drug Administration Staff."

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.

GENERAL COMMENTS:

In general, BIO finds the Draft Guidance to be very insightful and well written, providing useful examples and references to illustrate the important principles underlying most sections. In particular, the discussion of clinical, intermediate, composite, and surrogate endpoints, including their utility during development and their respective pre- and post-market data burdens, is helpful to Sponsors developing premarket approval (PMA) medical devices with the potential to address unmet medical needs for life threatening or irreversibly debilitating diseases or conditions.

Indeed, the Center for Devices and Radiological Health (CDRH) and Center for Biologics Evaluation and Research (CBER) are to be commended for crafting a draft guidance document that discusses in detail the rationale behind the Data Development Plan and the approach to benefit-risk for qualified Expedited Access PMA (EAP) devices, rather than simply the eligibility criteria and benefits of the EAP program, itself. There are several areas, however, for which BIO believes additional elaboration by the Agency would add value to the Draft Guidance document and, ultimately, the EAP Program.

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A. Additional Details on EAP Processes and Broadening of Scope

BIO believes that a central challenge for CDRH in developing the EAP Program will be to avoid putting processes in place that add more layers of review and requirements to the existing PMA process, but rather to establish processes that successfully streamline the PMA process for qualified EAP devices. While regulatory flexibility should be applied on a case-by-case basis, BIO requests additional details about the interactions available between FDA and Sponsors of EAP devices, including when in development or review they could occur. Such clarity would greatly inform how "FDA intends to engage with sponsors of EAP Devices earlier and more interactively during the device's development, assessment and review" and would help to avoid creating duplicative processes and additional layers of review and requirements. BIO is particularly interested in additional details about the interaction between the Sponsor and FDA to support the development of the Data Development Plan. Additionally, BIO believes that the inclusion of timeframes in *Attachment 1: Expedited Access PMA Process* would be helpful to Sponsors in planning for development of potential EAP devices.

Related to the scope of the program, BIO believes there would be value in expanding the Expedited Access program to include devices subject to 510(k) submission, or to develop a similar program that could accommodate these products, and encourages FDA to investigate this option. BIO believes that FDA should also outline how the EAP program, in complement to or in lieu of the Humanitarian Device Exemption (HDE) program, could help ensure a faster path to market for devices intended to address orphan indications.

B. Considerations for Companion Diagnostics

BIO strongly believes that additional details about how this guidance would apply to companion diagnostics would significantly help Sponsors prepare their drug/biologic and device applications and would potentially ensure coordinated and expedited access to drugs/biologics and devices. The benefit-risk determination criteria for a companion diagnostic (section III.C) can differ substantially from the criteria for an interventional medical device, as the benefit-risk of the companion diagnostic is inextricably linked to that of its accompanying drug or biologic therapy. As such, and given the implications of this guidance for companion diagnostic review and approval, BIO urges the Agency to clarify and expand the Companion Diagnostic Considerations section as a whole.

Specifically, BIO requests that CDRH clarify that EAP status will be granted for all companion diagnostics used in conjunction with drug and biologic therapies undergoing any expedited development through the Center for Drug Evaluation and Research (CDER)/CBER. Automatic EAP status for these companion diagnostics would enable the relevant offices at CDER, CBER, and CDRH to have earlier discussions regarding post-approval diagnostic/drug rollout plans and would facilitate a more timely review. This coordinated review would significantly assist with aligning decisions that affect both the companion diagnostic and the drug or biologic. Toward this end, BIO strongly encourages FDA to develop and publish a harmonized, multicenter (*i.e.*, CDER, CBER, and CDRH) guidance covering co-development of companion diagnostic products, which,

in addition to a detailed outline for highly coordinated administrative processes and management commitments for the review of companion diagnostics, should also harmonize the standards for Expedited Access designation and approval across centers.

C. Considerations for Combination Products

Similarly, neither this draft guidance, nor FDA's *Guidance for Industry on Expedited Programs for Serious Conditions – Drugs and Biologics,*[1] addresses or references combination products. With advances in new delivery technologies, there are an increasing number of opportunities for sponsors to develop combination products (*i.e.*, drug/device or drug/biologic) to address serious, life-threatening diseases. To that end, BIO encourages FDA to clarify, in both guidance documents, that for combination products wherein the drug or biologic is intended to treat a serious condition and qualifies for an expedited program, the device portion of the product automatically qualifies for the EAP program. Conversely, when the device component of a combination product is deemed to qualify for the EAP program, the drug or biologic portion should also be designated for an expedited development pathway. To achieve this, BIO strongly encourages FDA to include a section in the previously requested multicenter guidance covering co-development of combination products. BIO also encourages FDA to provide details on the approach to benefit-risk and the Data Development Plan unique to combination products.

CONCLUSION:

BIO appreciates this opportunity to comment on the "Expedited Access for Premarket Approval Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Diseases or Conditions; Draft Guidance for Industry and Food and Drug Administration Staff." Specific, detailed comments are included in the following chart. We would be pleased to provide further input or clarification of our comments, as needed.

Sincerely,

/S/

Paul Sheives, J.D.
Director, Diagnostics and Personalized Medicine
Biotechnology Industry Organization

/S/

Andrew W. Womack, Ph.D.
Director, Science & Regulatory Affairs
Biotechnology Industry Organization

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[1] FDA Guidance for Industry on *Expedited Programs for Serious Conditions – Drugs and Biologics*, available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf

SPECIFIC COMMENTS

SECTION	ISSUE	PROPOSED CHANGE
III. EXPEDITED ACCESS PMA		
Lines: 219-222:	BIO believes FDA should clarify that EAP Devices may provide a breakthrough technology over currently available ***approved or cleared*** devices (*i.e.*, devices approved under PMAs or cleared under 510(k)s).	BIO recommends that FDA revise to read: "For example, EAP Devices may offer a potential for clinically meaningful benefit as compared to existing alternatives (preventative, diagnostic, or therapeutic) or provide a breakthrough technology over currently available approved or cleared devices for patients with life threatening or irreversibly debilitating diseases or conditions."
A. CRITERIA FOR EXPEDITED ACCESS PMA DESIGNATION		
Lines 269-271:	BIO believes that the EAP criteria should be clear and equally applied in order to provide predictability and credibility to the program.	BIO requests FDA revise to read: "…would meet the EAP criteria. ~~However, even if a device meets the EAP criteria, FDA still has discretion over whether to grant the device the EAP Designation.~~ When determining whether…"
Lines 287-289:	BIO believes this sentence should be written to include diagnostic devices in its scope.	BIO requests FDA revise to read: "FDA also intends to consider devices that have a specific intended use to cure, detect, mitigate, or prevent a life-threatening or irreversibly debilitating disease or condition."
Lines 327-329:	BIO believes that outlining the points of consideration whereby FDA will determine whether an approved EAP Device for which the confirmatory post-approval studies have not been completed can be considered an "alternative treatment"	BIO requests that FDA, in order to ensure more consistent and fair evaluation across devices and situations, outline the points of consideration whereby the Agency will determine whether an approved EAP Device for which the confirmatory post-approval studies have not been completed can be considered an "alternative treatment" for

SECTION	ISSUE	PROPOSED CHANGE
	would ensure more consistent and fair evaluation across devices and situations.	purposes of EAP designation.
Lines 331-333:	BIO believes this sentence should be written to include devices cleared under 510(k)s, as well as diagnostic devices, including *in vitro* diagnostics (IVDs), in its scope.	BIO requests FDA revise to read: "There may be a substantial number of approved or cleared medical products with varying relevance in the current diagnosis and/or treatment ~~treating~~ of a life-threatening or irreversibly debilitating disease in the U.S., including devices that are no longer used or used rarely."
B. FEATURES OF EXPEDITED ACCESS PMA		
Lines 464-465:	As eligibility criteria for both the EAP Program and Priority Review of Premarket Submissions for Devices[2] are defined by section 515(d)(5) of the Federal Food, Drug, and Cosmetic Act, BIO believes that the PMA for all EAP devices should, by definition, receive priority review.	BIO requests that FDA revise to read: "~~FDA expects that t~~The PMA for an EAP Device will receive priority review under 515(d)(5) of the FD&C Act." BIO also requests that FDA provide benchmarks for standard and priority review periods.
D. TYPES OF CLINICAL EVIDENCE THAT MAY SUPPORT PMA APPROVAL OF EAP DEVICES		
Lines 543-546:	BIO believes that developing evidentiary standards for FDA qualification of Medical Device Development Tools (MDDTs) would provide much needed clarity to MDDT developers and would greatly benefit the finalized guidance document.	BIO encourages FDA to finalize the *Draft Guidance on Medical Device Development Tools* and, as part of that process, to work with stakeholders to develop evidentiary standards to support qualification of MDDTs for specific contexts of use. BIO encourages FDA to include or cross-reference these evidentiary standards in Sections VI.A.

[2] *FDA Guidance for Industry and Food and Drug Administration Staff on Priority Review of Premarket Submissions for Devices*, available at: http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089698.pdf

SECTION	ISSUE	PROPOSED CHANGE
		(Lines 418-420) and/or VI.B.3. (Lines 446-482) of the final guidance document.[3]
ATTACHMENT 1 – EXPEDITED ACCESS PMA PROCESS		
III. FDA RESPONSE		
Lines 1054-1055:	BIO believes this passage conflicts with an earlier statement made on lines 950-955 ("...FDA intends to be reasonably flexible about the timeframe for completing a post-approval study and submitting data to the Agency…"). BIO believes this previous statement better acknowledges the difficulties in providing a single benchmark for post-approval study completion for the diversity of EAP Devices, which may include companion diagnostics. The post-approval study for a companion diagnostic may be the same as that of the corresponding therapeutic; the timeline for its completion depends on the characteristics of the clinical study design, including the endpoints.	BIO recommends FDA revise to read: "Completion of the required post-approval study should occur within the timeframe specified in the approval order. This ~~should generally occur no later than three years after PMA approval, but~~ may vary depending on the device type and the type of post-approval study."

[3] *FDA Draft Guidance for Industry, Tool Developers, and Food and Drug Administration Staff on Medical Device Development Tools*, available at: http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM374432.pdf