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

Reference: Docket No. FDA-2023-D-5021 for "FDA Draft Guidance Processes and Practices Applicable to Bioresearch Monitoring Inspections, Request for Comments."

Dear Madam or Sir,

PDA appreciates the opportunity to provide feedback to the FDA as the agency develops and establishes best practices for the efficient prioritization, development, issuance, and use of guidance documents. In our attached comments, PDA offers specific comments and feedback that we believe will be helpful in further developing this program.

PDA is a non-profit international professional association of more than 10,000 individual members scientists having an interest in fields of pharmaceutical, biological, device manufacturing, and quality. Our comments have been prepared by a committee of PDA members with expertise in the areas covered in the Public Docket on behalf of PDA's Regulatory Affairs and Quality Advisory Board.

If you have any questions, please do not hesitate to contact me via email at wright@pda.org.

Sincerely,

Glenn E. Wright
President and CEO

cc. Josh Eaton, PDA; Carrie Horton, PDA;

PDA Member response to: FDA Draft Guidance on Processes and Practices Applicable to Bioresearch Monitoring Inspections (Docket: No. 2023-D-5021)

Responses to "FDA Draft Guidance Processes and Practices Applicable to Bioresearch Monitoring Inspections."

II. BACKGROUND pg. 2-3

Line #	Referenced Text	Comment / Suggestion
42-44	"The program assesses compliance with statutory requirements and FDA's regulations governing the conduct of nonclinical and clinical studies, and applicable postmarketing activities (e.g., in REMS and PADE).[9]"	The guidance document does not include information about the multiple levels and responsibilities of the BIMO investigators, including PHS personnel. PDA recommends adding text after line 44 about the different levels of BIMO investigators (Certified BIMO, Specialists, Program and National Experts, Dedicated Foreign Cadre, Foreign Office detailees). Including a brief note about PHS Commissioned Corps investigators (in uniform in domestic inspections). PDA believes this will assist the industry in understanding the range of experiences and qualifications of the BIMO investigators.
50-59	Specifically, in clarifying the Agency's BIMO inspection authority, section 704(a)(5) includes, among other things, the following: • the establishments subject to BIMO inspection, e.g., those used by sponsors in connection with developing an application or other submission to FDA for marketing authorization, or those conducting a study related to such an application or submission; and • the records and other information that may be inspected, e.g., information related to the conduct, results, and analyses of studies, including those involving human trial participants or animal subjects.	PDA recommends a brief explanation of the impact of the clarification on BIMO inspection processes and communication.

II. BACKGROUND pg. 2-3 (continued)

Line #	Referenced Text	Comment / Suggestion
72-79 Footnotes 14 & 15	RRAs under the BIMO Program may consist of: (1) Remote Interactive Evaluations and (2) requests for records or other information under section 704(a)(4) of the FD&C Act from sites and facilities subject to inspection under section 704(a)(5)(C)(i) (i.e., establishments subject to BIMO inspections) in advance of or in lieu of such inspections.[15]"	*PDA proposes to add additional text in bold to add clarity.* "RRAs under the BIMO Program may consist of: (1) Remote Interactive Evaluations[14] and (2) requests for records or other information under section 77 704(a)(4) of the FD&C Act from sites and facilities subject to inspection under section 704(a)(5)(C)(i) (i.e., establishments subject to BIMO inspections) in advance of or in lieu of such inspections.[15]" **As RRAs are not considered inspections by FDA, they are not within the scope of this guidance. The Draft RRA Guidance notes that the Agency does not intend to conduct an RRA at the same time as an inspection, the Draft RRA Guidance provides information about communications between industry and FDA during an RRA that may be relevant for communications during an inspection.**"
34-80	Background	The guidance does not have information about the Division of Field Investigations (DFI) processes regarding foreign inspections. This addition will clarify that foreign inspections are handled differently from domestic inspections. PDA proposes to add this language, which is currently in https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/foreign-inspections/chapter-1-international-inspection-program#SUB100: "The international inspection program is managed by the Division of Field Investigations (DFI), Office of Regional Operations within the Office of Regulatory Affairs. Within DFI, the day-to-day operations regarding international inspections, global harmonization, and related international activities are performed by the International Operations Branch (IOB)."

III. PROCESSES AND PRACTICES APPLICABLE TO BIORESEARCH MONITORING INSPECTIONS pg. 4

A. BIMO Processes and Practices pg. 4-5

Line #	Referenced Text	Comment / Suggestion
139-140	"FDA statutory and regulatory requirements (e.g. with respect to bioresearch inspections – to help ensure trial participant safety, and to evaluate data reliability)."	PDA proposes to add additional text in bold to add clarity. "…bioresearch inspections – to help ensure trial participant safety, to evaluate data reliability, and **to ensure adequate investigational product handling)**." Drug accountability, drug shipping and storage conditions, and control over unauthorized use are all part of CI, Sponsor, BEQ, and GLP inspections

C. International Inspections pg. 5-6

Line #	Referenced Text	Comment / Suggestion
155-156	"For domestic inspections, a notice of inspection (**e.g., Form FDA 482**[20]) is issued at the time of inspection."	PDA proposes adding the bold text below for clarity. "For domestic inspections, a **written** notice of inspection **(**e.g., Form FDA 482 **"Notice of Inspection"** [20]) is issued at the time of inspection." PDA is requesting clarity on whether the guidance is meant to refer to "written" notices of inspection in general, with Form FDA 482 as the typical, official form.
163-165	"FDA also collaborates with certain international regulatory partner agencies to conduct joint inspections, observe inspections, share inspection information and develop policy.[25]"	PDA proposes to add additional text in bold to add clarity. "FDA also collaborates with certain international regulatory partner agencies, **such as local regulatory authorities,** to conduct joint inspections, observe inspections, share inspection information, and develop policy."
165-166	"This collaboration is important to the BIMO program."	PDA suggests clarifying this statement for a reader to better understand why collaboration is important to the BIMO program.

IV. BEST PRACTICES FOR COMMUNICATION BETWEEN THE FDA AND INDUSTRY IN ADVANCE OF, DURING, OR AFTER AN INSPECTION pg. 6-7

A. Pre-announcement Notice and Communication pg. 6

Line #	Referenced Text	Comment / Suggestion
195-198	"FDA believes that an establishment's failure to acknowledge the pre-announcement notification should not be a reason to delay the start of an inspection. This pre-announcement notification should be provided within a **reasonable time** before the inspection is scheduled to occur."	PDA would ask the FDA to consider defining "within a **reasonable time.**" A more precise definition of "reasonable time" would help ensure consistency in preannouncements and equal treatment of all firms. We suggest aligning with Section 5.2.6.1 – Criteria for Consideration of the current IOM. "The pre-announcement of domestic inspections should generally be no less than five calendar days in advance of the inspection."

D. Communication After An Inspection pg. 8-9

Line #	Referenced Text	Comment / Suggestion
236-277	"For foreign inspections, if the establishment chooses to respond in writing to the observations discussed or listed on the Form FDA 483, the response should be addressed to the FDA center point of contact (POC) provided by the investigator."	PDA would suggest providing clarity on best practices for foreign inspection communication similar to domestic inspections. Related to the submission of Responses for Form FDA 483, suggest clarifying whether the process allows for confirmation of electronic receipt of a Response submitted by email.

E. Who to Contact at FDA for More Information? pg. 9

Line #	Referenced Text	Comment / Suggestion
284-285	"Questions about the inspection classification[38] can be directed to the FDA center POC identified in the post inspection correspondence or in the relevant compliance program."	PDA is proposing that the FDA should set a target timeframe in which they will be communicating the inspection outcome.

About PDA Regulatory Commenting

PDA submits comments to regulatory agencies and pharmacopeial bodies when draft guidance or legislation is issued for public comment. Members of the PDA community work together to provide feedback regarding the content to ensure a broad industry perspective is presented and considered for inclusion or revision of the draft document.

PDA Regulatory Commenting documents are consensus documents, prepared by member-driven teams (listed below) comprised of content experts, including scientists and engineers working in the pharmaceutical/biopharmaceutical industry, regulatory authorities and academia.

The final working draft is reviewed by the PDA Advisory Board(s) aligned to the PDA Commenting Effort subject matter. PDA's four Advisory Boards are classified as Science, Advanced Therapy Medicinal Products, Biopharmaceuticals, and Regulatory Affairs and Quality.

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