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Date: February 2, 2022

Dockets Management Staff
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Remote Interactive Evaluations of Drug Manufacturing and Bioresearch Monitoring Facilities During the COVID-19 Public Health Emergency: Guidance for Industry (Docket FDA-2020-D-1136-0057)

Dear Madam or Sir:

The Parenteral Drug Association (PDA) appreciates the opportunity to comment on the Guidance for Industry on Remote Interactive Evaluations of Drug Manufacturing and Bioresearch Monitoring Facilities During the COVID-19 Public Health Emergency.

PDA supports the concept of remote interactive evaluations (RIEs) and thanks FDA for providing more information about the process for these assessments. We understand that FDA's perspective is that RIEs cannot serve formally as "inspections," and our comments reflect that perspective.

After reviewing the guidance, and based on experience and its anticipated continued use, we have identified several areas in which FDA could provide additional information or guidance to industry, to further assist regulated sites to efficiently and effectively prepare for and respond to RIEs. This additional clarity can improve the performance of RIEs for both industry and the agency.

We provide our detailed suggestions in the attached comment table. Three of the themes raised in the attachment are of special significance:

1. Notice and Preparation

Because preparation is key to a successful remote assessment, PDA strongly encourages FDA to provide more information about the amount of notice that it will give sites in advance of an RIE. We encourage FDA to provide notice as far in advance as possible. As described in our recent PDA *Points to Consider in Remote and Hybrid GMP/GDP Inspections*, advance notification is necessary to allow the inspected site to prepare on-site and remote personnel, resources, and logistics, including the video communication platform and document-sharing platform.

2. Report and Observations

PDA members have a number of questions about the report and observations from an RIE, and request clarity on several topics as detailed in the attachment. Members seek

additional insights into the format and content of the report and the format for the observations. They also seek clarity on how observations made during this assessment, since it is not an inspection, will be reflected in the next inspection performed. While PDA supports FDA in its use of remote tools, additional clarity would be helpful in preventing confusion and/or misunderstanding by the agency staff as well as the staff of the site being assessed.

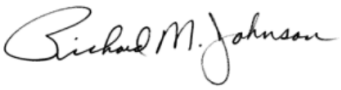
3. Livestream Video

Footnote 10 of the document states that CBER usually will expect facilities to provide livestream video of manufacturing operations during RIEs supporting pending biologics license applications. For the reasons more fully described in the attachment, PDA asks that CBER exercise patience in its discussions with facilities about these livestream videos, and accept prerecorded videos when necessary due to the manufacturing schedule or facility limitations. PDA would be happy to discuss further with FDA the provisions that could be put in place to ensure that prerecorded videos accurately reflect the facility's status.

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

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

Sincerely,



Richard Johnson
President and CEO

CC: Glenn Wright, PDA

U.S. Food and Drug Administration
Remote Interactive Evaluations of Drug Manufacturing and Bioresearch Monitoring Facilities During the COVID-19 Public Health Emergency: Guidance for Industry
14 April 2021

Section No.	Current Text	Comment / Suggestion
General	None	Regarding the remote interactive evaluations (RIEs), the metrics and data on observations would be very helpful to industry even if they were to be reported separately from inspections. PDA would suggest that the FDA develop a reporting process for this information. Similarly, PDA encourages FDA to discuss RIEs with other global health authorities with which it has a mutual recognition agreement covering inspections. While the RIE is not an inspection, the final report is likely to be useful to those health authorities.
III.A. page 7	"We will not accept requests from applicants or facilities for FDA to perform a remote interactive evaluation. Such decisions depend on many factors and information not always known to applicants or facilities, and it would be too burdensome on all parties to establish a request-based program."	While FDA will not accept request for applicants it might be helpful if FDA creates a method for companies to indicate that they are open to RIEs. As travel becomes safer again, some facilities may have a strong preference for on-site assessments.
III.A. page 7	"Correspondence or phone contact will include a request for confirmation of the facility's willingness and ability to participate in a remote interactive evaluation, including the use of teleconference, livestream video, and screen sharing of data and documents." "FDA will also work with facilities to procure information necessary to plan and coordinate the activities for a remote interactive evaluation. The facility should meet these requests or inform FDA of any challenges in meeting these requests as soon as possible."	For improved planning, it would be helpful if FDA could provide general information about timing for the different steps of a remote interactive evaluation. How much notice does FDA hope to provide?
III.A. page 7	"Declining FDA's request to perform a remote interactive evaluation could impede our ability to make	For clarity, PDA encourages FDA to state explicitly that declining the request will not constitute an inspection refusal. Without this clarity in

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	a timely regulatory decision (e.g., regarding adequacy of a clinical trial used in support of a pending application or adequacy of a drug manufacturing operation described in the application)."	the language the possibility of misinterpretation by both members of the industry and agency over time could occur.
III.A. page 8	"The prioritization of facilities, domestic and foreign, for remote interactive evaluations will follow the same risk-based approach currently used by FDA for surveillance inspections.[8] … [8]See, for example, the risk-based approach described in MAPP 5014.1 Understanding CDER's Risk-Based Site Selection Model, available at https://www.fda.gov/media/118214/download."	PDA recommends that FDA either revise the MAPP 5014.1 or create an additional MAPP to address the second risk assessment that is necessary for RIEs. While FDA can use the existing MAPP to determine whether the facility is high priority for assessment, FDA also will want to consider whether the facility is a good fit for a remote assessment. This may involve different factors than are considered for prioritization. For example, FDA may consider some product types, manufacturing activities, or dosage forms to be more conducive to remote assessments, while the manufacturing of others may, in FDA's view, require the presence of an investigator in the building.
IV. page 10, fn 10	"[10]For a remote interactive evaluation supporting a pending biologics license application, FDA usually will expect a facility to provide for livestream video of the manufacturing operations described in the application."	PDA recommend that FDA expands on the circumstances in which it would or would not expect live video of the manufacturing operations to be provided. PDA notes that the ability to provide live manufacturing video from a batch manufacturing facility will depend on the timing of the RIE. If FDA expects to see live, real-time video of manufacturing, the manufacturing schedule will need to be considered during the scheduling of the RIE. Changes to the manufacturing schedule are likely to have follow-on effects, including changes to the forecast supply and distribution schedules, as well as changes to the schedules for other products that use the same manufacturing line and/or staff. Even so, since some companies will not be manufacturing on an ongoing basis before approval, it would be helpful if FDA would consider accepting pre-recorded video in some circumstances.

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		Certainly, pre-recorded videos also present challenges for both the agency and manufacturer. PDA would be happy to discuss further with FDA the provisions that could be put in place to ensure that the prerecorded video reflects the current status. Other considerations, including the time required to obtain approvals internally within the inspected company, could be discussed at the time of the request. In seeking video, PDA also recommends FDA includes language related to working with the company as it navigates the data privacy concerns that may be present, particular in the application of the General Data Protection Regulation (GDPR). Due to GDPR, companies may need to take additional steps before any employee appears in a video that will be recorded. These steps may require additional time and consideration. Finally, if possible, it would be helpful if FDA could expand on this statement to describe the potential consequences for a site that is not able to provide video that meets CBER's needs.
IV.B. page 11	"However, we may request additional documents and other information, including video recordings, at any time during the remote interactive evaluation to address questions and to explain observations."	It would be helpful for industry if FDA could include examples of the types of video content the agency is thinking of.
IV.B. page 11	"However, if translation is needed during a livestream interaction, the facility may need to provide a translator."	PDA supports the agency's approach to live translation, as stated here, as the inspected facility may have easy access to appropriate and qualified live translation services. PDA does note, however, that this language is significantly different from the related language in the bioresearch monitoring (BIMO) Compliance Program document, which specifies that FDA will be responsible for coordinating translation services. (Food and Drug Compliance Program, Chapter 48 – Bioresearch Monitoring, Clinical Investigators and Sponsor-

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		Investigators, § III.S.2, July 22, 2020, available at https://www.fda.gov/media/75927/download) PDA recommends that FDA update the BIMO compliance document to match the language in this new guidance, as this approach could reduce burdens on the agency.
V. page 12	"This written list of observations will not be a final Agency action or decision. … As with an inspection, FDA encourages facilities to respond during the discussion and/or provide responses in writing to the observations within 15 U.S. business days."	PDA suggests that FDA consider clarifying in the guidance the status and impact of the observations. If the observations are not final Agency action or decision, what is their status? PDA also suggests that FDA expand on the potential consequences to the facility, if any, if it does not respond within 15 days.
V. page 12	"After the remote interactive evaluation concludes, FDA will provide a copy of the final remote interactive evaluation report to the facility."	While PDA understands this is an evolving area. PDA suggests that FDA provide more detail about what this report will include and how it will be used, to help ensure that this will be efficient and effective for both agency and facility. Will the report be used to address facility status? Availability of the Certificate of Pharmaceutical Product (CPP)? Will it describe whether a follow-up on-site inspection will be necessary? Will it address the GMP status of the facility? Will it use the same language that is used in "smart 483s"? Will it be listed in the Inspection Classification Database search engine? Any additional detail would help industry to know what to expect.
V. page 12, fn 13	"[13] If the remote interactive evaluation, including the review of any records before or during the evaluation, is intended to supplement a scheduled inspection, then FDA usually will combine any observations from the remote interactive evaluation(s) into a single written list of observations issued at the close of the inspection, which would be issued on a Form FDA 483, Inspectional Observations."	PDA recommends that additional language be added to indicate in more detail how observations made during the RIE will be treated in regard to the final FDA Form 483. As an example, how will observations made during the RIE, but corrected or adequately responded to before the beginning of the inspection, be treated in the final FDA Form 483?

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		PDA recommends that in such cases where an observation has been made during the RIE and corrected, or adequately responded to, before the beginning of the inspection, the observation should not be included in the final FDA Form 483. In regard to the timing of the RIE and subsequent inspection. To allow the facility to respond to the RIE, PDA recommends language be added that provides at least 15 business days, when possible, between the time the RIE observations are provided and the time the subsequent inspection occurs.