

September 23, 2022

Lauren K. Roth
Associate Commissioner for Policy
Food and Drug Administration, Dockets Management Staff
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

**RE: ACRO comment submission on:
Conducting Remote Regulatory Assessments—Questions and Answers; Draft Guidance for Industry
[Docket No. FDA-2022-D-0810]**

Dear Ms. Roth,

The Association of Clinical Research Organizations (ACRO) represents the world's leading clinical research and technology organizations. Our member companies provide a wide range of specialized services across the entire spectrum of development for new drugs, biologics and medical devices, from pre-clinical, proof of concept and first-in-man studies through post-approval and pharmacovigilance research. ACRO member companies manage or otherwise support a majority of all FDA-regulated clinical investigations worldwide. The member companies of ACRO advance clinical outsourcing to improve the quality, efficiency, and safety of biomedical research.

ACRO welcomes the opportunity to provide the following general and line-specific comments.

General Comments:

Since the Remote Regulatory Assessment (RRA) process was introduced during the COVID-19 pandemic, the absence of formal guidance on the program has created some confusion and concern for FDA-regulated establishments. ACRO supports the concept of appropriate risk-based remote assessments and therefore appreciates the Agency's efforts to provide some much-needed clarity. However, we believe there is an opportunity for the Agency to provide additional clarity in the final guidance.

We recognize that FDA is constrained by definitions in law such that the conduct of an RRA does not qualify as an inspection. But, for all practical purposes other than the onsite attendance by FDA and inspection reporting required by law, the approach to an RRA is essentially the same as that to an inspection. In comparison with the detailed guidance available on inspections across all FDA Centers (e.g., <https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/inspection-guides>), the information currently provided in the draft Questions-and-Answers could provide more detail to assist both FDA assessors and assessed entities. We recognize that the exact requirements of an RRA process will differ between FDA programs and Centers (for instance, ensuring protection of personal data during remote access will be of much greater concern during an RRA of a clinical investigator than during an RRA of a manufacturer of an FDA-regulated product). For this reason, and to provide the clarity that assessed entities need, we ask the Agency to consider expanding the draft Questions-and-Answers document to include additional sections that set out the essential process and principles for the conduct of an RRA – including the following content that discusses:

- FDA assessment of the feasibility and scope of an RRA
- initial contact with the entity to be assessed
- agreement on timelines and access/technology requirements
- opening meeting
- conduct of the assessment
- closing meeting
- reporting of the RRA conclusions to the assessed entity
- agreement on timelines for responses to findings
- close-out of the RRA

In addition, we strongly encourage FDA to consider including appendices to the Q&A that address methodological considerations for specific types of RRA. For example, in the biopharmaceutical area, separate dedicated appendices on the conduct of RRAs for assessing compliance with GMP, GLP, GCP and GPhVP requirements would be helpful.

Line-Specific Comments:

Line 224-227:

The draft guidance currently states: *“FDA will use a risk-based approach to determine whether to initiate or request an RRA. Factors that may be considered include, but are not limited to, firm location, inspection history, complexity of product and process, and travel restrictions. Programs and centers within FDA may assess risk differently based on the product.”*

ACRO fully supports the use of a risk-based approach and recommends that, within the examples of factors taken into account, the feasibility of conducting an RRA should be listed. We also recommend that the expanded Q&A confirms that the lead assessor will take a risk-based approach to define the scope of the RRA, and that the word “firm” is deleted to take account of individuals such as clinical investigators, who may be subject to an RRA. In the specific case of clinical investigators, we also recommend that the feasibility assessment should ensure that the RRA will not place any undue additional burden on the investigator site and must not impact routine clinical care of patients. Furthermore, given the potential remote access to confidential patient information, we recommend strongly that the final Q&A guidance should stress that expectations for the protection of personal data must be taken into account.

We ask the Agency to consider the following alternative language for the final guidance:

FDA will use a risk-based approach to determine whether to initiate or request an RRA. Factors that may be considered include, but are not limited to, location, inspection history, complexity of product and process, travel restrictions, expectations for the protection of personal data, and the feasibility of conducting an RRA. A risk-based approach will also be taken by the FDA’s lead assessor to define the scope of the RRA. Programs and centers within FDA may assess risk differently based on the product. When an RRA of a clinical investigator is planned, the FDA’s risk-based feasibility assessment will ensure that the RRA will not place any undue additional burden on the investigator site and will not impact the routine clinical care of patients or patient-investigator confidentiality.

Lines 287-290:

The current text in the draft guidance states: *“FDA correspondence or phone contact will include a request that the establishment’s top management official at the site, or their senior designee, provide written confirmation of the establishment’s willingness and ability to participate in the type of RRA requested.”*

We recommend that the final Q&A guidance should make clear that this initial contact will clearly define the scope of the requested RRA and asks the Agency to consider the following alternative language for the final guidance:

FDA correspondence or phone contact will include a request that the establishment’s top management official at the site, or their senior designee, provide written confirmation of the establishment’s willingness and ability to participate in the requested RRA. The FDA’s request will clearly define the type and scope of the planned RRA.

Lines 291-294:

The draft guidance states: *“Following the establishment’s written agreement to participate, subsequent to or during our initial contact, we will work with the establishment to schedule virtual interviews and meetings, confirm technological capabilities, and request records or other information for review, as appropriate.”*

The initial contact person may not be the most appropriate person within the establishment to undertake these tasks in preparation for the RRA. Consequently, we recommend strongly that the words “or during” be deleted from this sentence. Also, there are many other considerations beyond those listed here that need to be addressed in preparation for an RRA, especially where an overseas facility is concerned, and these should also be included in the final Q&A guidance. Therefore, we ask FDA to consider the following alternative language for the final guidance:

Following the establishment’s written agreement to participate, subsequent to our initial contact, we will work with the establishment to schedule virtual interviews and meetings, confirm technological capabilities, and request records or other information for review, as appropriate. Additionally, access to necessary systems and databases, whether directly by the FDA assessor or facilitated by the establishment’s staff, and including access to third-party systems and databases when appropriate, will be specified. If one or more video tours is considered necessary, the FDA assessor will confirm whether these may be pre-recorded or should be live-streamed. Establishments may find it helpful to involve appropriate IT staff in these early discussions in order to ensure the smooth conduct of the RRA. Additionally, in the case of establishments outside the USA, the need for interpreter services and complexity of time zone considerations will be addressed.

Line 320-321:

The draft guidance states: *“FDA may provide updates to the establishment on observations and outstanding issues, whenever feasible, throughout the RRA.”*

We recommend strongly that the word “may” is changed to “will” as this communication will facilitate the resolution of potential misunderstandings and issues during the RRA. We suggest that the final guidance state: *FDA will provide updates to the establishment on observations and outstanding issues, whenever feasible, throughout the RRA.*

Line 416-418:

The draft guidance states: *“Where applicable, FDA will take appropriate efforts to minimize the quantity of records or other information requested and may request that establishments take reasonable efforts to facilitate and expedite FDA’s collection and review of other records. See questions 14 and 15 for additional details.”*

We believe it would be helpful for establishments to know, and strongly recommend that the final Q&A notes, that documents provided under an RRA may be subject to disclosure under the Freedom of Information Act so that establishments may wish to redact personal and commercially confidential information before providing documents to FDA. We suggest the following text for the final guidance:

Where applicable, FDA will take appropriate efforts to minimize the quantity of records or other information requested and may request that establishments take reasonable efforts to facilitate and expedite FDA’s collection and review of other records. See questions 14 and 15 for additional details. Documents provided under an RRA may be subject to disclosure under the Freedom of Information Act, therefore establishments may wish to redact personal and commercially confidential information before providing documents to FDA.

Line 441-442:

The draft guidance currently states: *“For voluntary RRAs, FDA may suggest timeframes to ensure the RRA is completed in a reasonable amount of time and expects establishments to work diligently to provide the requested records.”*

Rather than “FDA may suggest timeframes”, we recommend the final Q&A should state that FDA will agree to timeframes with the establishment so that the final guidance would state: *For voluntary RRAs, FDA will agree to timeframes with the establishment to ensure the RRA is completed in a reasonable amount of time and expects establishments to work diligently to provide the requested records within the agreed timeframes.*

Line 480:

The draft guidance states: *“Upon completion of an RRA, FDA may have a meeting with the establishment’s management.”*

It is important that both parties are clear on the outcome of the RRA. We therefore recommend strongly that the word “may” is changed to “will” so that the final guidance would state: *Upon completion of an RRA, FDA will have a meeting with the establishment’s management.*

ACRO thanks the Agency for the opportunity to provide input on the draft Questions-and-Answers. Please do not hesitate to contact ACRO (knoonan@acrohealth.org) if we can provide further detail.

Respectfully submitted,



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