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ASSOCIATION OF CLINICAL RESEARCH ORGANIZATIONS

February 28, 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 Food and Drug Administration [Docket No. FDA–2021–D–1146] ***Real-World Data: Assessing Registries To Support Regulatory Decision-making for Drug and Biological Products***

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ACRO thanks the Agency for releasing this draft guidance on *Real-World Data: Assessing Registries To Support Regulatory Decision-making for Drug and Biological Products*. ACRO is pleased to provide the following feedback. ACRO would like to provide three general comments, before moving on to specific lines within the draft guidance.

I. General comments:
First, we were surprised that Section III.A (Using Registry Data to Support Regulatory Decisions) does not address the role of metadata to create a clearer understanding of the data elements contained in registries in order to achieve greater reliability and quality of information. We recommend that the final guidance should note that access to a standard and electronic set of complete and accurate metadata information can contribute to identifying the data sources suitable for a specific study, facilitate description of the data sources planned to be used in a study protocol or research proposal and contribute to assessing the evidentiary value of the results.

Second, we note an omission for the Agency to consider addressing in the final guidance. The draft guidance notes the *"Additional potential limitations of registries involve issues with data heterogeneity (e.g., different clinical characteristics across various populations) and variation in approaches used to address data quality"* (Lines 152-154) and Section III.D (Considerations When Linking a Registry to Another Registry or Another Data System) addresses the use of additional data sources to provide further information on patients in the registry. However, the draft guidance does not specifically address the use of combining data on different patients from multiple registries (e.g., when data are combined from the national registries of different countries). We recommend that the final guidance should include a specific section on this topic, which highlights the potential for heterogeneity in terms of measurement and collection of clinical variables and the need to ensure the relevance of the registry populations to the U.S. population.

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Finally, while we recognize that this guidance is directed as Guidance for Industry, its aims can only be achieved fully if the data custodian (i.e., the organization responsible for a registry) is completely transparent with industry in terms of what and how data are collected and validated for inclusion in the registry. We recommend that the final guidance should stress this expectation.

II. Line-Specific Comments:
ACRO supports the specific recommendations within the draft guideline, and we offer just two suggestions for the final guidance.

Lines 289-294:
The current text reads:

> *Sponsors also should ensure that a registry adheres to applicable jurisdictional human subject protection requirements, including protecting the privacy of patient health information, when designing a registry and developing protocols for the subsequent use of the data from the registry. FDA also recommends that an institutional review board or independent ethics committee be consulted when developing a registry to review data collection and other procedures associated with the registry.*

We recommend inclusion of the additional text that is highlighted in bold here in the final guidance, in order to ensure the appropriate and ethical use of registry data relative to human subject protections:

> *Sponsors also should ensure that a registry adheres to applicable jurisdictional human subject protection requirements, including protecting the privacy of patient health information, when designing a registry and developing protocols for the subsequent use of the data from the registry.* ***The informed consent given by subjects for inclusion of their data in the registry should allow for secondary research use of the data.*** *FDA also recommends that an institutional review board or independent ethics committee be consulted when developing a registry to review data collection and other procedures associated with the registry.*

Lines 375-377:
The current text reads:

> *Sponsors should use strategies to correct for redundant data, to resolve any inconsistencies in the data, and to address other potential problems.*

ACRO asks the Agency to consider listing the additional issues (highlighted in bold below) in the final guidance:

> *Sponsors should use strategies to correct for* ***selection bias, confounding data, missing data and*** *redundant data, to resolve any inconsistencies in the data, and to address other potential problems.*

Thank you for this opportunity to provide feedback. Please do not hesitate to contact ACRO (knoonan@acrohealth.org) if we can provide additional details or answer any questions.

Respectfully submitted,

Karen A. Noonan

Karen Noonan, Senior Vice President, Global Regulatory Policy