September 10, 2018

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Comments on Docket No. FDA-2018-D-1893-0002, "Patient-Focused Drug Development: Collecting Comprehensive and Representative Input."

Dear Sir or Madam:

The Association of Clinical Research Organizations (ACRO) appreciates the opportunity to comment on the Draft Guidance, "Patient-Focused Drug Development: Collecting Comprehensive and Representative Input."

General comments

ACRO welcomes the ongoing efforts by the Food and Drug Administration to facilitate the incorporation of the patient perspective into regulatory decision-making. Implementation of the Patient-Focused Drug Development program, supported by the fifth authorization of the Prescription Drug User Fee Act (PDUFA), has provided FDA and other stakeholders, including industry, a better understanding of patients' views of the impact of their diseases and conditions. Additional patient-focused activities called for under the 21st Century Cures Act will further help ensure that medical product development is directly informed by patients' experiences of disease and perspectives on the appropriate balancing of benefits and risks, ultimately enhancing the quality and efficiency of clinical trials and improving outcomes for patients.

ACRO appreciates the Agency's efforts in this Draft Guidance to provide industry and other stakeholders greater clarity on recommended methods and tools to use to collect and submit patient experience data. We also look forward to the additional guidance that FDA has indicated it intends to issue related to patient-focused drug development.

Line-specific comments
The following are ACRO's comments on specific sections of the Draft Guidance:

Lines 21-25
This guidance (Guidance 1) is the first of a series of four methodological patient-focused drug development (PFDD) guidance documents that FDA is developing to address, in a stepwise manner, how stakeholders (patients, researchers, medical product developers and others) can collect and submit patient experience data and other relevant information from patients and caregivers for medical product development and regulatory decision making.

ACRO requests that the agency consider adding "caregivers" to the list of stakeholders.

Lines 163-171
Patient experience data can be understood as including (but is not limited to) the experiences, perspectives, needs and priorities of patients related to:

- *the symptoms of their condition and its natural history;*
- *the impact of the condition on their functioning and quality of life;*
- *their experience with treatments;*
- *input on which outcomes are important to them;*
- *patient preferences for outcomes and treatments; and*
- *the relative importance of any of these issues as defined by patients*

ACRO requests the Agency to consider adding a bullet on the impact of disease on family and caregivers.
In addition, in Line 168 above (*"their experience with treatments"*), ACRO requests the addition of the following phrase – *"their experience with treatments, including unexpected outcomes as a result of treatment"*)

Lines 222—226 (in relation to Lines 1154 to 1158 below)
"Who can collect and submit patient experience data? Patient experience data can be collected by any persons including (but not limited to): patients, family members and caregivers of patients, patient advocacy organizations, disease research foundations, researchers, and drug manufacturers. It should be clear in any submission to FDA which person or group has collected the data."

Lines 1154—1158 (in relation to Lines 222 to 226 above)
"All personal participant data collected and processed for research should be managed by the research team with adequate precautions to ensure confidentiality of the data in accordance with applicable national and/or local laws and regulations on personal data protection."

Considering both the need to identify collectors of patient experience data (Lines 222-226) together with the personal data protection requirements (Lines 1154-1158), ACRO suggests that the Agency clarify the identification of patient experience data sources/collectors in the final guidance by stating that a role based identification would satisfy the requirement of identifying the person or group that has collected the data. Proper names are unnecessary and could add to privacy risk.

Lines 404-408
"However, more restrictive patient inclusion criteria (e.g., limiting patients to specific geographic regions), the less likely it is the information is generalizable to a broader sample. PD patients in California may have different views and preferences than those in another country or even another part of the US."

ACRO recommends that patient experience data from small or specific populations that are submitted to the Agency be accompanied by an explanation of relevance to broader populations.

Line 620
"For quantitative studies, the criteria for sample size calculation are usually quantifiable."

This statement suggests that there are some circumstances in which they are not. We recommend that the guidance provide examples of those circumstances and how they might be addressed.

Lines 890-893
Because this guidance focuses on sampling methods for collecting patient experience data through a variety of research contexts (including, but limited to, clinical trials, observational studies, advisory boards, public meetings, etc.), a full discussion of which laws may apply to these collection methods is beyond the scope of this guidance.

ACRO asks the Agency to consider adding the example of questionnaires: "(including, but limited to, clinical trials, observational studies, questionnaires, advisory boards, public meetings, etc.)

Lines 1080-1085
"Digital health technology can be one approach to mobile data collection and can include devices 1082 that allow participants to track some aspect of their health data. FDA recommends stakeholders 1083 who are collecting patient experience data with digital health technology to discuss the planned 1084 method early with FDA and obtain feedback from the relevant FDA review division."

ACRO looks forward to a separate guidance on the use of digital health technology as an approach to mobile data collection of patient experience data.

Glossary: Lines 1398-1409

"Data analysis plan:

> *A roadmap for how the data will be organized and analyzed and how results will be presented. A data analysis plan should be established when planning a research study (i.e., before data collection begins). Among other things, the data analysis plan should describe: (a) the data to be collected; (b) the analyses to be conducted to address the research objectives, including assumptions required by said analyses; (c) data cleaning and management procedures; (d) data transformations, if applicable; and (e) how the study results will be presented (e.g., graphs, tables).*

Data management plan (DMP):

> *A written document that describes the data you expect to acquire or generate during the course of your research study; how you intend to manage, describe, analyze, and store said data; and what mechanisms you will use at the end of your study to preserve and share your data. (Source: Stanford University Libraries n.d.(b))*

ACRO recommends clarifying how the Data Analysis Plan differs from the Analysis section of the Data Management Plan.

Conclusion

As the voice and trade association representing the world's leading, global clinical research organizations, ACRO stands ready to assist the Agency wherever possible in the development of this series of patient-focused drug development guidances. Our member companies provide a wide range of specialized services across the entire spectrum of development for new drugs, biologics and medical devices – from discovery, pre-clinical, proof of concept and first-in-man studies through post-approval and pharmacovigilance research. With more than 130,000 employees engaged in research activities around the world, ACRO advances clinical outsourcing to improve the quality, efficiency and safety of biomedical research. Each year, ACRO member companies conduct more than 7,000 clinical trials involving 1.3 million research participants in over 100 countries. On average, each of our member companies works with more than 700 research sponsors annually.

Thank you again for the opportunity to comment on this draft guidance. Please do not hesitate to contact ACRO (knoonan@acrohealth.org) if we can provide additional information or details.

Respectfully submitted,

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