ACRO
ASSOCIATION OF CLINICAL RESEARCH ORGANIZATIONS

July 6, 2016

Division of Dockets Management (HFA-305)
Food and Drug Administration
5360 Fishers Lane, Rm 1061
Rockville, MD 20852

Re: Docket No. **FDA–2016–D–1224**
Use of Electronic Health Record Data in Clinical Investigations; Draft Guidance for Industry

Dear Sir or Madam:

ACRO would like to thank FDA for issuing the public docket to solicit input from stakeholders on the use of EHRs as a source of data in clinical investigations. Founded in 2002, ACRO represents the world's leading clinical research organizations (CROs), which provide specialized services integral to the development of drugs, biologics and medical devices.

- ACRO's mission is to advance clinical outsourcing to improve the quality, efficiency and safety of biomedical research.
- Each year, ACRO members conduct more than 9,000 clinical trials in 140 countries involving nearly two million research participants.
- ACRO member companies employ more than 110,000 people worldwide.

ACRO is a leading voice for safe and ethical clinical trials, working with stakeholders globally to promote a better and more efficient clinical trial process. We are dedicated to bringing efficiency, innovation and value to the clinical research process and to highlighting the important contribution CROs make as partners in the development of new medicines and new treatments that benefit millions of patients worldwide.

ACRO applauds the Agency's issuance of this important draft guidance to address the use of EHRs in clinical investigations. As part of our commitment to unlocking the value of new technologies to help move clinical development forward[1], ACRO is pleased to provide the following comments.

[1] Please see ACRO comment on FDA docket no. FDA–2015–N–3579:
Using Technologies and Innovative Methods to Conduct Food and Drug Administration-Regulated Clinical Investigations of Investigational Drugs

Please see also ACRO's YouTube channel video on:
Sharing for Better Caring: Breaking Down Silos To Advance Medical Research

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General comments:

ACRO was pleased to see that the guidance connected the EHR usage to the predicate rules for Sponsor/CRO oversight expectations and investigator/Site expectations. In addition, ACRO appreciates the agency's approach to giving organizations the ability to use Meaningful Use (HITECH/ONC Health IT) certification program as a benchmark for acceptance of evidence of the privacy and security requirements of the IT system being met.

The draft guidance highlights the potential technical issues (which are significant) with exchange of information between the EHR and the EDC systems. This is, no doubt, compounded by the multiplicity of EHR systems – and security, access, and control issues that need to be appropriately managed. Additionally, as noted in the draft guidance, there are diverse data standards.

Systems involved in clinical trial data collection must be strictly validated. Moreover, system use, intent, and roles need to be clearly documented. The guideline does not set any such requirements; therefore, there seems to be an acceptance of data from a system of lower-level validation for use in clinical trials. ACRO looks forward to additional details in the final guidance.

The draft guidance does not include suggestions for situations where sites are already set-up and working on studies that were originally designed with paper records. Many hospitals and institutions are now transitioning to EHRs and destroying the original paper records once the records have been scanned. The UK Medicines and Healthcare Products Regulatory Agency (MHRA) has established guidance in this regard, and this language may be a helpful template for the FDA. According to the MHRA guidance, there must be a documented QC process in place and available.[2] Reference 1 associated with the entire guidance indicates that the document was drafted in consultation with HHS, which had been conducting compliance assessments/certifications with their Meaningful Use regulations. ACRO suggests that the final guidance include a sentence or two to clarify if the EHR guidance has any impact on the HHS certification for systems and proposes the following language: "*The introduction of this new FDA EHR guidance document has no direct effect on existing HHS certification processes and is meant to augment what has already been established.*"

[2] Please see MHRA Position Statement & Guidance on EHRs

> *2. For the scanning/ transfer process from paper to e-records:*
>
> - *A validated process to confirm scanned documents are certified copies e.g. QC checks (to include scan quality, legibility, completeness, page counts etc.) and a documented audit trail of this process. Supporting documentation should include what documents were transferred, when and how the scanning took place and by whom (i.e. metadata);*
> - *Written procedures in place to cover the above processes (these may also assure external sponsors that the system is GCP compliant).*

Specific comments:

Lines 15-25:
There is a key omission in this section of the draft guidance. It appears that the draft guidance implies or assumes that electronic source data for a patient comes from a *single* EHR system and does not address the situation of *multiple* EHRs for a *single* patient. ACRO looks forward to additional details in the final guidance.

Lines 90-91:
The draft guidance states: *"As provided in the eSource guidance, FDA does not intend to assess compliance of EHRs with 21 CFR part 11"*

This statement is unclear, as the Agency expects the same controls of the systems through the remainder of the guidance. Therefore, ACRO recommends this statement be clarified using the following more precise language:

"As provided in the eSource guidance, FDA does not intend to assess compliance of EHRs with 21 CFR part 11, however, an assessment of the validity, reliability, and integrity of EHR data used to support a marketing application for a medical product should be performed."

Lines 93-95:
The draft guidance states: *"Sponsors are responsible for assessing the validity, reliability, and integrity of any data used to support a marketing application for a medical product"*

ACRO recommends this statement be expanded by providing more details of the type of assessment or controls that the agency expects to see that it would consider effectively demonstrates validity, reliability and integrity of the data.

Line 113:
The draft guidance states: *"For the purposes of this guidance, interoperability refers to the ability of two or more systems or components to exchange information and to use the information that has been exchanged"*

To achieve greater clarity, ACRO recommends that the discussion around "interoperability" avoid the use of that general term when possible and, instead, use more specific terms such as:

- Interface
- Data mapping
- Data Flow
- Connectivity
- Data Security

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Lines 127-170:
ACRO suggests that the guidance encourage the use of data standards when possible to support consistent data mapping across systems by inserting a statement similar to the following:

"The data exchange between an EHR system and EDC or other clinical system should leverage the use of existing data exchange standards, such as CDISC, when possible while ensuring data security and data integrity are not compromised."

In addition, ACRO recommends that the final guidance clarify the expectations for data transfer and exchange between EHR systems used for day-to-day healthcare management of patient data and EHR systems used in clinical investigations where data controls are expected to be strong and reliable.

Lines 232-322:
ACRO welcomes the recommendation to include planned use of patient's EHR data in the informed consent and for the sponsor/CRO to consider the management and maintenance of that data.

However, the language is vague and general. To achieve greater clarity and specificity, ACRO recommends the following language:

"Data being transferred from a healthcare EHR system should be assessed or verified prior to initial inclusion into the clinical study system. Data elements that directly impact research trial data that may have been changed by a healthcare EHR should be assessed or verified prior to being pooled with the clinical study data."

While this draft guidance does not address the use of EHRs for patient recruitment purposes, ACRO sees tremendous potential for this application. We anticipate future guidance will address this issue and look forward to sharing our experiences with the agency at the appropriate time.

ACRO looks forward to being a resource to the agency as it moves ahead to create guidance for the use of EHRs in clinical investigations and – more generally – to promote the use and adoption of innovative new technologies and clinical trial methods.

Respectfully submitted,

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