March 23, 2015

National Institutes of Health/Department of Health and Human Services
42 CFR Part 11
[Docket Number NIH-2011-0003]
RIN: 0925-AA52
Notice of Proposed Rulemaking

Dear Director Collins:

On behalf of the Association of Clinical Research Organizations (ACRO,) thank you for the opportunity to comment on the Notice of Proposed Rulemaking regarding Clinical Trials Registration and Results Submission.

As the world's leading, global clinical research organizations (CROs,) ACRO 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 110,000 employees engaged in research activities around the world, each year ACRO member companies conduct more than 9,000 clinical trials involving nearly two million research participants.

Improving the utility of ClinicalTrials.gov to raise awareness of available clinical trials among patients and physicians with the goal of accelerating patient recruitment is one of ACRO's top policy priorities. We have been working closely with Congress on the 21st Century Cures initiative and commend the National Institutes of Health for this timely NPRM to address one of the major stumbling blocks to more efficient clinical trials.

As new technologies and applications are developed to facilitate clinical trials, such as the recently introduced Apple ResearchKit, it is imperative that ClinicalTrials.gov be brought up to current standards of technology and usability. Without a standardized, compatible database, the power of these emerging technologies will never be fully realized and clinical trial recruitment will continue to be one of the major impediments to the faster development and delivery of new treatments and cures to patients.

We see four fundamental shortcomings of the current website: 1) there is insufficient information entered to be truly useful for matching patients with appropriate trials; 2) the information is not provided in standard terminology format; 3) the site is very difficult to navigate and not consistent with current standards for usability and searchability; 4) the website currently is not designed for connectivity to electronic health records, which will ultimately drive usage.

The NPRM addresses these shortcomings and ACRO has specific recommendations in each area, in addition to other subjects where comment is requested. While it is not the purpose of the NPRM to discuss necessary funding for proposed changes to clinicaltrials.gov, ACRO would be supportive of efforts to ensure the National Library of

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Medicine is adequately funded to carry out this important mission. Our comments are largely focused on the Registration component of clinicaltrials.gov and we have only minor comments on the Results Submission section.

Specific Comments:

Responsible Party – The NPRM correctly identifies the party responsible for registering a clinical trial as either the sponsor or the principal investigator. While in most cases the sponsor or the principal investigator is the appropriate party, the NIH may want to consider the possibility of a contractor, like a CRO, being designated as the responsible party.

Adverse event reporting – ACRO endorses the implementation of a standard vocabulary for adverse event reporting and suggest that FDA standards be used with an appropriate lag in submission time between FDA reporting and posting in the data bank.

Clinical trial registration/recruitment information – In general, a full protocol is not necessary and a summary protocol may be adequate but the NIH should consider adding the "schedule of events" to provide subjects with information on the care that will be covered in a given study. Additionally, the inclusion/exclusion criteria must be adequate to facilitate, at a minimum, the initial screening and matching of trial participants. Here too, standardized terminology should be implemented. The content of all updates should be clearly identified. ACRO also recommends that the study be identified as being a biosimilar or a bioequivalent trial. If there is a specific biomarker that is being sought in the patient population, that should be specified as well. The NIH should consider including Phase I protocols, as these would be helpful to participants.

Further, there must be standardization of indication names to ensure the usefulness and consistency of the data bank. Our members have identified an inconsistency in terminology as a major limiting factor for effective patient recruitment. ACRO believes the use of SNOMED CT, which has been mapped MeSH, presents the best option to ensure uniformity. Other standards that have been mapped to MeSH may be acceptable but we believe SNOMED CT provides the most recognizable format and the format that will be easiest to integrate into electronic health records, which should be the ultimate goal for the data bank. Alternatively, ICD-10 could be considered. More important than the specific standard chosen is the ability for that standard to be mapped to EHRs.

Administrative data – ACRO strongly endorses the proposal to include the complete grant or contract number for any clinical trial that is funded, in whole or in part, by a U.S. federal government agency.

Facility information – ACRO supports inclusion of contact information for a knowledgeable person at each clinical trial site to the extent practicable.

Human Subjects Protection Review Board Status – ACRO agrees that inclusion of status of Institutional Review Board/Ethics Committee review would be helpful to

patients considering a clinical trial. We also believe highlighting this status could help promote the use of central or single IRBs for multicenter trials, which would facilitate greater efficiency in the clinical trial process.

Conclusion

We urge NIH/NLM to convene a stakeholder meeting or user testing group that includes patients, physicians, researchers and investigators to ensure ClinicalTrials.gov meets the needs of all interested parties. Further, NIH may want to consider the formation of an ongoing advisory committee to ensure that ClinicalTrials.gov keeps pace with changing research and technology needs.

Thank you again for the opportunity to comment. Please feel free to contact us if we can be of further assistance on this important matter.

Respectfully Submitted,

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Executive Director

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