

Comments of the Association of Academic Health Sciences Libraries (AAHSL), Medical Library Association (MLA), and Cancer Libraries Section of MLA

In Response to the NIH Request for Public Comments on the Draft NIH Policy on Dissemination of NIH-Funded Clinical Trial Information, 42 CFR Part 11 [Docket Number NIH-2011-0003]; RIN: 0925-AA52; Clinical Trials Registration and Results Submission

As health sciences librarians who fulfill requests for information from clinicians, scientists, and patients, we applaud efforts to expand and clarify the regulations for clinical trials registration and results submission.

On behalf of the Association of Academic Health Sciences Libraries (AAHSL), Medical Library Association (MLA), and Cancer Libraries Section of MLA, we strongly support approaches that will enhance the transparency of clinical trial results. The proposed regulations will provide patients with more information to make necessary health care decisions, including critical information about the safety of products and treatment options. Clinicians will have access to results information about efficacy, adverse effects, and safety; and biomedical researchers will have information on research design, safety, and scientific results that can inform future protocols and discoveries.

We also support timely, easily understood, and accurate reporting of all clinical trials, especially those supported by federal funding, regardless of agency and phase of the clinical trial.

Results Submission

Definitions and Descriptions of Outcome Measures. We are pleased that the draft policy includes modifications and additions to the data items listed in 402(j)(2)(A)(ii) of the Public Health Services (PHS) Act and believe these changes would improve the clinical trial information available to the public. In particular, the definitions and descriptions of outcome measures proposed under Section 11.48 of the draft policy will be strengthened and provide clearer information to those interested in a trial. The new definitions for primary, secondary, and other outcome measures should assist in the registration of the protocol, and the requirement for the specific measurement, specific metric, and timeframe of the outcome would support better understanding of the protocol and the measured outcomes.

Submission of results information for applicable clinical trials of unapproved, unlicensed, or uncleared products. Making these results available in ClinicalTrials.gov would provide clinicians, scientists, and patients with vital information which might otherwise be inaccessible. The benefits of having access to this information are many and include providing a more current and complete picture of results of clinical trials of FDA-regulated products, reducing potential sources of bias, protecting the safety of participants in clinical trials, enabling potential human subjects to make more informed decisions about participating in a trial, and broadening the

evidence base for systematic reviewers and others involved in assessing the benefits and harms of classes of drugs and devices.

Submission of non-technical and technical summaries. Health sciences librarians and health care providers are actively engaged in providing health literacy information services to patients and the general public. Many patients face challenges in understanding medical terminology and health information resources, including information found in ClinicalTrials.gov. To ensure compliance with the draft policy calling for the submission of non-technical and technical summaries of trial results, and for the provision of additional information to improve patient understanding, we recommend the development of guidelines for writing summaries in “plain language” that can be easily understood by non-health professionals and the public.

We concur with the decision to defer the requirement for the submission of narrative summaries until further research on this issue is undertaken, and recommend that guidelines be developed and ready for implementation within one year of the date the final policy is issued. We also support the recommendation that further investigation is needed to identify standards for providing technical summaries to the public that are unbiased and understandable. Having NIH continue to provide links, where possible, to related peer-reviewed literature and other authoritative information related to the intervention(s) studied or the disease or condition addressed is desirable, and will provide additional resources. To assist users in better understanding and interpreting of submitted clinical trial information, we suggest providing links to MedlinePlus, the National Library of Medicine’s consumer health web site. MedlinePlus has become the tried and true gold standard for providing patients with trusted information on more than 900 health topics including symptoms, causes, treatment and prevention, and also includes information on prescription drugs, over-the-counter medicines, dietary supplements and herbal remedies.

Another consideration is the optimum format for narrative, non-technical summaries. For example, two existing widely-endorsed and used formats intended for reporting results of individual clinical trials for technical or expert audiences are the CONSolidated Standards for Reporting Trials (CONSORT) Statement [Ref. 31], a checklist of best practices for producing journal articles that report the results of clinical trials of any type of intervention; and the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human use (ICH) topic E3 – Structure and Content of Clinical Study Reports (ICH E3) [Ref. 23], a required format for summarizing results of individual clinical trials of drugs in submissions to FDA and to agencies that regulate the use of drugs in other countries. Both of these formats require narratives and data tables, including information that is already submitted to ClinicalTrials.gov to meet the registration and results submission requirements under section 204(j) of the PHS Act.

Adverse Event Reporting

AAHSL, MLA, and the Cancer Libraries Section of MLA maintain that both expected and unexpected adverse events should be reported, regardless if it is or is not considered to be attributed to the intervention or device. However, we believe that attribution to an adverse event should not be derived solely based on the results. A better way to determine the cause of an adverse event would be to compare rates across all arms of the trial and identify where the highest rate of occurrences take place. We support continuing the requirement for two tables: one for serious adverse events, and one for those with a frequency of five percent or more in any arm of the trial. We also agree with the recommended time frame for the data collected as well as the approach used to collect the data—systematic or non-systematic. Reporting the number of patients experiencing the adverse event, as well as the participants at risk, and computing the frequency of events will provide a more accurate level of risk for the intervention.

We believe that requiring an all-cause mortality table would highlight information that is important for both patients and clinicians. Trying to pull this information from other reported data may not clearly indicate the mortality rates that occurred during the study, but it would provide a more comprehensible presentation and meaning of the data, such as identifying deaths not connected directly to the study.

From the patient's perspective, we believe that providing information indicating an adverse event could be attributable to the intervention is important. It might be possible to include an explanation or disclaimer that this statement is a subjective judgment and not a precise link to the intervention. This additional information and data regarding adverse events will aid patients and clinicians in making risk-benefit decisions for treatment options, as well as possibly informing future design of similar protocols.

Quality Control Procedures

As part of the quality control process we recommend posting a disclaimer with a time/date stamp in ClinicalTrials.gov when data is undergoing quality control review as a result of errors, deficiencies, and inconsistencies that may have been found. In many instances, data is corrected and posted within 30 days of receipt; however, this process sometimes takes longer than 30 days. We maintain that while adding a disclaimer is a good idea, the peer review process and submission of corrections should be completed within 30 days once the disclaimer is posted.

Posting a disclaimer also will ensure users are aware of the pending changes in study results and conclusions, and are informed that results will be reported in the future. We also recommend that the amended record should include the history of all corrections which would help users who viewed an earlier record and acted on then-incomplete information.