April 2, 2014

Bernard Lo, MD, and
Members of the Strategies for Responsible Sharing of Clinical Trial Data Committee
Board on Health Sciences Policy
Institute of Medicine
500 Fifth Street, NW
Washington, DC 20001

RE: Request for Public Feedback: Responsible Sharing of Clinical Trial Data (PIN IOM-HSP-13-12)

Comments submitted electronically to: RLenzi@nas.edu

Dear Dr. Lo and Committee Members:

The Federation of American Societies for Experimental Biology (FASEB) is composed of 26 scientific societies, collectively representing more than 120,000 researchers. FASEB believes that efforts to improve the responsible sharing of clinical trial data have the potential to enhance biomedical discovery and innovation, and we thank the Institute of Medicine (IOM) for the opportunity to provide comments on this important topic. We have three overarching recommendations in addition to feedback on the specific topics raised in the IOM discussion framework.

FASEB recommends that the IOM explicitly recognize two major categories of clinical trial data use by researchers: (1) re-analysis of the original study or analysis of aggregated data across similar studies; and (2) re-use of data to generate new hypotheses and to conduct research in areas beyond the aims of the original study. Both types of secondary data use have the potential to provide great benefits; however, the issues raised and the specific data and metadata needs will vary between these categories.

Development of metadata standards is critical to data sharing. Therefore, FASEB encourages government agencies and other organizations to support efforts to establish minimal metadata standards for clinical trial data. To succeed, these efforts must seek insight from stakeholders, especially from investigators conducting clinical trials and researchers who intend to reuse the resulting data. The metadata included in the minimal standards must be feasible to collect and be of value to secondary users.

The burden of metadata collection falls upon primary data collectors, whereas the benefits accrue to secondary data users. Reducing the effort required to generate metadata reduces the adverse social effects of this asymmetry. Therefore, in conjunction with the establishment of minimal metadata standards, it is highly desirable that instruments and software be designed and developed that can automate metadata collection and reporting, whenever possible. Minimal
metadata standards may be able to be expanded as the capabilities of these tools increase, thereby enhancing the value of shared clinical trial data.

In addition to these overarching recommendations, FASEB provides the following recommendations to address the topic areas highlighted in the IOM discussion framework;

**Global Implementation and Practical Consideration**

Regulations regarding data sharing, research participant protections and privacy, and medical data privacy vary greatly between nations. The adverse effect of this variation could be minimized with the development of minimal metadata standards for clinical trial data as described above. FASEB also recommends the development of adjusted standards specific to an individual country’s laws and regulations when necessary. Lists of these adjusted metadata standards should be compiled and publicly accessible to allow researchers to easily identify which countries do not permit the collection of a metadata field of interest and exclude data from trials conducted in those locations in their analyses.

**Timing and Prioritization**

As previously stated, FASEB considers the development of metadata standards to be a critical first step for productive clinical trial data sharing. In the field of microarray research, productive data sharing was greatly enhanced by the establishment of the Minimum Information About a Microarray Experiment (MIAME) standards. We encourage the IOM to look to existing models, such as MIAME, to guide the development of minimal metadata standards for clinical trials.

**Mitigating Risks**

As described in the IOM discussion framework, there are a number of risks associated with the sharing and reuse of clinical trial data. One such risk is inaccurate or statistically inappropriate analysis of data by researchers. To minimize this risk, FASEB recommends the development of standards for publications that reuse clinical trial data and that the standards include the following elements: (1) a description of which clinical trial data were accessed; (2) a detailed methodology section on how the data were used and analyzed; and (3) citations of the datasets utilized.

Privacy protection for research participants is of great importance, but data sharing places privacy at risk. In prior statements, FASEB has noted that de-identification cannot be guaranteed for certain types of data, including whole genomic sequences. As technology progresses and more data become publicly available – both in biomedical and non-biomedical databases – the instances in which re-identification becomes possible will continue to increase. Therefore, FASEB recommends that governments explore alternative models to protect human research subjects, such as shifting from a privacy-
protection paradigm to one that provides research subjects with substantive legal protections against the misuse or inappropriate accession of their data.

**Enhancing Incentives**

There are few incentives for researchers to share their data. The majority of the effort is borne by the initial investigator for the benefit of secondary users. Furthermore, less prestige is often assigned to sharing quality datasets as compared to the publication of articles that use the shared data. To reduce these disincentives, governments and other research-associated organizations should: (1) reduce barriers and burdens associated with data sharing for investigators; (2) provide or identify sources of support for the continued maintenance and curation of databases; and (3) work towards changing the research culture to ensure that the sharing of quality datasets receives appropriate consideration and recognition.

Requiring data sharing as a condition of journal publication has been a successful strategy in genetics and other fields. Similarly, in the U.S., clinical trials must be registered on [www.clinicaltrials.gov](http://www.clinicaltrials.gov) and summary data must be added for any “drug, biologic, or device that is approved, licensed, or cleared by FDA.” International journals can promote increased clinical trial data sharing by making access to data a requirement for the publication of clinical trials. This approach, however, is unlikely to enhance sharing of data from unpublished trials, including unsuccessful trials.

**Measuring Impact**

As sharing and reuse of clinical trial data increases, it is important to observe how datasets are being used and accepted by the broader research community. This experience will help inform what metrics for measuring impact would be of greatest utility.

FASEB appreciates your consideration of our comments and looks forward to working with the IOM on these issues. Please let us know if we can be of further assistance.

Sincerely,

Margaret K. Offermann, MD, PhD
FASEB President