FASEB
Federation of American Societies for Experimental Biology

Representing Over 120,000 Researchers

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Lawrence Tabak, DDS, PhD
Principal Deputy Director, NIH
Building 30, Room 524
30 Convent Drive
Bethesda, MD 20892

RE: Principles and Guidelines for Reporting Preclinical Research

SUBMITTED VIA EMAIL: lawrence.tabak@nih.gov

Dear Dr. Tabak:

The Federation of American Societies for Experimental Biology (FASEB) is composed of 27 scientific societies collectively representing over 120,000 scientists and engineers. A total of 62 peer-reviewed journals are published by member societies; therefore FASEB appreciates the efforts of the National Institutes of Health (NIH) and journal editors to develop the Principles and Guidelines for Reporting Preclinical Research released last November. Guidelines to encourage uniform reporting of data and experimental methods are valuable to the scientific community and the public, both to improve transparency of the research process and increase capacity to reproduce research findings. FASEB recognizes that strong actions are necessary, and we applaud NIH for its willingness to address this challenge. However, we have three specific concerns: the premature timing of the guidelines, the inability of the guidelines as proposed to take into account the diversity of biomedical research, and the increased administrative burden for researchers and reviewers.

Guidelines are premature and do not include all stakeholders

Effective guidelines should be based on demonstrated best practices. The first step must be to assess what data are needed to enhance rigor and increase transparency. Some of the factors where best reporting practices are needed include source, species, sex, age, husbandry, and inbred and strain characteristics of laboratory animals. In some work, other factors may also be important such as medications administered to laboratory animals, in particular analgesics and anesthetics. Other such data requirements exist, and FASEB is willing to assist NIH by convening experts to initiate the development of best practices. However, while it is important to be thorough, a “one size fits all” list could become burdensome, overwhelming, and ultimately ineffective if it requires everyone to report every factor regardless of its relevance to a particular kind of research.

Best practices for reporting and sharing data evolve in an ongoing manner that varies by field, discipline, and research technique. Therefore, FASEB supports the development of community-based standards that are flexible and can be adapted over time.

NIH should start by encouraging community discussions on data standards and helping to increase awareness of these activities within the research community. NIH should also assist in the development of tools and repositories to automate data collection, analysis, and submission. Such NIH support for data citation practices may incentivize researchers and enhance the professional prestige associated with data sharing. FASEB recognizes that such efforts are already underway as part of NIH's Big Data to Knowledge (BD2K) initiative, and we look forward to seeing progress in these areas.

Guidelines must reflect diversity of research

The Federation is concerned about several terms and definitions used in the guidelines. For instance, use of the verb "adhere" in the preamble seems to signify that the signatories envision a rigid application of these guidelines. Biomedical research is a vast enterprise with substantial variety in statistical methods, data types, and best practices within and between disciplines. To achieve the stated goals of enhancing rigor, reproducibility, robustness, and transparency, guidelines must allow flexibility and discretion by journal editors and reviewers. A statement clarifying the ability to apply other criteria may encourage additional journals to sign on to the guidelines.

Our community is also concerned about varied interpretation of the term "preclinical research." For example, *Nature*[1] defines preclinical research as "research involv[ing] the evaluation of potential therapeutic interventions in cells and animals," while the National Cancer Institute[2] defines preclinical research as "research using animals to find out if a drug, procedure, or treatment is likely to be useful." Yet Landis et al[3] note that the best practices outlined in their article "do not apply to early-stage observational experiments searching for possible differences among experimental groups." They go on to emphasize that, "Such exploratory testing is frequently conducted using a small sample size, does not have a primary outcome and is often unblinded." Since these definitions do not take into account basic, discovery-based research, there remains a great deal of confusion regarding what research is covered under these new guidelines. Therefore, FASEB recommends that NIH provide a clear definition of what is considered preclinical research.

Increased Administrative Burden for Researchers and Reviewers

Time lost due to unnecessary, duplicative, or overly complicated administrative tasks is a long-standing concern of the scientific community that FASEB represents. Implementation of these principles and guidelines will obviously require additional time and effort and will make preparation, submission, and peer review of manuscripts more onerous. Furthermore, over-zealous interpretation or excessively rigid implementation of the guidelines could exacerbate the problem.

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[1] http://www.nature.com/subjects/pre-clinical-studies
[2] http://www.cancer.gov/dictionary?cdrid=44517
[3] Landis et al. A call for transparent reporting to optimize the predictive value of preclinical research. *Nature.* 490(7419):187-191, 2012.

If these guidelines fail to allow for flexibility, significantly more administrative effort may be required at every step of the manuscript development, submission, and review process. Journal reviewers, editors, and publishers will become the arbiters of adherence to the new standards. Recruiting high-quality peer reviewers is already challenging, and the additional time and burden associated with evaluating science in light of rigid "checklists" may further diminish the pool of those willing to serve as reviewers. Nothing could be more detrimental to the rigor and reproducibility of published science than a weakening of the peer review process. Therefore, FASEB strongly urges that the research community be included as an active and equal participant in future discussions with NIH leadership and journal editors to determine best practices for ensuring quality data and method reporting while also maintaining a healthy publication process.

In conclusion, FASEB finds these guidelines to be premature, to lack the appropriate flexibility to be applicable across disciplines, and to likely produce significant and in some cases unjustified burden associated with the preparation and review of scientific manuscripts. We appreciate NIH's willingness to address this challenge head-on; however, we encourage NIH to broaden stakeholder input on future decisions involving research reporting to enhance reproducibility. Should you have any questions or wish to discuss these comments further, please do not hesitate to contact me.

Sincerely,

Joseph R. Haywood, PhD
FASEB President