October 8, 2014

Francis S. Collins, MD, PhD
Director, National Institutes of Health
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1 Center Drive
Bethesda, Maryland 20814

Janine A. Clayton, MD
Director, Office of Research on Women’s Health
National Institutes of Health
Building 2DEM Room 400
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Bethesda, Maryland 20817

Dear Dr. Collins and Dr. Clayton,

The Federation of American Societies for Experimental Biology (FASEB) is composed of 27 scientific societies, collectively representing over 120,000 biological and biomedical researchers. As noted in your article in the May 15, 2014 issue of *Nature*, the inclusion of women in NIH-supported clinical studies has increased dramatically over the past two decades as a result of concerted action and NIH policy. FASEB commends NIH for its leadership in developing policies to address the disparities in the scientific literature between sexes in preclinical research.

The Federation also recognizes the scientific need to study both male and female animals and cells in preclinical research, as sex is an important biological variable. New policies to address the imbalance, however, will require educational efforts, clear delineation of covered research, and a plan for dealing with the financial implications of the changes. Below we describe three key areas for consideration as NIH develops its policy to address sex as a variable in biological research.

**Enhanced Training of Trainees, Investigators, and Scientific Review Officers**

Clear guidance and training modules will be imperative for those involved in the development and review of research proposals. The entire peer review community (Scientific Review Officers, institute program staff, and individuals recruited to serve on study section panels) should participate in the development and dissemination of guidance and training materials to aid in determining how sex should be considered in the review of research proposals. Without clear guidelines for reviewers, the success of a proposal may be determined by opinion rather than by scientific merit. Guidelines could facilitate consistency among reviewers within and across study sections when considering the balance of sex in preclinical research. We suggest that NIH consider a model similar to the Office of Human Research Protections’ Human Subjects...
Regulations Decision Charts\(^1\) to assist PIs, reviewers, and program staff in determining the extent to which sex differences should be assessed for a specific project.

**Clear Delineation of Research Covered by or Exempt from Policy**

The potential lack of clarity regarding the types of research that would be covered by the policy is another area of concern for FASEB members. Therefore, we encourage NIH to clearly define research that would be covered under the proposed policy as well as delineate exempt research prior to implementation. While research on conditions that affect only one sex (e.g., cervical cancer, prostate cancer) are obvious examples of exemptions, the need for inclusion or exclusion will be less well defined for some conditions. To reduce confusion, FASEB strongly recommends that NIH supplement the final policy with a workflow diagram or chart to help investigators and reviewers navigate and implement the policy as intended.

**Increased Costs Associated with the Conduct and Analysis of Animal and Cell Studies**

Finally, implementation of the new policy will increase the cost of individual research projects, likely resulting in fewer total projects funded by NIH. In fiscal year 2013, the success rate for research project grant applications was 16.8 percent—an all-time low. The increased cost associated with balancing sex could drive that rate even lower. Therefore, we urge NIH to develop this policy in a manner that ensures a vibrant and diverse portfolio of funded research, while still achieving the goal of evaluating the similarities and differences between sexes in preclinical research (e.g., targeted RFAs, administrative supplements to existing grants).

We recognize the important role that balancing sex in pre-clinical research plays in advancing safe and effective treatments for both male and female patients. As you take into consideration the points raised in this letter, we also urge NIH to continue to engage and solicit input from the research community and allow sufficient time for formulation of responses as it develops policies for balancing sex in preclinical research.

On behalf of FASEB, I thank you for considering our perspective. Please do not hesitate to contact me if I can provide you with any additional information.

Sincerely,

Joseph R. Haywood, PhD
FASEB President

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