September 16, 2019

The Honorable Alex Azar
Secretary
U.S. Department of Health and Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Dear Secretary Azar:

We write to express our concerns regarding two NIH guide notices "Changes to NIH Requirements Regarding Proposed Human Fetal Tissue Research" (NOT-OD-19-128) and "Clarifying Competing Application Instructions and Notice of Publication of Frequently Asked Questions (FAQs) Regarding Proposed Human Fetal Tissue Research" (NOT-OD-19-137). We are concerned that both the policy underlying these notices (i.e., the requirement that human fetal tissue research proposals be subject to an additional layer of review) and the specific requirements of these notices will create substantial barriers to important biomedical research, jeopardize the integrity of the peer-review process, and create an unnecessarily cumbersome and bureaucratic process for reviewing crucial research. The new policies upend the existing legal and ethical frameworks for human fetal tissue (HFT) research, which have provided rigorous and appropriate oversight for decades and allowed important biomedical research to progress. Unless significant changes are made to the new requirements, lifesaving research will be encumbered, delaying the development of new treatments for patients.

As our coalition noted during the fetal tissue review, HFT remains scientifically critical because of its unique and valuable properties that cannot be replaced by other research materials. HFT is an essential resource for studying complex interactions between cells, and it is critical for studying immune responses and infectious diseases like HIV and Zika. It is necessary to understand human development and allows researchers to more fully understand congenital defects such as those of the heart and nervous system. While there have been some advances in recent years that have reduced the need for fetal tissue in certain areas of research, HFT remains critical to advance discovery and new therapies in other areas. Considering the scientific significance of HFT for biomedical research, we urge you to eliminate the new layer of review that is being imposed on research proposals in this area. If the new requirements remain in place, we ask that you consider modifying the procedures described in the recent NIH notices to protect the scientific peer-review process, ease compliance, and clarify the new requirements, as described below.

The Integrity of the Scientific Peer Review Process

The NIH's two-step system of peer-review (Scientific Review Group and Council Review) for extramural research must be preserved to allow each institute to identify and support the most scientifically meritorious projects. The new requirements subvert

the peer review process by inappropriately defining the scope of the ethics advisory board's charge to include a review of the scientific justification for research, the amount of HFT proposed to be used, and the consideration of alternative models (e.g., research design). These requirements are inconsistent with Section 492A of the Public Health Service Act, which provides the statutory authority for such ethics advisory boards and limits their purview to "ethical considerations." The NIH's peer-review process is the "gold standard" for evaluating research proposals and must remain the principal process to assess scientific merit.

Ease Administrative Burdens for Important Biomedical Research

The new HFT requirements will have a chilling effect on HFT research due to the complexity and burdens of applying for and receiving federal funding for research that involves HFT. It will not only delay and interrupt important biomedical research that gives patients hope but will also hamper the development of alternatives to HFT. We encourage the NIH to reduce the administrative hurdles and ease compliance with the new HFT requirements.

- Requiring an IRB-approved informed consent form for all research using covered human fetal tissue is inappropriate for basic science research involving HFT. The IRB review of consent forms is required by the Common Rule (45 CFR §46.206) only when an individual is participating in human subject research, as defined in the regulations, not for basic science research that involves use of de-identified tissue and that does not involve interaction or intervention with an individual human subject. Fetal tissue is typically de-identified, and researchers generally do not interact with the tissue donors or otherwise intervene in the donation process; such non-clinical research is not human subjects research. Accordingly, we believe that investigators who are engaged in non-human subjects research should not be required to submit to NIH a sample IRB-approved form, and should not be required to include in their applications information about the consent process beyond providing an assurance that the supplier of the fetal tissue verified that the material complies with rules and regulations governing the donation, including the tissue donation consent process

- The placement of the new "Human Fetal Tissue Justification" within the page-limited Research Strategy section of grant applications will impede investigators from adequately justifying the significance and innovation of their research. We urge the NIH to either exempt the new justification from the existing page limits or move it to a different section of the application, like the justification for vertebrate animals.

- The new requirements discourage existing grantees from adding research involving HFT because the new rules consider such an addition to be a change of scope, requiring the submission of a competing revision application. We believe this additional application and review will impede important biomedical research.

- Donated human tissue for biomedical research is a precious resource that must be handled with care, regardless of the source, and its use and disposal are already institutionally regulated. We urge the NIH to remove the obligation to describe plans for the treatment and disposal of HFT in the new Human Fetal Tissue Justification.

Clarifications are Needed to Ensure Compliance

We recommend revising the Guide Notice to clarify how the new requirements impact trainees, fellows, and labs with existing human fetal tissue supplies.

- We urge NIH to revise the Guide Notice NOT-OD-19-128 to clarify that, consistent with the guidance posted on August 6, 2019, research trainees and fellows supported by NIH grants are still allowed to conduct research using HFT. We are concerned that the discussion of training grants in connection with this new policy will discourage trainees from pursuing potentially productive and important research using HFT. We encourage NIH to clearly state that there is no prohibition on trainees learning how to use this important biomedical resource through involvement in grants other than the specified training awards, which are not intended to fund research.

- The definition of fetal tissue in the guide notice differs significantly from the definition in the statute and the NIH Grants Policy Statement and is overly broad.

As organizations representing scientists, clinicians, and patients who are driven by a desire to improve the health and well-being of all, we urge you to consider the scientific and medical significance of fetal tissue research and its crucial role in the development of new therapies. Thank you for considering our views.

Sincerely,

Academic Pediatric Association
AIDS Action Baltimore
AIDS Foundation of Chicago
Alliance for Aging Research
American Academy of HIV Medicine
American Academy of Neurology
American Academy of Pediatrics
American Association for Anatomy
American Association for the Advancement of Science
American Association of Colleges of Pharmacy
American Association of Immunologists
American Pediatric Society
American Physiological Society
American Society for Cell Biology

American Society for Investigative Pathology
American Society for Reproductive Medicine
American Society of Hematology
American Thoracic Society
APLA Health
Association for Research in Vision and Ophthalmology (ARVO)
Association of American Medical Colleges
Association of American Universities
Association of Independent Research Institutes
Association of Medical School Pediatric Department Chairs
Association of Public & Land-Grant Universities
AVAC
Axis Advocacy
Coalition for the Life Sciences
Columbia University Irving Medical Center
Cornell University
Council on Governmental Relations
Duke University
Elizabeth Glaser Pediatric AIDS Foundation
Endocrine Society
Fellowship in Family Planning
Global Healthy Living Foundation
Harvard University
HealthHIV
HIV Medicine Association
HIV+Aging Research Project-Palm Springs
Infectious Diseases Society of America
International Society for Stem Cell Research
ISCT, International Society for Cell & Gene Therapy
Jacobs Institute of Women's Health
Johns Hopkins University
Medical College of Wisconsin
National Alliance for Eye and Vision Research
National Alliance on Mental Illness
National Multiple Sclerosis Society
Northwestern University
Pediatric Policy Council
Princeton University
Research!America
Rutgers Biomedical and Health Sciences
Sexuality Information and Education Council of the United States (SIECUS)
Society for Pediatric Research
Society of Family Planning
Stanford University
Stony Brook University
SUNY Upstate Medical University

Texans for Cures
The Center for HIV Law and Policy
The Michael J. Fox Foundation
The Nebraska Coalition for Lifesaving Cures
The State University of New York
Treatment Action Group (TAG)
Tuberous Sclerosis Alliance
UC San Francisco (UCSF)
United States People living with HIV Caucus
University at Buffalo
University of California
University of California San Diego
University of California, Davis
University of California, Irvine
University of California, Los Angeles
University of Massachusetts Medical School
University of Michigan
University of Pittsburgh
University of Washington
University of Wisconsin-Madison
UW Medicine
Yale University

Cc: Francis Collins, NIH Director