Summary Testimony for
the
United States Senate Committee on Health, Education, Labor and Pensions
for Hearing on
"Gene Editing Technology: Innovation and Impact"

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Chairman Alexander and Ranking Member Murray, thank you for the opportunity to submit testimony on this timely and vitally important subject.

I am Director of the Johns Hopkins Berman Institute of Bioethics in Baltimore, where I also hold an endowed professorship in bioethics and public policy. Relevant to my comments today I was a member of the National Academy of Sciences international consensus committee on human genome editing.

I will focus my comments today on three topics: (1) policy history in related areas of science and biomedical research; (2) existing ethical frameworks and oversight; and (3) ethical issues raised by the use of gene editing technologies in humans and considerations for future oversight.

Related policy history

The relevant policy history started in 1975 with the Asilomar Conference on Recombinant DNA Molecules, whose summary statement focused on containment of the risks of creating and working with genetically modified organisms, and with the admonition to avoid experiments that pose "such serious dangers that their performance should not be undertaken at this time" along with a call for continuing reassessment of issues arising in light of new knowledge gained with experience with the then-new genetic technology. These voluntary suggestions gave way to more robust oversight as use of genetic technologies became more refined and with initial attempts to treat diseases in humans, with a now longstanding body called the NIH

Recombinant DNA Advisory Committee or RAC charged with review of proposed gene transfer research involving humans.

Existing ethical frameworks and oversight

Ethical concerns in genetic modification in humans have been addressed through a range of policy and oversight approaches, in order to limit certain types of research or to provide prospective oversight prior to particular proposals being undertaken.

Institutional oversight

There are a number of institution-level oversight mechanisms that will apply to gene editing research. While there is no single institution-level committee that is currently responsible for gene editing research, there is robust oversight with some combination of committees responsible for oversight depending on the specifics of the research proposed. Those include:

Institutional Biosafety Committees (IBCs), charged oversight of research with recombinant or synthetic nucleic acid molecules;

Institutional Stem Cell Research Oversight Committees (SCROs), charged with institutional and ethical oversight of research on human embryonic stem cells and related areas of research.

While specifics of gene editing research will determine which if any of these existing institutional oversight mechanisms will apply, any research involving human participants must be also be reviewed and approved by *Institutional Review Boards*, charged with prospective review of all research involving humans, requiring appropriate risk-benefit balancing, informed consent of subjects, and monitoring adverse events that occur, in order to protect the rights and interests of those participating in research.

Regulatory oversight

In addition to institutional oversight requirements there are regulatory bodies with roles that are relevant to gene editing research. The aforementioned NIH Recombinant DNA Advisory Committee (RAC) is charged with making recommendations to the NIH Director "on matters related to the conduct and

oversight of research involving recombinant DNA."[1] In addition, the NIH Guidelines currently state that "RAC will not at present entertain proposals for germ line alterations."[2] This indicates a current effective prohibition on the use of germline modifying technologies for areas of research within the purview of the RAC, with every indication that applications of gene editing tools to humans will be subject to such oversight and review.

FDA review and approval would also be required prior to the administration of gene editing techniques in humans, a process that in the case of gene transfer takes place in parallel with and informed by the review process of the RAC.

Ethical Issues Raised by the Use of Gene Editing Technologies in Humans and Considerations for Future Oversight

There are a range of ethical issues posed by gene editing and related technologies for modifying human DNA, and I will focus on just three in my testimony today: (1) the expanded use of therapies beyond indications on which any approvals might be based; (2) interventions that result in heritable genetic modification; and (3) some challenges that genome-editing poses for regulatory oversight.

The first concern is related to the use of somatic gene-editing approaches that have clear therapeutic applications being used for other indications, including moving beyond therapies or preventive uses, and instead for enhancement beyond "normal" abilities, a challenge long known within the gene therapy oversight process and effectively blunted through very limited clinical trials with inclusion criteria for research participants. But as applications begin to make their way into the market, FDA will need to evaluate and apply its regulatory tools to assure that what has been termed "indication creep" or uses for what are unintended indications can be prevented or at least limited.

The second concern has been the focus of much ethical analysis in the application of manipulation of genetic information in humans, and that is the potential to introduce changes that affect the germline. The basis of this concern relates to the uncertainty

[1] Charter, NIH Recombinant DNA Advisory Committee, June 30, 2013.
[2] NIH Guidelines, Nov. 2012, Appendix M.

of the effects of genetic modification, the inability to "undo" unintended genetic changes, and the risks of passing on such unintended changes to future generations. As the NAS international consensus committee noted, "improvements in genome-editing techniques are driving increases in the efficiency and accuracy of genome editing while also decreasing the risk of off-target events. Because germline genome edits would be heritable, however, their effects could be multigenerational. As a result, both the potential benefits and the potential harms could be multiplied."[3]

While acknowledging these concerns, if and when such technologies have developed sufficiently, policy decisions must be made that balance the individual-level benefits of using gene editing against societal-level risks. The NAS committee recognized and analyzed this balancing and made recommendations about when if ever a clinical trial employing heritable genome editing could be acceptable, setting a very high bar—some have said with criteria that would be impossible to meet. I think the criteria are appropriately restrictive, and if they cannot be met, then such applications of gene editing tools would and should not be permissible.

Third, while existing oversight is robust and has proven effective at governing areas like gene therapy, the two ethical issues I've described thus far, along with others, must be addressed in policy as gene editing tools become more widely used. At the same time, prohibitions should not be the logical conclusion of addressing areas that require attention. We need only look to two of our closest allies for real-world comparison of two policy approaches and how differences in regulatory approach will have very different effects. Just last week in Canada, a major group of researchers called for change to their federal law that makes it a criminal offense with penalties of up to 10 years in prison for using gene-editing tools on cells that could lead to heritable genetic change in humans. The concern expressed by the group is that research has been stopped in ways that mean Canadian scientists are falling behind their international colleagues.

The counterexample is the United Kingdom, where scientists are taking the lead internationally in research involving potential human applications of these technologies. This owes not to lax oversight but rather the contrary—strict oversight with clear pathways for licensure by the responsible regulatory agency, allowing

[3] *Human Genome Editing: Science, Ethics, and Governance*, National Academies Press, 2017, pp. 111-112.

careful and controlled progress with clear reporting and evaluation of results before proceeding, creating a clear path forward.

There is no comprehensive regulatory approach, however, the absence of which creates an opportunity for some jurisdictions to craft lenient or nonexistent regulation, leading to the emergence of so-called "regulatory havens," the encouragement of both scientific flight and medical tourism, and more near-term concerns around scientific leadership and competitiveness, and a loss of abitlity to control research that is outside of U.S. jurisdiction.

In conclusion, the United States has long played a leadership role in both science and in the responsible use of the advances created by scientific discovery. This was certainly the case with the introduction of recombinant DNA technologies in the 1970s and it is critical that we continue to do so as the new and powerful genetic technologies become both more precise and more widely available. Existing oversight approaches are appropriate for providing part of a framework for addressing many of the issues raised by gene editing technologies. However, some areas require additional clarification or refinement, and my caution is that they not be addressed through additional bans or prohibitions. Instead work must be done to (1) identify gaps or areas requiring updated approaches to oversight in both in the near and longer terms, and (2) craft appropriate guidelines to address the areas identified, in order to create pathways to allow innovative science to go forward carefully and responsibly, and with appropriate oversight. This work must reflect input and contributions from the scientific community, ethics experts, policy makers, and a range of public stakeholders. Only then will we achieve a robust and credible policy framework that will assure the responsible use of these technologies while achieving their promise for advancing scientific knowledge and human health.

Thank you.