Testimony for the Record
Submitted to the
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Subcommittee on Research and Technology
for Hearing on
"The Science and Ethics of Genetically Engineered Human DNA"

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Chairwoman Comstock and Ranking Member Lipinski, thank you for the opportunity to submit testimony on this timely and vitally important subject.

I am a Professor of Bioethics and Public Policy at the Johns Hopkins Berman Institute of Bioethics in Baltimore. Relevant to my comments today I am also currently chairing an IOM consensus study commissioned by the FDA on Ethical and Social Policy Considerations of Novel Techniques for Prevention of Maternal Transmission of Mitochondrial DNA Diseases. Given that the study is considering related issues to the topic of today's hearing and our work is ongoing, I will restrict my comments to general observations and an overview of the ethical and policy landscape and issues so as not to give the impression of prematurely forecasting the conclusions and recommendations of that committee. I will focus my comments on three main topics: (1) policy history in related areas of science and biomedical research; (2) ethical issues raised by gene editing technologies; and (3) relevant existing ethical frameworks and approaches to oversight.

Related policy history

Starting in the 1970s with the initial discovery and development of recombinant DNA technologies and the ability they brought to manipulate DNA—whether in bacteria, plants, animals, or humans—the scientific community recognized the social and ethical implications of the potential uses of these new technologies.

This began 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. The summary also identified so-called "experiments to be deferred," which were in its words "feasible experiments which present such serious dangers that their performance should not be undertaken at this time . . ."[1] This admonition was paired with a call for continuing

[1] Berg et al., "Summary Statement of the Asilomar Conference on Recombinant DNA Molecules," Proc. Nat. Acad. Sci. 72(6):1981-1984; June 1975.

reassessment of issues arising in light of new knowledge gained with experience with the then-new genetic technology, and included the suggestion of a series of annual workshops, some of which should be at the international level—prescient for today's discussion given the truly global nature of the science. 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, as I will outline later in my testimony.

Ethical issues raised by gene editing technologies

Scholars and commentators have identified a range of ethical issues posed by gene editing and related technologies for modifying human DNA. They fall into three general categories of concerns: (1) the implications of modification of germline DNA; (2) the implications of interfering in processes that should be off-limits to humans; and (3) the potential for selection or introduction of traits for other than treatment or avoidance of disease, such as physical or behavioral traits or enhancements.

The focus of much ethical analysis in the application of manipulation of genetic information in humans is on changes that affect the germline, that is changes that are heritable and are therefore passed on to future generations of individuals. The basis of these concerns relate to the uncertainty 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.

The manipulation of human DNA in such fundamental ways is open to criticisms of interference in processes that we do not sufficiently understand, or that should be beyond human intervention—sometimes noted by the shorthand of "playing God". These concerns reflect the general unease over tampering with the very features that determine our identity, and even our humanity.

With greater precision of the technologies will come the ability to modify genes not only to avoid or cure diseases but to remove or introduce other traits in the interest of enhancement, which some consider a form of eugenics.

How then has the scientific community addressed these concerns?

Existing ethical frameworks and oversight

A range of approaches have been created or promulgated in order to limit certain types of research or to provide prospective oversight prior to particular proposals being undertaken.

Since early stage human gene editing research will require the use of human embryos, existing rules on such research will play an important role. The so-called Dickey-Wicker Amendment prohibits

the use of federal funds for research that creates, destroys, or knowingly harms a human embryo.[2] Privately funded research is not affected by these restrictions, though the convention is that research on embryos should take place no later than 14 days after fertilization, a limit also accepted by most countries engaged in research on human embryos.

Institutional oversight

There are a number of institution-level oversight mechanisms that will apply to gene editing research, which apply to various types of proposed research. While there is no single institution-level committee that is currently responsible for gene editing research, one or more may apply depending on the specifics of the research proposed:

Institutional Biosafety Committees (IBCs)—IBCs are charged with oversight of research involving recombinant or synthetic nucleic acid molecules, and review is required for any such research that is "performed at or sponsored by an institution that receives any NIH funding for such research."[3]

Institutional Stem Cell Research Oversight Committees (SCROs)—SCROs are charged with institutional and ethical oversight of research on human embryonic stem cells and related areas of research, following guidelines from the National Academies[4] and relevant state policy where applicable.

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 approved by Institutional Review Boards.

Institutional Review Boards (IRBs)—IRBs prospectively review 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 NIH Recombinant DNA Advisory Committee (RAC) is charged with making recommendations to the NIH Director "on matters related to (l) the conduct and oversight of research involving recombinant DNA, including the content and implementation of the NIH Guidelines for Research Involving Recombinant DNA Molecules, . . . and (2) other NIH activities pertinent to recombinant DNA technology," and it "makes recommendations on research involving the use of recombinant DNA and on developments in recombinant DNA technology."[5] Critical to the area of RAC recommendations, the NIH Guidelines currently state that "RAC will not at present entertain proposals for germ line alterations . . . Germ line alteration involves a specific attempt to introduce genetic changes into the germ (reproductive) cells of an

[2] P.L. 104-99. Thomas H.R.2880. The Library of Congress. Retrieved June 12, 2015.
[3] NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines), Nov. 2013.
[4] Guidelines for Human Embryonic Stem Cell Research, Washington, DC, National Academies Press, 2005.
[5] Charter, NIH Recombinant DNA Advisory Committee, June 30, 2013.

individual, with the aim of changing the set of genes passed on to the individual's offspring."[6] This indicates a current effective prohibition on the use of germline modifying technologies for areas of research within the purview of the RAC.

Should there be application for an Investigational New Drug, FDA review and approval would be required prior to the administration 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.

The role of scientific journals

Lastly, scientific journal publishers have an increasingly important role to play in setting and enforcing standards of behavior within the scientific community. The goal of credible researchers worldwide is publication of their work in the peer-reviewed scientific literature, which signifies the endorsement of the community of researchers working in similar areas and acts as a means of sharing advances in ways that credits the researchers and labs that achieve them as well as moving the field forward. But journals play an additional critical role with requirements that ethics standards are respected, through assurances by authors regarding their contributions, that human subjects protection standards are met, and that conflicts of interest are disclosed and sufficiently addressed.[7] Journals could play a similar role in relation to the publication of research involving gene editing technologies in humans. The study recently published in *Protein & Cell* was reportedly rejected by both *Science* and *Nature* prior to its acceptance and eventual publication, with some reportage indicating that ethics reviews played a role in the decision to reject it. There has been at least one editorial suggesting that journals could add to existing requirements and require that authors provide the details of the ethics review of any gene editing-related research as a condition for consideration of publication.[8]

Conclusion

The United States has long played a leadership role in both science and in the responsible use of the advances discovered or developed. This was certainly the case with the introduction of recombinant DNA technologies. It is critical that we continue to do so as the new and powerful genetic technologies we are discussing today become both more precise and more widely available. Existing oversight approaches may provide part of what can be the framework for addressing many of the issues raised by gene editing technologies. However, there are likely to be gaps in oversight of applications of these technologies, and work must be done to (1) identify these gaps in both in the near and longer terms, and (2) craft appropriate guidelines to bridge these gaps in order to most

[6] NIH Guidelines, Nov. 2012, Appendix M.

[7] International Committee of Medical Journal Editors, "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals," December 2014; http://www.icmje.org/recommendations/.

[8] A. Sharma, C.T. Scott, "The Ethics of Publishing Human Germline Research," Nature Biotechnology 33(6):590-592; June 2015.

appropriately and successfully address the ethics and oversight issues arising as the use of these technologies expands and becomes more sophisticated. 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.