To: Nuffield Council on Bioethics — Genome Editing Working Group
From: Marcy Darnovsky, PhD, Executive Director, Center for Genetics and Society
Re: Open Call for Evidence, 2017
Date: June 30, 2017

Addendum to the Center for Genetics and Society's Response to the 2016 Call for Evidence

Thank you for an additional opportunity to contribute evidence toward your deliberations about genome editing. We would hereby like to reaffirm both our 2016 response to your previous call for evidence and the points we shared in our telephone conversation of 11 March 2016, and to submit the following additional comments for your consideration.

As in our 2016 comments, unless indicated otherwise, the remarks below refer to the application of genome editing techniques to human reproduction (which we will refer to as "human gene editing for reproduction," "germline gene editing," or "human germline modification").

Outline of this submission

1. The February 2017 report issued by a committee of the US National Academies of Sciences and Medicine provides examples of misleading characterizations and/or inadequate considerations that too often characterize conversations about human gene editing for reproduction.
2. Another recent development – several unapproved births using nuclear transfer techniques, both to treat severe mitochondrial disease and to purportedly treat infertility – provides ample reason for concern about 1) unauthorized clinical use of human germline editing and 2) the likelihood of "function creep" – that is, the difficulty of limiting germline editing to particular purposes.
3. Despite calls for public participation, input, and engagement in deliberations about human gene editing for reproduction, no significant resources have been dedicated to this purpose.
4. It is essential that any evaluation of the use of human gene editing for reproduction foreground its potential social consequences – its impacts on communities (especially vulnerable groups), on cultural assumptions, and on societies – rather than only on individuals or couples.
5. Human germline interventions are indeed distinctly significant.
6. Existing international laws, treaties, and declarations on human germline modification must be taken seriously.

Comments

1. **One recent development in the conversation about human gene editing for reproduction that provides many examples of misleading characterizations and/or inadequate considerations is the publication of *Human Genome Editing: Science, Ethics, and Governance*,** a report by a committee convened by the U.S. National Academy of Sciences and National Academy of Medicine (NAS/NAM), released on February 14, 2017.

   The report recommends that "clinical trials using heritable germline genome editing should be permitted" under certain conditions. This represents a striking departure both from the existing international policy consensus on human germline modification, and from the concluding statement of the organizing committee of the 2015 International Summit on Human Gene Editing, of which the NAS/NAM was the main organizer.

The report was criticized by numerous observers, including the Center for Genetics and Society. We direct you to our press statement of February 14, which concluded, "Permitting human germline editing for any reason would likely lead to its escape from regulatory limits, to its adoption for enhancement purposes, and to the emergence of a market-based eugenics that would exacerbate already existing discrimination, inequality, and conflict. We need not and should not risk these outcomes." CGS's views on the report were cited in more than two dozen media outlets including *The New York Times, Washington Post, Reuters, National Public Radio, Science, The Scientist, Forbes, Scientific American,* and *The Guardian.*

We further discuss several of the report's shortcomings in a forthcoming article (Lowthorp and Darnovsky, see attached). They include:

I. **The report barely acknowledges the 2015 statement after the International Summit on Human Gene Editing, which called for a "broad societal consensus"** before any clinical use of germline editing could proceed, and provides no justification for or discussion of its abandonment. This is particularly disturbing because no meaningful resources have been devoted to any kind of public engagement since the 2015 statement. (See Françoise Baylis, "Human germline genome editing: An 'impressive' sleight of hand?")

II. **Though the 2017 report refers numerous times to the need for public engagement, it denies the public the ability to weigh in on the most pressing issue: whether human germline modification is acceptable in the first place.** The report's conclusion that germline editing for reproduction should be permissible was reached in the absence of substantive public engagement. In other words, the report and the process surrounding it are exclusionary moves that overrule democratic participation in the decision that really matters.

III. **The report all but ignores the widespread international opposition to human germline modification**, codified by legal prohibitions in more than 40 nations and in a binding international treaty, the Council of Europe's influential Oviedo Convention. It mentions the Oviedo Convention only twice in eight chapters—once in order to explain why it should not be considered significant.

In a webinar about the report sponsored by Genetic Alliance, one of the NAS /NAM committee co-chairs presented a slide titled "Heritable Genome Editing - Regulations," which included the point: "Other countries vary, from prohibition to possible authorization under strict regulation." This formulation fails to mention 1) the prohibitions that currently exist in dozens of countries, and 2) the fact that no country currently authorizes heritable genome editing. Like the consideration of international policy in the report itself, it is highly misleading.

IV. **The report replaces the widely accepted bright line between somatic and germline modification with the inherently blurred line between germline modification for medical purposes and for enhancement purposes.** While the report acknowledges that the latter distinction is conceptually and technically unclear, and that it would be impossible to maintain a firm policy line between medical application and

enhancement, the report makes no sustained argument to support its embrace of this shift.

V. **Though the report portrays its conclusion as a cautious approach to human germline modification, interpretive comments by its co-authors belie this claim.** The report states that germline gene editing should be used only in medical circumstances when there is an "absence of reasonable alternatives." What would constitute such a situation? In answering a question posed at the press event accompanying the report's release, one of the co-authors stated that a prospective parent's moral objection to pre-implantation diagnosis would qualify as a reason to permit germline editing. This suggests that one of the restrictions at the center of the report's claim to caution is so elastic as to be all but meaningless.

2. **Another recent set of developments, surrounding the births of several children using nuclear transfer techniques, sheds light on several aspects of the likely trajectory of germline gene editing if it were to be approved for even limited applications.**

In September 2016, it was reported that New York fertility doctor John Zhang went to Mexico where, in his words, "there are no rules," in order to evade US regulations and impregnate a Jordanian woman with an embryo created with a nuclear transfer technique. Less than two weeks later, reports emerged of two pregnancies in the Ukraine using the techniques initiated by fertility doctor Valery Zukin, purportedly to treat infertility rather than to prevent transmission of mtDNA disease.

In June 2017, *MIT Technology Review* reported that Zhang has started a company called Darwin Life to market nuclear transfer for age-related infertility. He plans to create the manipulated embryos in the US and take them to Mexico for implantation. In Zhang's words, "Everything we do is a step toward designer babies," and a child created according to his plan would be "very much like an iPhone that's designed in California and assembled in China." (See the CGS press statement on this development.)

These developments demonstrate both the commercial incentives operating in the fertility industry, and the rapidity with which "function creep" can occur with these types of technologies.

3. **Despite calls for public participation, input, and engagement in deliberations about human gene editing for reproduction, no significant resources have been dedicated to this purpose**.

In our 2016 submission to the Nuffield Council, we affirmed that a broad range of voices must be included in the conversation about human gene editing for reproduction. In our telephone consultation with Pete Mills and Andy Greenfield, we elaborated that this biotechnology, like certain other new and emerging technologies, would powerfully shape social relationships, political relationships, and power dynamics, and therefore is properly an object of democratic governance – and not a matter that can legitimately be decided by individuals or clinicians. Among the perspectives that must be included are those from civil society groups, artists and cultural producers, community-based organizations, rights and justice advocates, and social movements.

Unfortunately, no significant resources have yet been dedicated to encouraging or enabling such public participation. The Center for Genetics and Society, however, has shown that public interest in

this topic is strong. In partnership with other civil society organizations, we have organized two public webinars this year on human gene editing, each with over 300 registrants: Gene Editing and the Future of Reproductive Justice and Disability Justice & Gene Editing: Exploring Multiple Perspectives.

4. **It is essential that any evaluation of the use of human gene editing for reproduction foreground its potential social consequences – its impacts on communities (especially vulnerable groups), on cultural assumptions, and on societies – rather than only on individuals or couples.** Unfortunately, the Nuffield Council's public survey that is currently open for responses is structured so as to focus respondents' attention only on the situations and desires of individuals and couples contemplating their personal reproductive decisions, with no mention of the dire consequences these decisions may have on society and humanity at large.

   In addition, the survey fails to mention that germline editing is medically unnecessary due to the existence of alternatives for preventing the births of children with serious transmitted genetic diseases; that judgments about "safe enough" are themselves subject to contestation and disagreement; and that governments around the world prohibit human gene editing for reproduction, mostly because of the risks it poses for introducing a new high-tech eugenics.

5. **Human germline interventions are indeed distinctly significant.** Human gene editing for reproduction has the potential to exacerbate social inequities in a way unprecedented in human history. Once adopted for non-medical purposes, it would be marketed using claims that it could engineer superior traits. Commercial incentives and imperatives would vie with realistic assessments about genetic contribution to desirable traits. Whether or not it objectively introduced inequality into the human genome, it would be understood in that way. Popular perceptions that some people had been born genetically superior could in and of themselves lead to a society of genetic "haves" and "have-nots."

   In addition, as Roberto Andorno has noted (forthcoming), human germline modification is fundamentally different from previous technologies in the sense that it aims at changing not the tools that we use, but the users themselves (or rather, our descendants), and in a manner that is for all intents and purposes irreversible.

6. **Existing international laws, treaties, and declarations on human germline modification must be taken seriously.** It is deeply significant that every country whose legislature has seriously considered human germline modification has decided to prohibit it, and that these decisions account for the majority of the world's nations with advanced biomedical and biotechnology sectors. Similarly, statements by UNESCO, the World Medical Association, and the Human Genome Organization that the human genome is the "common heritage of humanity" bespeak a strong and important commitment to our shared humanity, and a profound aversion to discriminatory beliefs about human difference that would undermine this commitment.

   As a global society, we have recently witnessed assaults on international agreements. In particular, the withdrawal of the United States, under the current presidential administration, from the Paris climate agreement highlights the fragile and precious nature of hard-won international accords. Both of the prospects in question – catastrophic climate change, and the advent of a new high-tech eugenics – pose grave threats to the future of humanity as a species. We ignore, weaken, or undermine global agreements against these threats at our own great peril.

Resources and References

Authored/produced by the Center for Genetics and Society

- Reproductive Genome Editing and the U.S. National Academies Report: Knocking on a Closed Door or Throwing it Wide Open?, Leah Lowthorp and Marcy Darnovsky, *Bioethica Forum* (forthcoming, attached)

  Lowthorp and Darnovsky discuss several problematic elements of the recent US National Academies report.
- Gene Editing and the Future of Reproductive Justice Webinar (video), with Lisa Ikemoto, Ruha Benjamin and Dorothy Roberts (June 13, 2017)

  Addresses the role that advocates of reproductive health, rights, and justice can play in preventing a high-tech eugenic future in which some people's genes are deemed more valuable for reproducing than others featuring Dorothy Roberts, professor of law and sociology at University of Pennsylvania; Ruha Benjamin, professor of African-American Studies at Princeton University; and Lisa Ikemoto, professor of law at UC Davis.
- Disability Justice and Gene Editing Webinar (video), with Anita Cameron, Mia Mingus, Rosemarie Garland-Thomson and Tom Shakespeare (April 24, 2017)

  Disability rights activists Anita Cameron and Mia Mingus, sociologist and bioethicist Tom Shakespeare, and feminist disability studies scholar Rosemarie Garland-Thomson discuss how emerging biotechnologies shape our ideas about disability rights and justice.
- Why I'm speaking about human genetic engineering as a Black woman with disabilities, Anita Cameron, *Biopolitical Times* (April 20, 2017)

  Black civil rights activist with disabilities Anita Cameron discusses how gene editing could affect her communities.
- The fertility industry is 3-person IVF's ultimate prize, Leah Lowthorp, *Biopolitical Times* (April 20, 2017)

  Lowthorp charts how fertility doctors using "3-person IVF" to treat mitochondrial disease have their eye on a more lucrative, prize – treating infertility.
- The Social and Political Dangers of Human Germline Interventions, Marcy Darnovsky and Elliot Hosman, *GeneWatch* (Jan-Mar 2017)

  Darnovsky and Hosman describe such dangers as market-driven mission creep leading to enhancement, a dangerous risk-benefit imbalance for future generations, and the potential of reinforcing inequalities and discrimination while creating a new form of eugenics.
- Editing Humans, Marcy Darnovsky, *Bioscience Technology* (February 27, 2017)

  As part of the "Tech for Humanity" series at South by Southwest, Darnovsky makes the case against human gene editing for reproduction.
- 2016 Fear vs Hope: Gene Editing— Terrible turning point?, Pete Shanks, *Deccan Chronicle* (January 1, 2017)

  Pete Shanks discusses the risks of initiating a techno-eugenic future.
- Dangers of an Unscientific Policy Process: Why the UK's legalization of "three-person babies" should not be the model for CRISPR, Jessica Cussins, *Biopolitical Times* (October 24, 2016)

  Cussins evidences how the UK process that led to legalizing mitochondrial replacement therapy cherry picked data and sidelined dissenting views and scientific results, arguing that policymaking on CRISPR should be guided by greater transparency and more inclusive debate.

- Con: Do Not Open the Door to Editing Genes in Future Humans, Marcy Darnovsky, *National Geographic* (July 15, 2016)
    Published alongside a "pro" contribution by John Harris.
- Should Heritable Gene Editing Be Used on Humans?, Marcy Darnovsky, *The Wall Street Journal* (April 10, 2016)
    Opposing opinions by Marcy Darnovsky and George Church.
- The perils of human gene editing for reproduction, Marcy Darnovsky, *Washington Examiner* (March 8, 2016)
    Darnovsky argues that commercial dynamics would lead to gene editing being offered as an "upgrade" in fertility clinics – with disastrous social outcomes.

Bioethics and social science articles

- Can human germline alterations be ethically justified?, Roberto Andorno, *Bioethica Forum* (forthcoming)
    Andorno poses the questions: Can a risk that may unpredictably shape future people be regarded as "minimal?" Is there any way to ensure that inheritable genetic modification would not lead to non-therapeutic design of future children? Since this technology would irreversibly change the users rather than the tools, is a classic risk-benefit analysis applicable?
- Who will pay for CRISPR?, Jim Kozubek, *STAT* (June 26, 2017)
    Kozubek details how insurance companies are already excluding CRISPR treatments from coverage. Will they put added pressure on the health care system? Will only the wealthy be able to access them?
- CRISPR, human genetic modification, & a needed course correction, Paul Knoepfler, *The Niche* (June 26, 2017)
    UC Davis stem cell biologist Paul Knoepler reviews recent articles promoting human germline modification, and advocates for more assertive policy stances by scientists and scientific bodies to prevent threats to society.
- The Fertility Doctor Trying to Commercialize Three-Parent Babies, Emily Mullin, *MIT Technology Review* (June 13, 2017)
    Mullin reports how controversial fertility doctor John Zhang's new start-up, Darwin Life, plans to commercialize experimental nuclear transfer techniques as an age-related fertility treatment. Zhang wants to combine the technique with gene editing "so that parents can select hair or eye color, or maybe improve their children's IQ."
- Fixing genes won't fix us, Jim Kozubek, *Boston Globe* (June 1, 2017)
    Kozubek argues that efforts to engineer genes often mistake social problems for biological issues, and could channel more resources to wealthy scientists while diverting them from social services.
- Human germline genome editing and broad societal consensus, Françoise Baylis, *Nature* (May 8, 2017)
    Baylis advocates for setting aside the 2017 NAS/NAM report that recommends permitting germline gene editing for therapeutic purposes, and makes a wider call to embrace the challenge of seeking broad societal consensus on this ethically controversial issue.
- Human Germline Gene Editing: An 'Impressive' Sleight of Hand?, Françoise Baylis, *Impact Ethics* (February 17, 2017)

Baylis contrasts the 2015 call for "broad societal consensus" surrounding gene editing for human reproduction with the 2017 recommendation to move ahead by a different committee of the National Academies of Sciences and Medicine.

- Human Nuclear Genome Transfer (So-Called Mitochondrial Replacement): Clearing the Underbrush, Françoise Baylis, *Bioethics* (December 14, 2016)

  In the context of evaluating mitochondrial replacement, Baylis provides a compelling critique of the purported "need" for genetically-related children.

- A "Better Baby" with Gene Editing?, George Annas, *Cell* (April 21, 2016)

  Boston University bioethicist George Annas reviews Paul Knoepfler's *GMO Sapiens: The Life-Changing Science of Designer Babies.*