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Novel Tech Ethics
Faculty of Medicine

Attention:
Dr. Bettina Schmietow
Research Officer
Nuffield Council on Bioethics
28 Bedford Square, London, WC1B 3JS

February 20, 2016,

Dear Dr. Bettina Schmietow and Members of the Nuffield Council on Bioethics Genome Editing project Working Group,

Thank you for the opportunity to provide input into the Open Call for Evidence on Genome Editing. Attached are suggestions for information, insight, and evaluation of gene editing technology. We have placed particular emphasis on the ethical and social questions that arise with respect to the following:

A. The Perspectives on Genome Editing
1) *Linguistic framing of gene editing*
2) *Conceptual framework for analyses*

B. The Application of Genome Editing
3) *Considerations related to the fertility industry and other under-regulated industries*
4) *Considerations related to military intelligence and security*

Thank you,

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Response to Genome Editing: Open Call for Evidence

A. Perspectives on genome modification

1) *Linguistic Framing of Gene Editing*

The language used by the Nuffield Council and others to describe gene editing is likely to contribute to the ethically relevant social perceptions of this technology. For example, the if gene editing is described as "editing," as opposed to "replacing" or "manipulations," it carries with it connotations of control and the type of alteration taking place. Some ways of naming gene editing might have more positive public responses than other ways of naming it, given the particular social context and perceived relationship with other, more accepted technologies. The importance of language can also be evidenced in other biotechnologies, such as the so-called mitochondrial replacement. Arguably, there are potential benefits related to the public perception of this technology if one called it "mitochondrial replacement," as opposed to "nuclear genome transfer." The latter name conjures the (correct) impression that the technique in question is the same as the technique used in cloning (See Baylis 2016). Moreover, mitochondrial replacement suggests that only the mitochondria are being exchanged, rather than an entire cell and its biochemical machinery. Given that the third party's cellular construction and mitochondria will exist in each and every cell of the resulting child, to ignore the importance and potential effects of the third party's contribution seems misleading.

In the context of gene editing, the public perception of this technology can be shaped and manipulated (for better or for worse) by such semantic choices. (See O'Keefe, et al. 2015). The ethical provision of gene editing requires transparency with respect to the nature of the technology. The use of euphemistic descriptions for this technology can unduly colour the lay public and relevant stakeholders' perceptions of what this technology is and how it works. Such misguided perceptions are likely to influence whether or not they find general or particular uses of this technology ethically permissibly. The ethical provision of biotechnologies thus requires that the general public and key stakeholders are not primed with language (in naming or description) to accept its use.

Baylis, Françoise, "A Cautious Approach to Mitochondrial Replacement," Impact Ethics. February 3, 2016.

Meaghan, O'Keefe, Sarah Perrault, Jodi Halpern, and Lisa Ikemoto, "Editing" Genes" A Case Study about How Language Matters in Bioethics," American Journal of Bioethics. 2015 15(12): 3-10.

2) *Conceptual Framework for Analyses*

The conceptual framework for evaluating gene editing technology also matters. We maintain that it is imperative that this technology is understood as revolutionary, as opposed to analogous with past technologies. To be clear, this is not because this technology raises many new ethical questions, but rather, because:

a. New genome editing technologies, such as CRISPR are now fast, efficiently, and more widely available. In this way, CRISPR gene editing is a revolutionary technology. It re-introduces familiar ethical challenges surrounding past genetic technologies and makes addressing these familiar ethical questions all the more pressing to address. If gene editing is framed as "a familiar technology," there is a risk that we might assume ethical questions, surrounding issues related to justice, dignity, and wellbeing, for example, have long been addressed with previous biotechnologies. Arguably, this is not the case. In the provision of genome editing as it advances at an unprecedented pace with CRISPR, researchers and policy makers ought to be attentive to the revolutionary nature of this technology. (See Mariscal and Petropanagos, manuscript under review.) Insofar as biological systems are complex, some argue that it is appropriate to classify the use of gene editing as a "social experiment" as opposed to merely employing the precautionary principle for evaluating new gene editing technologies. (See Hawkins 2015).
b. The revolutionary nature of this technology also means that genome editing will become increasingly relevant across a number of new and interrelated domains. For example, genome editing will have implications for various aspects of health care, including assisted reproduction, as well as agriculture, the environment, various ecological systems. All the different domains of application are interrelated and should not only be addressed in isolation. For example, there is a growing literature on the genetic modification of mosquitoes aimed at the eradication of malaria and other diseases (Hammond et al. 2016). The proposal to genetically modify mosquitos to eradicate disease are not merely important from the perspective of public health, but they intersect with ecological concerns, scientific concerns of off-target effects, international justice concerns, and so on. It is likely that no single person or perspective adequately grasps all of the interrelated implications of the widespread use and normalization of genome editing.
c. Gene-editing technologies are likely to be disruptive both economically and socially. There is money to be made in the patenting, use, and commercial applications of gene editing. The start of the commercial gene editing trend is evidenced by the creation and sale of gene-edited micropigs. In addition, gene editing will have implications social implications for kinship, social

norms surrounding fitness and disability, as well as the pressures and values surrounding human enhancement, for example.

What is important with respect to the revolutionary nature of new gene editing technologies (such as CRISPR) is that it will be difficult to control, as its full impact will only become apparent as it develops, if not in hindsight.

By virtue of its revolutionary nature, we would like to stress the importance of facilitating, promoting, and requiring broad social discussions with a diversity of stakeholders. Groups that have been underrepresented and marginalized thus far include:

- Persons with various different kinds of disabilities, particularly disability rights activists
- Individuals and groups from certain geographic regions, such as Africa and Asia (with the exclusion of China).

Understanding the ways that the use of gene editing should be regulated will require that the social values and needs of marginalized groups be taken into consideration. We don't want to further marginalize or harm already vulnerable groups. The direction that gene editing takes us will largely depend on the social values that are prioritized by those with research and governing powers.

Mariscal, Carlos and Angel Petropanagos. "CRISPR A Driving Force: The *Model T* of Biotechnology" (manuscript under review.)

Hawkins, Ronnie "Facing up to Complexity: Implications for our Social Experiments. Science and Engineering Ethics. (Online) 2015 1-40.

Hammond, Andrew et al. "A CRISPR-Cas9 gene drive system targeting female reproduction in the malaria mosquito vector Anopheles gambiae. Nature Bioetechnology. 2016 34: 78-83.

B. The Application of Genome Editing

3) *Considerations related to the fertility industry and other under-regulated industries*

As human (clinical) applications of gene editing develop, they reveal risks from the use of this technology in largely unregulated industries, such as the fertility industry. The concern here is that technologies are often introduced as treatments, when in fact they are experimental or unproven. This has been the case with the

initial introduction of in vitro fertilization, oocyte cryopreservation, and more recently AUGMENT technology. There are a number of concerns with the lack of regulation in the fertility industry (See Preisler 2013.) In addition to concerns related to the off-target effects of genome editing and the effects on future generations are additional concerns about the safety, efficacy, cost, misrepresentation and potentially negative normative force of introduction of genome editing into largely unregulated industries, such as the fertility industry. One can imagine that the use of CRISPR to select for particular traits might be offered in the clinical setting well before the appropriate clinical research has been conducted. It is particularly important to pay attention to the intersection of poor oversight in under-regulated industries and the availability of technologies that are novel and far-reaching.

The lines between research and therapies are easily blurred. Unregulated settings make this even more concerning when experimental therapies are introduced as innovative therapies. This magnifies concerns related to the commercial uses of gene editing and the potential for off-target effects when used in reproduction (germline).

Preisler, Andrea "Assisted Reproductive Technology: The Dangers of an Unregulated Market and the Need for Reform" DePaul J. Health Care Law 2013 5(2): 213- 236.

4) Considerations related to military intelligence and security

Of note, less attention has been given to particular military and security considerations. These should receive detailed analysis by experts in the ethics of military applications. By the very nature of security concerns, such uses will be less public, though likely interface more with the international community. Uses of biological technologies and organisms in warfare have waned since the Second World War, likely because biology is a stochastic and difficult to control. Nevertheless, all of the microorganisms, animal, and human applications of gene-modification technologies are likely to be relevant in military and security contexts. Others may be particularly troubling in these contexts – performance enhancement, a concern in sports, may be especially problematic in the military context. Military personnel are particularly vulnerable to effectively being human research subjects in military research and operations because of their position. As such, it is appropriate to classify these areas of gene editing research/ application as "dual use research of concern."

In addition, controlled genetic alteration also raises new possibilities, such as the hiding of messages in biological tissue. Such issues must be considered as potentially in need of government regulation. The ability to use the genomes of persons, animals, or plants to send encoded messages across international borders without detection raises new possibilities for intelligence and security. The new possibilities raised by such technologies in these contexts makes it particularly troubling that these perspectives have been largely unexpressed in the discussion of gene modification.