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Genome editing open call for evidence: updated response

This submission is a supplementary update to our previous response from January 2016, which still stands. In this response we update some of the general points we originally made and also add some more detailed answers in response to the questions raised by this latest call for evidence.

Many of the same endpoints potentially possible using germline editing can be reached using currently available techniques that do not have the risks and uncertainties that are associated with germline editing, for example, pre-implantation diagnosis. Given the existence of these technologies, it is challenging to justify the use of germline editing, particularly in the context of human reproduction when the benefits and harms are so uncertain. Therefore it might be premature to try to answer these questions definitively, however they can be revisited as evidence accumulates.

Variations on these technologies have been used for decades if not centuries. We are concerned that limiting the focus of this enquiry to germline impacts in humans is unduly narrow and results in a failure to take account of the wider innovative and regulatory context within which reproductive decisions are situated. It could also result in less attention being paid to applications of gene-editing in plants and animals which cumulatively might have profound global impacts although individual applications may pose fewer ethical challenges.

We also consider if the community is asking the right questions. The use of genome editing in therapeutic clinical applications is happening now, with more clinical trials in the pipeline. We think that more attention should be paid to the implications of implementing these technologies into clinical use, including how existing authorisations can be scaled up.

The PHG Foundation is non-profit health policy think tank. We work to achieve the prompt, effective and responsible application of biomedical and digital technologies within health systems

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Our approach to this consultation

This document should be read as a supplement to our previous response and as such will focus on the additional points we wish to make in response to the questions outlined in the latest call for evidence. We will also highlight some of the uses of genome editing that are closest to delivering clinical benefits and why we think there should be more of a focus on these uses.

Perspectives on genome modification

The significance of genome interventions
In addition to previous submission (section 3):

- A precedent for germline changes to the genome already exists in the form of mitochondrial technologies. These cases are characterised by small numbers of patients, affected by conditions which are usually severe with onset in early childhood, therefore the balance of likely benefits and harms of utilising novel technologies in this context is favourable. However this technology has been developed in order to allow parents to have genetically related children and in all cases the challenges of genetic disease can be overcome by donation of healthy gametes. A discussion is needed on the balance of rights of parents to have genetically related children versus the ethical challenges of altering the germline.
- Over the last year, increasing evidence has emerged about the potential benefits and harms associated with genome editing technologies such that the balance of benefits and harms remains unclear and continues to be an unknown quantity. For example there might be more off-target effects generated than previously thought however this is currently under debate.
- Uptake of CRISPR has been particularly fast in the research arena and is being used as a valuable tool to generate new cell and animals models for research. In terms of clinical use, clinical trials ongoing and planned using CRISPR-Cas9 are currently limited geographically – 9 of 10 listed on clinicaltrials.gov are in China – and also in terms of application, with 8/10 of these trials being in cancer. There is a danger of more impactful applications being overlooked, however trials are also ongoing using more established genome editing technologies such as TALENs and zinc finger nucleases. Examples of these are outlined in our previous submission, section 7.
- Predicating the need for policy on the emergence of particular technologies suggests a danger of technological exceptionalism which seems short-sighted. This approach is unlikely to be robust and future proofed, as technologies are likely to evolve beyond gene editing. This suggests a need for proportionate policy responses that emphasise undesirable policy endpoints rather than processes.

The obligations of scientists
See previous submission, section 4.

The intersecting nature of genome editing applications
See previous submission, section 5.

Science, morality and the law

See previous submission (section 6), in addition:

What conventional moral principles are threatened?

Germline gene-editing potentially threatens the autonomous choices of future generations: extensive philosophical debate already exists on epistemic status of future persons and how the interests of future persons can be reflected in debates about the relative benefits and risks associated with these techniques.

If implemented into clinical practice, these technologies are likely to be limited to those countries (and individuals within those countries) who can afford them. The lack of distributive justice in accessing these technologies for reproductive purposes but also for therapeutic purposes is a significant concern (see section 14). In addition, the widespread introduction of gene-editing technologies in plants and animals could impact on the extent to which individuals can make autonomous choices about their exposure to such technologies.

Are existing moral frameworks/approaches sufficient?

Although it might be desirable to create harmonised (even standardised) approaches, the breadth of ethical, moral, religious and cultural perspectives on these issues suggests that it will also be important to develop frameworks that can take account of moral pluralism in the form of multiple, even conflicting perspectives.

To what extent are laws/legal frameworks necessary?

As stated in our previous response, the UK has robust processes to deliberate the risks, benefits and uncertainties associated with novel technologies, and to develop legal frameworks that provide proportionate checks and balances. For example, the Human Fertilisation and Embryology Authority has established precedents for managing novel technologies in the context of reproductive decision making: these systems and processes are enshrined in the Human Fertilisation and Embryology Act 2008. These processes and concerns are well-developed within England and Wales but creating robust international legal/regulatory frameworks that can take account of multiple divergent perspectives is a potential challenge.

Additional issues

We cover additional issues on equity and equitable access in section 14 of this submission.

The lack of distributive justice in accessing these technologies for reproductive purposes but also for therapeutic purposes is a significant concern

Biomedical research and human applications: Genome editing (non-germline)

Direction of travel
See previous submission, section 7.

Only very recently have there been calls to extend the deadline to allow research into older embryos to take place. In part, this is because the science has finally caught up with the ethics

Biomedical research and human applications: Germline genome editing

Direction of travel

See previous submission (section 8). In addition:

Embryo research in the UK is limited to embryos which are less than 14 days post fertilisation. Although regarded as somewhat arbitrary and pragmatic at the time of its inception, this threshold has been widely supported by most stakeholder groups. Only very recently have there been calls to extend this deadline to allow research into older embryos to take place. In part, this is because the science has finally caught up with the ethics: it was only in 2017 that researchers reporting growing embryos in the lab to 13 days old and having to destroy potentially viable embryos as a result of this restriction. The current position provides certainty, is pragmatic and allows valuable research to proceed as there are many aspects of embryo development which remain unresolved. If the current rule is extended, this could re-open heated arguments about the moral status of the embryo, which could ultimately result in a more restrictive position being taken.

Role of international ethical debates

See previous submission (section 9). In addition:

The National Academy of Sciences in the US released a report on human genome editing in February 2017, which differed in its stance on germline editing – while previous international debates recommended a complete moratorium on germline editing (apart from regulated research purposes) – the NAS report recommended that, subject to stringent criteria, human germline editing could be permissible if it was to prevent serious heritable disease only. This stance highlights the importance of continued and rigorous public debate on the issue and also the need for robust regulation of these technologies.

Significant decisions that need to be taken/responsibility for decision making

See previous submission (section 10). In addition:

Engagement with the public is important in terms of gauging the strength of public opinion and also providing a foundation for good policy development. This process also helps to mitigate individuals' more visceral responses to technology which can form unchecked in the absence of clear communication about a technology and how it might be used.

Equity and equitable access

See previous submission (section 11). In addition:

The most promising clinical applications of genome editing are in the provision of medicinal products for the treatment of disease (covered

in section 7 of our 2016 submission). Within the UK, the delivery of specialised technologies via a small number of centres of excellence has the potential to introduce inequality through 'postcode lottery'. Therefore commissioning of these therapies as specialist treatments should ensure that there is equity of access across the NHS. Some of these products are made using a mix of technologies, therefore appropriate regulation of the end product, rather than the process used to make it, should help to reduce delays in access that might be caused by over burdensome regulation.

The delivery of specialised technologies via a small number of centres of excellence has the potential to introduce inequality through 'postcode lottery'

From an international perspective, access to these technologies is likely to be limited to those countries that have gone ahead with development, which might not have the same ethical or safety standards. Access might be limited to those who can pay, particularly if a technology/treatment is not available in their home country. This also puts patients at risk since safety and ethical standards are not consistent worldwide. In the case of germline editing, given the uncertainty over its effectiveness, it is currently difficult to justify proceeding with a technology that could move reproductive technologies further out of reach of many people, and who could benefit from the techniques that we already have at our disposal.

However, the greatest impact of genome editing is likely to be in agriculture. This is outside the scope of PHG Foundation expertise, but we think that more debate should be focused on these issues, particularly given previous negative public responses to, and handling of the debate on, genetically modified crops.