# The Royal Society

## Public Call for Evidence for the International Commission on the Clinical Use of Human Germline Genome Editing

**27 September 2019**

## Response from the Scottish Council on Human Bioethics

**1. Which diseases and conditions, if any, do you see as appropriate for human germline genome editing?**

None

Intentional germline genome editing is not a form of therapy but of eugenic selection based on the quality of life of possible future persons.
In other words, it indicates that some lives are preferable than others, thereby undermining the very basis of equality of all human life in a civilised society.

This is one of the reasons why the 1997 European Convention on Human Rights and Biomedicine (Oviedo Convention) of the Council of Europe indicated in Article 13 that:

'An intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants.'

This means, according to paragraph 91 of the Explanatory Report to this convention, that:

'Interventions seeking to introduce any modification in the genome of any descendants are prohibited. Consequently, in particular genetic modifications of spermatozoa or ova for fertilisation are not allowed.'

The Scottish Council on Human Bioethics is very concerned that this is the first question being asked in this consultation.

**2. If there were to be an appropriate use case for human germline genome editing, what evidence would be needed to proceed to first in human use?**

There will never be an appropriate use of intentional human germline genome editing since it is a reproductive eugenic procedure.
In this regard, the EU Charter of Fundamental Rights which stresses in Article 3(2) that: 'In the fields of medicine and biology...the prohibition of eugenic practices, in particular those aiming at the selection of persons' must be respected.

The Scottish Council on Human Bioethics is very concerned that an appropriate examination of the ethical challenges relating to intentional human germline genome editing does not seem to be taking place.

**3. What is the status of editing mechanisms for early stage human embryos (e.g., using different editing techniques, improving homology directed repair, etc.)? What are the factors that predict whether single nucleotide changes or other intended modifications in human embryos will be correct? To what extent will genome editing affect the viability of embryos?**

Genetic Modifications of Sperm, Eggs, and During Fertilisation

In the specific context of a genetic modification which takes place either on the sperm and egg cells before they are used for conception or during fertilisation resulting in the formation of a one-cell fertilised egg, a new individual, who would not otherwise have existed, is being brought into being. This would happen because any change (no matter how small) of any of the variables in bringing an individual into existence would result in a very different individual existing in time. In other words, any individual brought into existence through these procedures would be a totally different person, from a numerical identity perspective, to the one who would, otherwise, have existed.

If such a conclusion is accepted then this again has a clear eugenic element since a new individual is being brought into existence in preference to another who may, for example, have qualities which were seen as less valuable than the new individual. What is being proposed, therefore, is not a form of therapy. No existing person is being treated for a disorder. Instead, it is making sure that only certain persons are brought into existence based on the quality of their genomes.
But here again it should be noted that the modification of sperm and eggs cells may be acceptable under international regulations but only as a secondary effect of the main genetic treatment of an existing person for clinical reasons.

Genetic Modifications of Very Early Embryos

Interestingly, if a genetic modification takes place on a very early post-conception human embryo (such as a two-cell embryo), a number of additional ethical challenges arise. Indeed, it would be difficult to know whether any significant genetic change would bring about a completely new individual or whether the original embryonic individual continues to exist and is simply modified. In other words, whether the procedure would have a numerical or only a qualitative effect on identity.
In a way, this philosophical conundrum is not new and comes in many different forms. It is similar to the one mentioned by the Greek historian Plutarch (c. 46–120) in his Life of Theseus (the mythical founder-king of Athens). In this, Plutarch questions in a thought experiment whether a ship which is restored by replacing every one of its wooden parts remains the same ship. This is especially relevant if the old parts are then used to build another ship. In the same way, it is possible to ask whether an embryo in which a certain number of genes have been edited remains the same embryo or whether a change in numerical identity has taken place.

From an ethical perspective, if the genetic modification does not give rise to any significant change in the already existing embryo, it would no doubt be seen as being similar to classical (somatic) therapy in which the original individual remains and the masterpiece is restored. However, if the genetic modification substantially modifies the genome of a very early embryo, more questions relating to the continued existence of the original embryonic individual could be asked. Genetic modification may then be considered to end the life of the original embryo (a form of death) while creating another. Indeed, if this did happen, then a clear eugenic element

would exist since it would mean preferring one new being over another based on the quality of his or her genome.

**4. What is the status of the technology for validating that a correct edit (on target characterization) has been made and that unintended edits (e.g., off target effects, mosaicism, etc.) have not occurred in a range of cell and tissue types? If possible, please provide evidence drawn from work on induced pluripotent stem cells, embryonic stem cells, and/or early stage human embryos.**

The Scottish Council on Human Bioethics will not be responding to this question.

**5. What is the status of generating cell lines from human and non-human germline stem cells?**

The Scottish Council on Human Bioethics will not be responding to this question.

**6. How might animal models inform the editing in human embryos (inclusive of analysis of phenotypic correction)?**

The Scottish Council on Human Bioethics will not be responding to this question.

**7. To what extent do different genetic backgrounds affect success and phenotypic outcomes after genome editing?**

The Scottish Council on Human Bioethics will not be responding to this question.

**8. What is the success rate of full term pregnancies following pre-implantation genetic diagnosis? What affects this (e.g., age, number of oocytes harvested, technique used, etc.)?**

The Scottish Council on Human Bioethics will not be responding to this question.

**9. What are the appropriate mechanisms for obtaining informed consent, long-term monitoring of the future children, assessing potential effects in subsequent generations, and addressing untoward effects? Are there best practices from: a) assisted reproductive technologies; b) pre-implantation genetic diagnosis; c) gene transfer research for children; d) mitochondrial replacement therapy; and e) somatic genome editing?**

Obtaining informed consent for germline genome editing will be impossible. Moreover, the question does not specify whether this consent procedure is for (1) the person wanting a child, (2) the resulting child or for (3) society.
It is clear that the resulting child will not be able to consent to being brought into existence. But this is similar to the present (natural) situation.

With respect to obtaining informed consent from the person wanting a child and from society, the main problem will related to the information being provided before consent is obtained and how much this will be understood. Will they be told, for example, that such procedures are eugenic in nature and will result in undermining the equality of value and worth of all human persons in society?
With germline genome editing it will also be impossible to withdraw consent once the child exists (unless one supports infanticide).

For an example of consent and the long-term monitoring of the resulting child, necessary in germline genome editing, it may be useful to consider the Council of Europe report on xenotransplantation (page 67) see:
https://www.coe.int/t/dg3/healthbioethic/Activities/06_Xenotransplantation_en/XENO(2003)1_SAR.pdf

**10. How should we think about the inter-generational medical (e.g., genetic changes to the genome) and ethical implications of human germline genome editing (e.g., potential harms and benefits)? How should the rights of future generations and the wider human population be taken into account?**

Looking of the rights of future generations and the wider human population is difficult because they do not exist.
Only existing persons have rights.
Moreover, based on the non-identity principle, anything undertaken before a child is created will create a different child from the ones who would, otherwise, have existed.

All these philosophical and existential dilemmas need to be taken into account in the Royal Society's consultation. It is very concerning (and unprofessional) that the Society has not sought the advice of leading philosophers on the non-identity principle.

**11. What international oversight structures would need to be in place to facilitate, in a responsible way, a path forward for germline genome editing?**

The only international oversight structure which would need to be in place for the responsible oversight of germline genome editing is an International Court of Human Rights together with a suitable prison to incarcerate anyone undertaking such a procedure.

**12. Are there any topics or issues that are not covered by the above questions that you think the Commission should attend to during its deliberations?**

International legislation clearly prohibits intentional germline modifications and eugenic practices. For example:

UNESCO's Universal Declaration on the Human Genome and Human Rights indicates in Article 24 that germ-line interventions could be considered as a practice that would be 'contrary to human dignity'.

The Council of Europe Convention on Human Rights and Biomedicine (5), indicates in Article 13 regarding 'interventions on the human genome' that, '[an] intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants'.

The EU Charter of Fundamental Rights which stresses in Article 3(2) that: 'In the fields of medicine and biology...the prohibition of eugenic practices, in particular those aiming at the selection of persons' must be respected.

Moreover, a 2015 UNESCO International Bioethics Committee report has clearly highlighted the eugenic dangers of germline procedures. This indicated that if any intentional germline selection was accepted (such as with gene editing), this would ‘jeopardize the inherent and therefore

equal dignity of all human beings and renew eugenics, disguised as the fulfilment of the wish for a better, improved life.’

This consultation does not seem to understand that germline genome editing involves eugenic selection. Moreover, any selection procedure between the very existence of different persons can only mean preferences. In other words, that it would be better that some persons should exist instead of others and that there may such a thing as 'a life unworthy of life'!
But such a position undermines the very basis of civilised society which does not believe in any differences in value and worth between persons.