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Consultation: *Genomics and genome-editing*

Consultation response on behalf of the Scottish Council on Human Bioethics:

1. The **Scottish Council on Human Bioethics** (SCHB) is an independent, non-religious registered Scottish charity composed of doctors, lawyers, biomedical scientists, ethicists and other professionals from disciplines associated with medical ethics.
The principles to which the Scottish Council on Human Bioethics subscribes are set out in the ***United Nations Universal Declaration of Human Rights*** which was adopted and proclaimed by the UN General Assembly resolution 217A (III) on the 10th of December 1948.
The SCHB is very grateful to the House of Commons Science and Technology Committee for this opportunity to respond to the consultation on ***Genomic and genome-editing***. It welcomes its intention to promote public consultation, understanding and discussion on this topic.

Executive Summary:

2. While it is clear that the safety and efficiency of preconception and early embryonic gene editing procedures give rise to significant biomedical challenges, a number of other ethical questions need to be addressed. These include aspects of germ line modification and eugenic practice as well as whether the very existence of an embryo has been ended in some procedures.

Scottish Council on Human Bioethics Response

The Scottish Council on Human Bioethics will only respond to the questions of the enquiry which relate to its remit. These are:

Question 1: The impact of genomics and genome-editing on human health, with regard to treating disease, avoiding genetic disease and human enhancement.

3. Before gene editing can be used in human reproduction a number of biomedical challenges still need to be addressed. For example, inserting or deleting specific DNA in the right place of the genome of a developing embryo, foetus or post-natal individual without upsetting the biological equilibrium of the cell(s) is a difficult operation. A certain gene may influence a number of different characteristics so that even if a gene was modified to address a certain dysfunction this may give rise to unexpected consequences. The overall result would be a modification that may be less than beneficial.

Gene Editing on Mature Embryos, Foetus or Post-natal Individuals

4. If gene editing tools are used with the aim of addressing a genetic disorder of an existing mature embryo, foetus or post-natal individual, without any intention to change the germ line, this may be seen as a very positive development.
It would be similar to already existing somatic cell gene therapy which is supported by the Council of Europe's *Convention on Human Rights and Biomedicine*¹ which indicates in Article 13 that:

¹ Since the UK is one of the few countries that has not signed or ratified this Convention it only has the force of 'Soft Law'.

“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.”

Thus, such applications would not raise many new significant ethical problems apart from safety and efficacy.

Gene Editing on Early Human Embryos

5. With respect to the editing of the genome of early human embryos, one ethical difficulty relates to the development stage at which this change occurs.
If fertilisation has already been completed and gene editing, takes place on one of the cells of a very early embryo, such as a two cell embryo, a specific ethical concern would be whether any genetic changes would bring about a new embryonic individual. This would then mean that the original embryo would cease to exist (a form of death for this embryo).
Alternatively, if the genetic modification does not give rise to any significant changes in the already existing embryo, it would be possible to consider that the original embryo continues to exist and is simply modified. This may then be seen as similar to any other form of medical somatic cell genetic treatment in which the original individual remains.
6. In a way, this philosophical conundrum is not new and comes in many 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 used to build another ship.² 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 becomes, instead, a new embryo with a new identity.

Ethical Dilemmas and Concerns

7. With respect to preconception and early embryonic gene editing, such as when a genetic modification takes place either (1) on sperm and eggs before they are used in conception or (2) during fertilisation, such as in the formation of one-cell embryos, an important ethical dilemma arises for which very different perspectives can exist.
Careful philosophical analysis is required and it is impossible to do justice to the issue of the ‘non-identity problem’ in a 3,000 word consultation response. The SCHB would, therefore, advise the House of Commons Science and Technology Committee to seek expert comments.³
The following is a very brief summary of the dilemma.
8. First, it is possible to accept that when gene editing takes place either before or during conception to bring into existence a certain kind of future possible person, no identity change takes place. For example, if the gene editing is done so that a possible future person is healthy this could be considered as a form of treatment.
9. Those holding this view may then believe that it is appropriate to seek to bring into existence healthy individuals. Since parents now have a choice with gene editing, their aim should be to improve the lives of their potential children.
From this perspective, the procedure would not create any new ethical problems apart from safety and efficacy.
10. Alternatively, it is possible to consider that making any deliberate gene editing intervention before or during the creation of a being, is in itself, a statement that a choice is being made between two possible future persons based on quality of life, which has a clear eugenic element, if this term is defined as *“strategies or decisions aimed at affecting, in a manner which is considered to be positive, the genetic heritage of a child, a community or humanity in general.”*^{4,5}

² What makes me me? BBC, <https://www.youtube.com/watch?v=wbpQSI95k6I>

³ D. Parfit, 1987. *Reasons and Persons*, Oxford: Clarendon Press.

⁴ Calum MacKellar and Christopher Bechtel (Editors), *The Ethics of the New Eugenics*, New York: Berghahn Books, 2014, p.3.

11. In this case, what is being proposed is not a form of therapy if dysfunctional genes are being replaced by healthy ones either in the sperm, egg cells or during conception. No existing person is being treated or cured for a disorder. Instead, it is making sure that only a certain possible future person is brought into existence. Any individual brought into existence through gene editing would be a very different person (in his or her very identity) from the one who would, otherwise, have existed with the genetic disorder.⁶
12. It follows, that when parents make a decision that only a certain kind of child should be brought into existence, based solely on genetic factors, this decision contradicts the important principle that the lives of all possible future human beings have the same worth and value, regardless of their state of health. Indeed, if “*all human beings are born free and equal in dignity*”, as stipulated in Article 1 of the UN’s Universal Declaration of Human Rights⁷, how can a choice between two supposedly equal future persons be made?
Suggesting that choice should be available to make sure that certain kinds of children are not brought into existence may also mean that there is such as thing as a ‘life unworthy of life’ in society.⁸
This would also mean that the UK would begin to classify the worth of all lives and start walking down a eugenic road.
13. Moreover, if parents do make a choice and decide to avoid having a child affected by a serious genetic disorder and have another one instead, the indirect message being given to persons, who have already been born with the same disorder, is that they should also not have existed. This is clearly discriminatory and would undermine the inherent equality of all human persons.
For clear evidence of the feeling of offence being taken by persons with disability in such a situation, it is useful to refer to the disability witnesses in the prominent French ‘Nicolas Peruche’ court case. In giving evidence to the French Senate in 2001 relating to this case, Mr. Patrick Gohet, Director General of the French Union of Associations of Parents and Friends of Persons with a Handicap (Union des associations de parents et amis de personnes handicapées) insisted that society had a duty to remind all its members that they have an equal intrinsic value and worth. He also believed that it was crucial for society to react to any decision giving the indirect message that there were some lives of less value than others and/or which did not merit to be brought into existence.⁹
14. The fact that some of these gene editing procedures may deliberately change succeeding generations or be considered as eugenic is significant since international legislation clearly prohibits intentional germline modifications and eugenic practices. For example:

(1) 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*”.

(2) The Council of Europe *Convention on Human Rights and Biomedicine*,¹⁰ indicates in Article 13 regarding “*interventions on the human genome*” that, “[a]n 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”.

⁵ It should be noted that Sir Francis Galton (1822-1911), who coined the term ‘eugenics’ in 1883, did not restrict the definition of eugenic procedures to those which were organised by a state/community or which were enforced.

⁶ This is the non-identity problem which arises, for example, in cases where an individual appears to be wronged by the very action upon which his or her own existence depends. See: Derek Parfit. ‘Rights, Interests and Possible People’. In S. Gorovitz et al (ed) *Moral Problems in Medicine*, p369-375. Prentice Hall, 1 July 1976.

⁷ United Nations’ Universal Declaration of Human Rights (1948), <http://www.un.org/en/documents/udhr/index.shtml#atop> (Accessed on 7 April 2011)

⁸ The term a “life unworthy of life” (in German “Lebensunwertes Leben”) first occurred in the title of a book by German psychiatrist Alfred Hoche and lawyer Karl Binding, *Die Freigabe der Vernichtung Lebensunwerten Lebens*, in 1920.

⁹ Public Hearings of the French Senat on the 18th of December 2001 relating to the jurisprudence of the ‘Perruche’ case; http://www.senat.fr/evenement/dossier_perruche.html

¹⁰ Council of Europe. 1997. *Convention for the Protection of Human Rights and Dignity of the Human Being with Regard To The Application of Biology and Medicine*, ETS – No. 164.

Which means, according to paragraph 91 of the Explanatory Report for Article 13, 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.”*

(3) The EU Clinical Trials Directive 2001/20/EC or the new **Regulation EU 536/2014** which will replace this Directive, which both indicate in Articles 9(6) and 90, respectively, that: *“No gene therapy trials may be carried out which result in modifications to the subject's germ line genetic identity.”*

(4) The EU Directive 98/44/EC on the legal protection of biotechnological inventions which indicates in Article 6 that: *“Inventions shall be considered unpatentable where their commercial exploitation would be contrary to ordre public or morality ..., in particular, shall be considered unpatentable: ... processes for modifying the germ line genetic identity of human beings”.*

(5) The EU Charter of Fundamental Rights which stresses in Article 3 (2) that:¹¹ *“In the fields of medicine and biology ... the prohibition of eugenic practices, in particular those aiming at the selection of persons”* must be respected.

15. In the UK, the clinical use of gene editing procedures in human beings would not be possible under the UK *Human Fertilisation and Embryology Act 2008* which states in Section 3(5) that any cell of an embryo used for human reproduction should not have been genetically altered. The only exception would be if the embryo has *“had applied to it in prescribed circumstances a prescribed process designed to prevent the transmission of serious mitochondrial disease”*.
16. Whether the UK would eventually enact legislation enabling gene editing for mitochondrial disorders is an open question. Interestingly, a precedent for germ-line modifications has already been set by the UK's *Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015*. This legislation regulates the transfer of chromosomes from fertilised or unfertilised eggs, in which dysfunctional mitochondria are present, into healthy fertilised or unfertilised eggs, respectively, which were previously emptied of their own chromosomes. It should further be noted that the UK has already accepted, in 2015, gene editing procedures in human embryos for research.¹²

The importance of equality

17. Because every person is different and unequal from a biological perspective, it should be remembered that the only real basis for the equality of human beings is their inherent dignity. This concept, of course, is difficult to define since it cannot just be reduced to scientific or measurable concepts but this does not make it unimportant. Indeed, equality remains the very foundation of civilised society such as in the establishment of democratic parliaments.
18. Certainly, the advancement of autonomy, the reduction of suffering, and the increase in flourishing of human persons are very important goals in any ethical appraisal. But these aims, by themselves, do not give any true value or worth to human life. At least not the kind of value and worth that is equal to all persons, which is expressed in the concept of inherent dignity by the UN Universal Declaration of Human Rights.
19. The SCHB believes that a civilised society must always be prepared to equally value, without selection or choice, each and every human individual. In the same way, a civilised society must welcome into existence all possible future persons independently of their biological or other characteristics such as their genetic qualities or disorders.

¹¹ Charter of Fundamental Rights of the European Union (Proclaimed in Nice on 7 December 2000).

¹² Such as the use of Clustered regularly-interspaced short palindromic repeats with the Cas 9 protein. i.e. the CRISPR/Cas 9 system

20. This is one of the reasons why eugenics was condemned in the past. It was not only seen as wrong because a degree of coercion existed in some of the reproductive procedures. Eugenics was also considered unacceptable because it undermined the very basis of equality between all existing or possible future persons.
21. Thus, if intentional eugenic selection through gene editing was made possible, it would in the words of the 2015 United Nations Educational, Scientific and Cultural Organization's Bioethics Committee: *"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"*.¹³

Question 2: Whether current regulations in particular areas of genomics and genome-editing are consistent, and whether they are adequate to meet the requirements of different 'product' and 'process' based approval processes

22. Under UK and EU law, eugenic research on reproductive cells and early embryos would not come under clinical trials legislation, such as the Clinical Trials Directive 2001/20/EC (or the new Regulation EU 536/2014 which will replace this Directive) but only under the tissue and cells regulations such as the Tissue and Cells Directive 2004/23/EC which does not really address clinical research and does not prohibit germ line modifications.
23. Thus the following questions remain:
1. How can all the protective requirements associated with clinical trials be implemented with gene editing, such as the need for review by a Research Ethics Committee, if they are not being considered as clinical trials?
 2. Can the use of certain gene editing interventions in creating very early embryos just be accepted as procedures/techniques or do they actually involve substances such as medicinal products?
 3. Can the materials being used in the interventions only be considered as cells or manufactures products derived from cells, as such, (so that the interventions come under the Tissue and Cells Directive 2004/23/EC) or can they also be seen as parts of cells or substances (so that the interventions may be considered under the Clinical Trials Directive 2001/20/EC)?
 4. Can the use of certain procedures be considered as gene therapy taking place on a subject since some gene editing procedures may be considered, by a number of commentators, as bringing into existence a subject and not modifying an already existing subject's germ line genetic identity?
 5. How is it possible to study and regulate inter-generational germ line research?
 6. How is it possible to regulate germ line research from an international perspective?
24. Current UK regulations in the areas of genomics and genome-editing are not, therefore, adequate. Moreover, as it stands, the UK still has to guarantee, under Recital 12 of the Preamble of the Tissue and Cells Directive 2004/23/EC, respect for fundamental rights which, according to the EU Charter of Fundamental Rights should include the prohibition of eugenic practices (Article 3(2)).
25. The UK cannot, moreover, side-step the clear condemnation in international legal instruments of deliberate germ-line interventions, such as in Article 13 of the Council of Europe Convention on Human Rights and Biomedicine.

¹³ UNESCO International Bioethics Committee Report: <http://unesdoc.unesco.org/images/0023/002332/233258E.pdf> (Accessed on 1 May 2016)