

This response was submitted to the Call for Evidence held by the Nuffield Council on Bioethics on *Genome editing* between 27 November 2015 and 1 February 2016. The views expressed are solely those of the respondent(s) and not those of the Council.

Personal Consultation Response from Dr. Calum MacKellar **(Based on Article from BioNews 801: 11 May 2015)**

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 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 influence a certain dysfunction this may give rise to unexpected consequences. The overall result would be a modification that may be less than beneficial.¹

Another important difficulty related to the gene editing of developing embryos is that this may represent a form of germline modification since changes would appear not only in the children resulting from the procedure but in all succeeding generations.

In addition, gene editing manipulations in early developing embryos are obviously eugenic 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.”²

In this regard, 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. A voluntary eugenic procedure can also be undertaken by an individual or a couple.

The fact that some of these gene editing procedures may 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,³ 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”.

(3) 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.

Even in the UK, the use of gene editing procedures 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”.

Whether this would eventually result in new UK legislation enabling gene editing for mitochondrial disorders is an open question. Interestingly, a precedent for germline 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.

¹ President’s Council on Bioethics, *Beyond Therapy: Biotechnology and the Pursuit of Happiness*, The President’s Council on Bioethics Washington, D.C., October 2003, p. 38-39

² Calum MacKellar and Christopher Bechtel (Editors), *The Ethics of the New Eugenics*, New York: Berghahn Books, 2014, p.3.

³ 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.

Another ethical difficulty relating to the editing of a human embryo's genome concerns the development stage at which this change occurs.

If a genetic modification takes place either (1) on the gametes before they are used or (2) during fertilisation, such as in the formation of pronuclear (one-cell) zygotes,⁴ a new individual, who would not otherwise have existed, is being brought into being. In other words, it is a statement that this individual should exist and not another which has a clear eugenic element.

It may also send the message to certain persons born with a disability that society believes that it is acceptable to make sure that other persons, similar to them, are not brought into existence which would be a very distressing message for them to hear. 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 court case of Nicolas Peruche.

In giving evidence to the French Senate 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 which did not merit to be brought into existence.⁵

Alternatively, if gene editing takes place once fertilisation has been completed whereby an individual already exists, another set of questions may arise. This would happen, for example, if a certain gene in one of the cells of a two cell embryo was edited.

Here the ethical concern would be whether any genetic changes would bring about a new individual while the original embryo would cease to exist (a form of death) or whether it would be possible to consider that the original embryo continues to exist and is simply modified.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. 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.

If the genetic modification does not give rise to any significant change in the already existing embryo, it would no doubt be seen as similar to any other form of medical somatic genetic treatment in which the original individual remains.

However, if a future procedure could substantially modify the genome of a very early embryo, more questions relating to the continued existence of the original embryo could be asked. Genetic modification may then actually end the life of one embryo while creating another.

In summary, while it is clear that the safety and efficiency of gene editing procedures on very early embryos give rise to significant biomedical challenges, a number of other ethical questions need to be addressed. These include aspects of germline modification and eugenic practices as well as looking at whether the existence of an embryo has been ended. Until such questions are answered it would be appropriate for a common position to be taken by the international community. For example, countries could sign or support the Council of Europe *Convention on Human Rights and Biomedicine* (which may be ratified by any non-European state).

⁴ Pronuclear zygotes are not considered to be embryos in certain European legislations such as in Germany.

⁵ 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

⁶ P.N. Ossorio. 2003. 'Inheritable Genetic Modifications' in Chapman and Frankel, *Designing Our Descendants*, Baltimore: Johns Hopkins University Press, 259-262.