Nuffield Council on Bioethics
CONSULTATION ON GENOME EDITING

Response from CARE

Christian Action Research & Education (CARE) is a well-established Christian social policy charity providing resources and helping to bring Christian insight and experience to matters of public policy. It believes in the value and application of new emerging technologies but also recognises the importance of upstream engagement to add traction to ongoing advances and developments in this area. CARE welcomes this opportunity to comment on the work being carried out by the Nuffield Council on Bioethics' consultation on genome editing. We hope that these brief comments will be helpful.

SUMMARY

- CARE wishes to highlight the safety and ethical concerns surrounding germline editing and how failing to distinguish between germline and somatic cell editing may well adversely affect the progress being made in the clinical development of ethical approaches to cure potentially serious debilitating diseases.
- CARE welcomes and supports beneficial and ethical applications of genome editing on somatic cells, but strongly opposes those that modify germ cells.
- Opening up questions of risk to democratic debate is on the whole good for science and innovation and helps to shape the way forward in determining which values and worldviews ought to be protected.
- In the specific case of genomic editing, the human genome is not the property of any particular culture, nation, or region; still less is it the property of science alone.
- There are obligations on the part of international bodies to uphold the protection of the health and well-being of all citizens. It is important to note that many other countries and scientists consider inheritable genetic modification as being the worst of several options for preventing the transmission of genetic diseases.
- Gene editing manipulations in early developing embryos can be seen to represent a significant step towards genetic enhancement and eugenics.
- Serious consideration needs to be given to whether or not there is compelling medical evidence to support the advance of this technology and whether this outweighs the risks of inaccurate editing and unanticipated effects of the intended edits.

1. Genomic editing: understanding the distinction

1.1 Genome editing should be understood to be an emerging family of biological techniques that can make precise genetic alterations to cells.

1.2 Distinctions should be made according to the type of cells being edited. First, the genetic material of somatic cells in just one individual patient can be edited and altered without affecting the sperm or eggs. Second, germline cells within sperm or eggs or early embryos can be edited which allows for any changes to be passed down to all future children, changing their genetic inheritance.

1.3 Techniques being developed using somatic cells present great potential and are being widely worked on for therapies across the globe, including those to help the human immune system's T cells resist HIV and those for leukemia (Le Page 2015; Lander 2015; Moreno 2015).

1.4 The development of techniques using germline cells have, to date, been prohibited and widely condemned, on the grounds of unknown risks and the impact upon future generations. Making this distinction clear and understandable to all is essential if the technology is to advance.

1.5 **CARE wishes to highlight the safety and ethical concerns surrounding germline editing and how failing to distinguish between germline and somatic cell editing may well adversely affect the progress being made in the clinical development of ethical approaches to cure potentially serious debilitating diseases.**

1.6 CARE welcomes and support beneficial and ethical applications of genome editing on somatic cells, but strongly opposes those that modify germ cells.

2. What obligations do scientists involved in developing and using genome editing technologies owe to society and what freedoms should society allow to these scientists?

2.1 Good science practice should involve adhering to and recognizing legal and ethical boundaries. Law and ethics should not be regarded as obstacles to the advancement of science and technology.

2.2 A key part to developing this good practice involves a two-way conversation with the public, which is based on transparency and proceeds to build a relationship of trust between the public and the scientific community. The risks, realistic benefits, purposes and any vested interests need to be honestly and openly discussed, so that expectations are managed responsibly without being fuelled by hype. This should be the case for all research, whether it is morally controversial or not.

2.3 Opening up questions of risk to democratic debate is on the whole good for science and innovation and helps to shape the way forward in determining which values and worldviews ought to be protected (Sarewitz 2015). To simply dismiss such a stance on the basis that the public are supposedly not able to grasp and understand the complexity of the issue is wrong. Social scientists have a wealth of material to refute this argument, clearly evidencing the capacity of people to learn about and consider wisely the technical aspects of complex dilemmas (see Sarewitz 2015). Dialogue on the ethics of science, needs to involve both the scientific community with non-

scientists (Moreno 2015).

2.4 In the specific case of genomic editing, the human genome is not the property of any particular culture, nation, or region; still less is it the property of science alone. As Jasonhoff et al have argued it belongs equally to every member of our species, and decisions about how far we should go in tinkering with it have to be accountable to humanity as a whole (Jasonhoff et al 2015).

Setting priorities

2.5 Alternatives to ethically controversial work should be prioritised. From even a cursory review of media reports on this issue it is clear that human germline modification is presented as a way in which to prevent transmission of inherited diseases.

2.6 Yet in many cases where couples are at risk of passing on genetic diseases alternative techniques such as prenatal screening, pre-implantation diagnosis, adoption or donated gametes, could be used to allow them to have healthy and genetically related children, without manipulating genes (Dickenson 2015).

2.7 At the International Summit on Human Gene Editing convened by the National Academy of Sciences and the National Academy of Medicine's Human Gene-Editing Initiative in Washington DC, December 2015, several prominent scientists and biotech industry leaders expressed their skepticism about germline gene editing explicitly. Lander, who has spent his career working to develop genomic medicine, noted that the overwhelming majority of people at risk of passing on a genetic disease can have healthy and genetically related children without gene editing (Darnovsky 2015). He argued, "to avoid most cases of genetic diseases … the most important intervention would be ensuring access to genetic testing so carrier couples know they are at risk" (Darnovsky 2015).

3. Do genome scientists have any special obligations to society that are distinct from those of other scientists?

3.1 Yes. This is a very new technology that presents significant questions concerning safety and ethics. The potential benefit of germline genome modification can also be regarded as its greatest danger because of its impact on future generations, the irreversibility of the technique and its potential for unintended consequences and off-target harm.

3.2 It is therefore imperative that scientists build relationships of trust (as discussed above). One way in which this can be achieved is through adhering to national and international safety and ethical guidelines.

3.3 The economic impact of new genomic techniques should not be underestimated. Techniques such as CRISPR-Cas9, are providing genomic scientists with tools that could lead to the development of new research and therapies, at a pace which allows the modification of DNA to become cheaper and easier. This opens up greater possibility of amateur biologists working in converted garages or community laboratories, helping to challenge legal and/or ethical boundaries, pursue ideological driven agendas and who simply ignore international agreements (Odling-Smee et al

2015; Ledford 2015b).

3.4 To date there has been only one published study that describes genome editing of human germ cells. The Chinese research group have attempted to genetically modify non-viable human embryos (Cyranoski & Reardon 2015). The treatment killed nearly one in five embryos and only half of the surviving cells had their DNA modified. Of the cells that were even modified, only a fraction had the disease mutation repaired. The study also revealed off-target DNA cutting and incomplete editing among all the cells of a single embryo.

3.5 These research findings tend not to be widely communicated in the media and public conversation surrounding germline modification. Instead more attention is given to the anticipated benefits - which may or may not be justified.

4. What obligations do governments have towards society to ensure 'safe' science or otherwise to shape the scientific research and development?

4.1 Governments have an obligation ensure the safety and well-being of their citizens. To do this involves balance the harms of potential research with therapies that could help to treat and heal.

4.2 The International Summit on Human Editing in 2015 in effect called for a moratorium on making inheritable changes to the human genome. This was based on the fact that in their expert opinion it was felt "irresponsible to proceed" until the risks could be better assessed and until there was "broad societal consensus about the appropriateness" of any proposed change (Wade 2015). Accompanying such a move should be a continuing forum in which potential uses of germline editing can be discussed, with the hope of developing a coordinated approach.

4.3 CARE supports the international call for a voluntary moratorium among genome scientists for human germline modification, including on human embryos. This would not harm or impede all genome research but would rather help to focus attention, expertise and time to exploring fully the benefits of somatic genetic editing.

4.4 It is noted that the Chinese research team's 'proof of concept' experiment on non-viable human embryos took place weeks after the summit's call for a moratorium and falls within an ethical grey area. This demonstrates the need for international cooperation in taking clear and decisive steps in this area. As Dickenson and others have noted this kind of cooperation has caused scientific endeavor to flourish (Dickenson 2015). The Human Genome Project, which has allowed the gene editing techniques to be subsequently developed, was based on international cooperation and partnership.

International obligations

4.5 There are also obligations on the part of international bodies to uphold the protection of the health and well-being of all citizens. It is important to note that many other countries and scientists consider inheritable genetic modification as being the worst of several options for preventing the transmission of genetic diseases, owing to risks both biologically and socially (Darnovsky 2015; Baltimore

2015). This places the UK in an isolated position, one that goes against international consensus.

4.6 On this basis it has been prohibited by law in some 40 countries and by a binding Council of Europe treaty, the Convention on Human Rights and Biomedicine. There is a breadth of guidance from international bodies:

4.6.1 **The EU Charter of Fundamental Rights Article 3 (2)** states 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.

4.6.2 **UNESCO Universal Declaration on the Human Genome and Human Rights** (UNESCO 1997). Article 24 states that germ-line interventions "could be considered as a practice' that would be 'contrary to human dignity".

4.6.3 **The International Bioethics Committee of the UNESCO** recently published a report on Germline Gene Therapy with a re-emphasis that: "interventions on the human genome should be admitted only for preventive, diagnostic or therapeutic reasons and without enacting modifications for descendants, as affirmed in Article 13 of the Oviedo Convention. The alternative would be to jeopardize the inherent and therefore equal dignity of all human beings and renew eugenics, disguised as the fulfillment of the wish for a better, improved life" (UNESCO IBC 2015, para. 107).

4.6.4 **The Council of Europe's Convention on Human Rights and Biomedicine.** Article 13 states that "an intervention seeking to modify the human genome may only be undertaken...if its aim is not to introduce any modification in the genome of any descendants" (Council of Europe 1997).

5. What conventional moral principles, if any, does genome editing challenge?

5.1 In order to fully consider the moral principles in relation to genome editing requires the need to make clear distinctions about what it does and does not entail, as addressed in section (1).

5.2 Significant principles are challenged when germline genome editing is considered and it is with regard to this that the following points are offered:

The future child

5.3 Taking to ourselves the power and ability to alter the genomes of our offspring and all subsequent generations, representing irreversibly change.

5.4 It is likely that some may well argue for the rights of the parent to exercise autonomy without restriction, similar to using preimplantation genetic diagnosis (PGD) to avoid genetic diseases. Nevertheless parental autonomy must be weighed against the interests of future generations who cannot consent to the genetic modifications being considered (Lander 2015). The future child must be placed at the centre of ethical decision-making concerning germline modification.

5.5 A key question that needs to be asked is does a human being have a right not to be designed, not to be manufactured, not to be the object of commercial deals, to come into existence with his or her own unique, naturally created characteristics and life?

5.6 The impact of this must also be considered in the wider social context. How does editing the germline affect our respect for human life and beliefs that parents have unconditional love for their children and that human life is priceless and must never be considered and treated as a commodity?

Eugenic concerns

5.7 Gene editing manipulations in early developing embryos can be seen to represent a significant step towards genetic enhancement and eugenics, if the term is defined as any "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" (Mackellar & Bechtel 2014: 3)

5.8 Several scientists have warned of this danger writing in *Nature,* "Such research could be exploited for non-therapeutic modifications...permitting even unambiguously therapeutic interventions could start us down a path towards non- therapeutic genetic enhancement" (Lanphier et al 2015).

5.9 It is all too easy to dismiss claims of eugenics as helping to scaremonger but the fact remains that any action that helps to reinforce discrimination by improving human genetic traits should be vigorously opposed.

5.10 In the name of upholding personal freedom to choose, taking steps to modify the human germline helps to bring closer the potential to determine what are 'bad' genes that need to be replaced and what are 'good' genes that need to be introduced. Of crucial significance is the criteria set to determine this selection process and who is able to shape and determine the criteria. Whilst Harris (2005), Savulescu (2005; Alleyne 2012) and others will argue that parents influence their children in many ways through choice of schools, opportunity to engage in extra curricular activities and so forth, there remains a fundamental difference between these choices and the decision to change the genetic code, which represents the core make-up of a person and which is passed down to future generations.

Safety

5.1 CRISPR/Cas9 is not a perfect procedure with evidence indicating that it can often find unintended targets and can cut the DNA in the wrong spot (Ledford 2015a). This clearly poses significant challenges and safety concerns if applied in humans. Given that the technology is still in its infancy very little is known as to its impact on future generations.

5.2 The research carried out by the Chinese team found 'a surprising number of 'off-target' mutations assumed to be introduced by the CRISPR/Cas9 complex acting on other parts of the genome. It was noted that the rates of such mutations were much higher than those observed in gene-editing studies of mouse embryos or human adult cells. The team also acknowledge their work only looked at a portion of the genome. If the whole genome sequence was taken there could be many more. These unintended mutations could be harmful and potentially catastrophic if they occurred in humans.

5.3 Serious consideration needs to be given to whether or not there is compelling medical evidence to support the advance of this technology and whether this outweighs the risks

of inaccurate editing and unanticipated effects of the intended edits (Lander 2015). Being able to justifiably distinguish between what is hope and hype is difficult but nonetheless necessary.

5.4 As Lander (2015) argues, to reduce the incidence of monogenic disease embryo editing is not what is needed but rather routine genetic testing so that the many couples who do not know they are at risk can consider the options available to them.

[2,701 words]

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