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.

Nuffield Council on Bioethics – Genome Editing: open call for evidence

Cystic Fibrosis Trust response – February 2016

About cystic fibrosis and the Cystic Fibrosis Trust

Cystic fibrosis is a life-limiting, recessive, autosomal genetic disorder. Over 10,500 people in the UK have cystic fibrosis and more than 2.5 million people in the UK are thought to carry the faulty gene.

The Cystic Fibrosis Trust is the only UK-wide charity making a daily difference to the lives of people with cystic fibrosis, and those who care for them.

Whilst life expectancy has increased dramatically in the Cystic Fibrosis Trust's 50 years, only half of people with the condition alive today will live to see their 40th birthday.

We are committed to promoting world-class research and clinical excellence, focused on the development of innovative and life-changing treatments and care shaped by people with cystic fibrosis.

Our research programme helps us develop treatments that both limit the impact of cystic fibrosis, and will one day find a treatment to beat it for good.

Our research strategy aims to build on past achievements and ensure we can play a leading role in responding to the new and exciting opportunities within cystic fibrosis research for the benefit of people with cystic fibrosis.

Cystic fibrosis and genome editing

Genome editing research has huge potential for the mission to beat cystic fibrosis for good and we want to ensure that the unprecedented pace of development in the field is nurtured, whilst ensuring that a transparent ethical debate can develop and embed public confidence in the exploitation of the technology, particularly for applications beyond research.

Supporting the Nuffield Council on Bioethics call for evidence

The Cystic Fibrosis Trust is connected to a number of leading researchers in the field of genome editing and called upon their expertise to support the development of our submission.

We give special thanks to Professor Ludovic Vallier, Senior Group Leader, Cambridge Stem Cell Institute; Dr Patrick Harrison, Senior Lecturer in Molecular Physiology, University College Cork; Professor Eric Alton, Chair in Gene Therapy and Respiratory Medicine, National Heart & Lung Institute, Imperial College London; and Dr Chris Boyd, Gene Therapy Group Leader and Senior Research Fellow, MRC Centre for Inflammation Research, University of Edinburgh.

We focus our response on five themes.

- **What is the rate of travel in genome editing science and what are the expected timescales?**

The pace of change in genome editing since the publication of Jinek et al in 2012 has accelerated like nothing else in the field over the last 40 years. The unprecedented rate makes it challenging to identify useful timescales but it is likely that ex vivo gene editing in man will be achieved before in vivo genome editing in man, due to the greater technical challenge posed by delivery and immune response.

However, with 2017 considered a plausible date for the first clinical trials using CRISPR technology, there is an undoubted appetite to accelerate progression of the science still faster. This, of course, makes it all the more important that we are able to confidently guide, support and hold to account the ethical considerations of such activity.

- **Does genome editing raise any distinctively new moral questions or simply cast familiar questions in a new light?**

Genome editing's broader moral framework has been open for debate for more than 40 years, with the only distinctively new moral challenge being that applications that were once understood as only a vague possibility could now be cited as reasonable probabilities.

In that context, the main challenge must be to define an ethical framework that allows for specific clinical applications of genome editing technology, while avoiding inappropriate and/or eugenic applications.

With germline modification via genome editing tools such as CRISPR likely to be possible in humans, it is important to reflect that the ethical considerations of germline modification remain the same, regardless of the mechanism, and that mitochondrial donation was approved by the UK Parliament after widespread consultation in 2015 and is close to being licensed for human testing.

- **What are the current technical limitations and constraints of genome editing technologies in clinical applications?**

Despite iterative improvements in specificity, efficiency and fidelity, combined with the pace of progress, concerns about the impact of off-target effects persist.

Therefore, an important ethical consideration and an important exercise in defining limits of acceptability in clinical genome editing innovation is to interrogate the acceptability of risk in a clinical setting.

Separately, the technical challenges of delivery and immune response to initial and repeat will need to be explored thoroughly and are likely to provide novel challenges to trial design.

Our consultation also raised the challenge of our own understanding of biology and genetics, in a broader sense, and the danger of overestimating its comprehensiveness when applying that knowledge in the field of genome editing.

We must, therefore, foster coordination and collaboration to collectively bring forward the advances of genome editing, in a way which appropriately balances risk and reward.

- **To what extent can government or other agencies support the advance of genome editing and what bearing do international ethical debates and agreements have on the pace or organisation of research?**

One of the key interventions that the government can make is to support the concept of genome editing to be considered holistically, by not purely investing resource in the editing itself but broadening, stimulating and enriching study that brings together those advances with delivery studies and immunological consequences.

This would accelerate the translational potential of genome editing, which will likely be an expensive but highly-reward enterprise. To this end, it is perhaps important to consider disease-specific supplementary funding of clinical translation of the technologies, which will focus resource to advance a positive outcome.

- **Is genome editing simply a more powerful tool or a transformative technology?**

The scale of the potential of genome editing make it hard to resist describing it as transformative. In research, that transformational quality has been realised.

The leap across to clinical application is a hurdle that may prove to diminish the scale of effectiveness we hope for – particularly in respect of in vivo treatment modes. Nevertheless, efforts to adapt the technology to clinical application are clearly warranted and should be supported enthusiastically.

Next steps

The Cystic Fibrosis Trust very much welcomes the work of the Nuffield Council on Bioethics and we are very keen to play a role in the future development of this work beyond this initial phase.

You can read more about the research we are funding relating to genome editing below:

http://www.cysticfibrosis.org.uk/research-care/research/about-cystic-fibrosis-research/areas-of-research/gene-therapy/second-generation-cftr-gene-repair

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