**CALL FOR EVIDENCE**

The Royal Society and the U.S. National Academies of Sciences and Medicine have convened an international commission to develop a framework for considering technical, scientific, medical, regulatory, and ethical requirements for human germline genome editing, should society conclude such applications are acceptable.

To inform its deliberations, the Commission is engaging with external expertise and invites responses to the questions below.  This call for evidence is open until **Friday 27 September 2019.**  You may limit responses to those questions most relevant to your particular area of expertise. When appropriate, you are encouraged to provide citations and/or links to evidence in support of your responses.

The U.S. National Academies will list all written submissions in a Public Access File (PAF) established for the International Commission. These submissions will be made available to the public upon request. If you prefer that personally identifiable details not be included in the PAF, you must not include your name, contact information, or other such specifics in your comments.

The call for evidence asks the following questions:

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

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?

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?

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 early stage human embryos.

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

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

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

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

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?

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?

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

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?

Because respondents to the call for evidence are self-selected, the National Academies and Royal Society will not necessarily use submissions to judge the prevalence of attitudes or opinions.