

# Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing

## REPORT OF THE FIRST MEETING

### Background

The World Health Organization (WHO) has established a global, multi-disciplinary expert panel to examine the scientific, ethical, social and legal challenges associated with human genome editing (both somatic and germline).<sup>1</sup> The Committee includes members from Africa, Asia, Europe, the Middle East, Oceania, North America and South America.

The Committee has been tasked to advise and make recommendations on appropriate institutional, national, regional and global governance mechanisms for human genome editing. During the course of its work, the Committee will review literature on current human genome editing research and its applications, consider existing proposals for governance and relevant ongoing initiatives, as well as solicit information about societal attitudes towards the different uses of this technology. The Committee will explore how best to promote transparent and trustworthy practices and how to ensure appropriate assessments are performed prior to any relevant work being undertaken.

The recent application of tools such as CRISPR-Cas9 to edit the human genome with the intention of treating or avoiding disease has highlighted the need for robust oversight in this area. The Committee will work in a consultative manner and build on existing initiatives to develop a responsible and responsive governance framework for the application of genome editing technologies going forward. It will liaise with relevant UN and other international agencies, and communicate with Academies of Science and Medicine as well as with other national or professional bodies, patient groups and civil society organizations that have worked, or are working, in this area.

### Work of the meeting

From 18-19 March 2019, 17 out of the 18 members of the Committee, and observers from eight organizations met in Geneva, Switzerland (Annex). The meeting was opened by Dr Tedros Adhanom Ghebreyesus, Director-General of the WHO. As part of its work, the Committee considered declared interests amongst its members, discussed the roles and responsibilities of membership, and reviewed its statement of task.

In its first substantive session, the meeting was briefed by Robin Lovell-Badge, senior group leader and head, Laboratory of Stem Cell Biology and Developmental Genetics, Francis Crick Institute, UK. He provided an overview of:

- (i) Common components of editing tools;
- (ii) Editing tools currently being used in clinical trials;
- (iii) Scope of potential for use;
- (iv) How editing tools enable different functional changes in genetic material and its expression, such as insertions, deletions, exchanges of sequences, and base editing;

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<sup>1</sup> <https://www.who.int/ethics/topics/human-genome-editing/en/>

- (v) Examples of *in vitro* and *in vivo* somatic genome editing; including the possibility of *in utero* interventions.
- (vi) Applications of *in vitro* genome editing of the human germline, such as editing cells that give rise to gametes, or editing the early embryo;
- (vii) Potential for *in vivo* human germline editing with genome editing tools;
- (viii) Challenges to clinical application of genome editing, such as mosaicism, or shortcomings in efficiency and accuracy of homology directed repair, and potential technical approaches for overcoming them;
- (ix) Methods of delivering genome editing tools into cells; and
- (x) Capabilities for detecting whether genomes have been edited.

The Committee also heard about:

- (i) *In vitro* and *in silico* methods for detecting and measuring off-target effects;
- (ii) Differentiating between mutations due to editing from natural background levels of mutation;
- (iii) Potential future developments for clinical application of somatic genome editing;
- (iv) Potential harms and potential benefits of genome editing; and
- (v) Technical developments in detecting negative impacts of genome editing.

The meeting then heard short briefings on existing initiatives and reports relevant to its work, including:

- “Genome editing: an ethical review” and “Genome editing and human reproduction: social and ethical issues” - published in 2016 and 2018 respectively by the Nuffield Council on Bioethics;<sup>2</sup>
- Human Genome Editing Initiatives by the US National Academy of Sciences and National Academy of Medicine;<sup>3</sup>
- Universal Declaration on the Human Genome and Human Rights (1997),<sup>4</sup> International Declaration on Human Genetic Data (2003),<sup>5</sup> Universal Declaration on Bioethics and Human Rights (2005),<sup>6</sup> the Report of the International Bioethics Committee of UNESCO on Updating Its Reflection on the Human Genome and Human Rights (2015);<sup>7</sup>
- Intergovernmental committee on bioethics, and the Convention on human rights and biomedicine by the Council of Europe.<sup>8</sup>

The WHO introduced a series of documents commissioned to provide background on the Committee’s work, including: on the governance of human genome editing technologies; on the governance of other genome editing technologies, including those related to food security, environmental security, and global health security; the ethics of human genome editing; as well as an overarching paper that provided a summary of key issues. These papers had been sent to, and reviewed by, Committee members prior to the meeting. The Committee heard that genome editing can have both direct and indirect health implications, for example, offering ways to prevent or treat genetic diseases, or enabling progress in nutrition and food security, environmental health, and global health security.

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<sup>2</sup> <http://nuffieldbioethics.org/project/genome-editing>

<sup>3</sup> <http://nationalacademies.org/gene-editing/index.htm>

<sup>4</sup> <http://www.unesco.org/new/en/social-and-human-sciences/themes/bioethics/human-genome-and-human-rights/>

<sup>5</sup> <http://www.unesco.org/new/en/social-and-human-sciences/themes/bioethics/human-genetic-data/>

<sup>6</sup> <http://www.unesco.org/new/en/social-and-human-sciences/themes/bioethics/bioethics-and-human-rights/>

<sup>7</sup> <https://unesdoc.unesco.org/ark:/48223/pf0000233258>

<sup>8</sup> <https://www.coe.int/en/web/bioethics>

The Committee then held a closed session where it reflected on the information provided. Committee members exchanged views on the group's mandate, substantive issues relevant to its work, as well as how to structure its activities so as to successfully conclude its task. The Committee identified both somatic and germline genome editing relevant to its mandate and determined to consider governance measures and develop recommendations relevant to both. The Committee noted that its work programme was ambitious given the timeframe available.

On the second day of the meeting, participants worked in small groups to identify and discuss specific issues, mechanisms and stakeholders that could comprise, or contribute to the development of, a governance framework. The Committee also considered how these elements may differ at international, regional, national or local levels.

Following this discussion, Committee members were invited to identify guiding principles or actions on which there might be agreement. Three action items and corresponding principles were identified.

The final afternoon of the meeting, including a closed session, saw the Committee discuss and develop a project plan for its future work and consider arrangements for its next meeting.

## **Outcomes**

At its first meeting, the Committee produced three recommendations.

1. Having agreed on the need to provide a more structured mechanism for collecting and curating details of planned and ongoing research relevant to its work, and anchoring this need in the principle of transparency, the Committee requested WHO to immediately start work to develop a registry. The Committee called on anyone, regardless of whether they are in government, academia, industry, or community labs undertaking research and development relevant to its mandate to register this to receive a registration number, once the registry becomes available. The Committee considered that any failure to register relevant research must be considered a fundamental violation of responsible research. The Committee called on those funding research to require registration in the database and that journals publish the results of research only with a registration number. The registry needs to include provisions to capture products and clinical applications in future. The Committee will establish a working group to develop the architecture of the registry, whose task will include agreeing the types of research that must be included in this registry and the metadata that should be submitted to describe the research in appropriate detail.

2. The Committee agreed with the views previously expressed that "it would be irresponsible at this time for anyone to proceed with clinical applications of human germline genome editing." Consistent with the principle of responsible stewardship of science and noting that relevant work might already be underway, the Committee requested and urged all those conducting, or aware of research and development relevant to its mandate, in particular genome editing of human germline cells and embryos, to engage with the Committee immediately. Interactions with these researchers is critical for the Committee's evidence-gathering work in order better to understand the technical environment, as well as the governance arrangements currently in place. The Committee noted the importance of understanding what has not been published to date, including negative or inconclusive findings, as well as successful efforts.

3. Having agreed on the importance of inclusivity, the Committee stressed its desire for input from the broadest possible range of stakeholders and is exploring opportunities for an open, online mechanism for seeking input. The Committee requested the Director General to enhance WHO's capacity to share information with, and collect information from, both technical and lay audiences. Two strategies were identified: an enhanced website; and targeted outreach to regional and country offices. Specifically, the Committee requested the Director General to engage WHO's regional and country offices and urge them to

canvass societal views on human genome editing and to act as a vehicle for engagement, in particular leveraging WHO's ability to operate in multiple languages. The Committee also highlighted the importance of language-independent resources, such as cartoons and memes. This process will enhance the inclusivity of the Committee's work.

### **Future work of the Committee**

Noting that no single mechanism or actor could effectively address all the issues connected to human genome editing, the Committee concluded that a comprehensive governance framework is needed. This framework must:

- (i) Identify relevant issues, a range of specific mechanisms to address them, and be developed in collaboration with the widest possible range of stakeholders.
- (ii) Be scalable, sustainable and appropriate for use at the international, regional, national and local levels.
- (iii) Work in parts of the world where there is traditionally weaker regulation of scientific and clinical research and practice, and where genome editing may not yet be pursued with great intensity
- (iv) Provide all those responsible for the oversight of genome editing with the tools and guidance they need.

The Committee charted its future work programme, including a series of in-person meetings over the next 12-18 months interspaced with online consultations to provide for a broad and inclusive debate. The Committee will continue to work on standards and practices for the responsible stewardship of science, as well as attributes of effective governance frameworks. The Committee will meet identified milestones and produce specific deliverables. At its next meeting proposed to take place during the week beginning 26 August 2019, the Committee will begin to flesh out elements of a governance framework, mapping specific elements and how they might operate at different levels. Future work of the committee will complement, and not replicate, other efforts to ensure appropriate governance of genome editing technologies.

ANNEX

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