SASHG Committee Consensus Statement on Heritable Human Genome Editing

Background:

On Wednesday, 11 December 2024, the South African Society of Human Genetics (SASHG) Committee hosted an Indaba titled *Ethical, Legal, and Social Implications of Heritable Human Genome Editing: A South African Perspective.* The event was prompted by the recent inclusion of a section on heritable human genome editing (HHGE) in South Africa's health research ethics guidelines. There were 119 participants. The Indaba featured presentations from a multidisciplinary panel of experts in Human Genetics, Bioethics, and Law:

Dr Janine Scholefield (Research Group Leader at the Council for Scientific and Industrial Research (CSIR)) outlined genome engineering technologies, their mechanisms, applications, and limitations.

Prof. Michele Ramsay (Professor in Human Genetics, Director of the Sydney Brenner Institute for Molecular Biosciences, and South African Research Chair for Bioinformatics and Genomics of African Populations) provided an overview of the international debate, guidelines, and recommendations for heritable human genome editing.

Prof. Michael Pepper (Director of the Institute for Cellular and Molecular Medicine and the SAMRC Extramural Unit for Stem Cell Research and Therapy; Professor in Medical Immunology at the University of Pretoria) discussed the potential clinical applications of genome editing in South Africa, focusing on conditions like HIV and TB, as well as the implications of existing laws and governance.

Prof. Safia Mahomed (UNISA's School of Law) explored legal and ethical gaps in South Africa's regulatory framework concerning genome editing.

Prof. Jantina de Vries (Director of the Ethics Lab and Professor of Medicine at the University of Cape Town) talked about the ethical considerations for heritable genome editing, emphasising best practice and policy recommendations.

Key Points from the Indaba:

1. **Scientific and Technical Developments**:

Genome editing technologies offer **unprecedented opportunities for research** and clinical applications. However, concerns about **off-target effects and long-term consequences remain significant barriers to clinical use.**

2. **Global Ethical and Regulatory Considerations**:

Currently, no country explicitly permits heritable human genome editing (HHGE). The overwhelming international consensus is that **clinical use is premature, and research should proceed cautiously within strict ethical and regulatory frameworks**. A moratorium on HHGE in clinical settings is supported, given the potential for irreversible effects on future generations and current uncertainties around safety and efficacy. A 2020 policy survey by Baylis et al., spanning 106 countries, found that 96 had policies on genome editing in early human embryos, gametes or precursor cells. Of these, 75 countries explicitly prohibit using genetically modified embryos to initiate pregnancies, effectively banning HHGE. **However, legal frameworks remain unclear both locally and internationally, underscoring the need for greater regulatory clarity.**

3. **Guiding Principles for Future Applications**:
   - Research should focus on **refining safety and efficacy**.
   - Initial applications, if/when considered, should be **restricted to severe monogenic disorders** with no viable alternative treatments.
   - **Equity in access** to technologies must be a priority to avoid exacerbating health disparities.
   - Any policy development should **align with international guidelines** and be subject to ongoing public discourse.

Our Position:

The SASHG committee thank (1) the panelists for guiding us through the nuances of this subject, (2) the South African National Health Research Ethics Council (NHREC) for attending the Indaba, and (3) the audience for engaging in thought-provoking discussions. We support the international moratorium on HHGE until robust safety, efficacy, and governance frameworks are established, and endorse continued dialogue on the subject.

The **phrasing and terminology** used in the revised South African National Health Research Ethics Council (NHREC) guidelines on HHGE are **problematic and ambiguous**. References to “individuals born as a result of HHGE interventions” and “prospective parents” suggest clinical reproductive applications, conflicting with statements like “researchers must adhere to the fourteen-day rule” and “researchers must adhere to all relevant laws governing HHGE research”. We feel that this inconsistency reflects **insufficient consultation with the genetics and bioethics experts**. Consultation with the SASHG community should be prioritized to gain access to crucial expertise and insights.

Furthermore, **we disagree with assertions that South African law permits HHGE simply because it is not explicitly prohibited**. In our view, the National Health Act should be interpreted within a broader context. While HHGE is not specifically mentioned, the Act clearly prohibits the manipulation of “any genetic material, including genetic material of human gametes, zygotes, or embryos” in a reproductive context.

Members of the NHREC attending the Indaba agreed that **revisions to the terminology and content of the guidelines are necessary** and should be made in consultation with local experts and stakeholders. The SASHG considers this an urgent matter and is committed to supporting the NHREC in this effort, **to mitigate any potential for unethical and harmful practice**. Correct terminology and conceptualization are essential for the document's clarity and crucial for ensuring that legal frameworks align with ethical principles, while fostering responsible innovation. Engaging with communities, policymakers, and stakeholders is essential to creating an inclusive regulatory and governance structure.

In conclusion:

The Southern African Society for Human Genetics (SASHG) recognises the rapid advancements in genome engineering technologies and their transformative potential for addressing genetic disorders. However, we emphasise the importance of proceeding cautiously, considering the ethical, social, and legal implications unique to our context. We urge South African researchers, policymakers, and the public to engage in open discussions on the implications of HHGE, ensuring that our national policies reflect our societal values and global standards.