Heritable human genome editing in South Africa – time for a reality check

Referring to the third edition of the *South African Ethics in Health Research Guidelines: Principles, Processes and Structures* (the guidelines) dated May 2024,[1] Baylis and Hasson[2] assert that the guidelines support heritable human genome editing (HHGE), which allows for children conceived from 'gene-edited' cells to be born. On 7 November 2024, a news item appeared in *Nature* titled 'Will South Africa become first country to accept controversial form of human genome editing?'[3] As South African (SA) scholars in the fields of genetics, biology, law and ethics, we wish to express our dismay that national and international audiences should be misled to believe that SA law accommodates or should be changed to allow for the clinical application of HHGE. What is at stake is not whether HHGE is permissible for research purposes in SA, but whether it is permissible to create live births.

Origins of the current controversy

The crux is whether existing legislation can be interpreted to allow for HHGE. Section 57(1) of the SA National Health Act 61 of 2003 (NHA) states that 'A person may not – (a) manipulate any genetic material, including genetic material of human gametes, zygotes or embryos; or (b) engage in any activity, including nuclear transfer or embryo splitting, for the purpose of the reproductive cloning of a human being'.

Section 57(6)(a) of the NHA defines reproductive cloning of a human being as 'the manipulation of genetic material to achieve the reproduction of a human being and includes nuclear transfer or embryo splitting for such purpose'. Genome editing is a form of genetic manipulation, as it changes the DNA code of an individual. Whether reproductive cloning as defined herein includes the propagation of edited cells (gametes, zygotes, embryos) for the purpose of a live birth is rejected by an SA research group.[4] Assuming, as the authors propose, that section 57(6)(a) does not include HHGE, a critical question arises: if the legislation is silent on a specific matter, does this make it 'legal'? They appear to interpret the lack of explicit prohibition as providing a green light to proceed with HHGE in SA. Their exclusively legal interpretation in the case of HHGE is insufficient on its own to justify this stance. The potential consequences of HHGE (mostly unknown, but possibly harmful) would therefore be of greater importance in the absence of explicit legislation in determining the way forward. Omission to deal statutorily with a particular situation explicitly (especially one not envisaged at the time of enactment) does not result in a void. Rather it is filled by the rest of the statute, its setting, and inferences from what is enacted, and in the context of HHGE, we reason that other factors such as ethics, morality and societal views take on added importance.

The global view on HHGE is largely the result of its potential consequences, which at present remain unknown. The Third International Summit on Human Genome Editing (London, March 2023) issued a statement[5] that includes: 'Heritable human genome editing remains unacceptable at this time. Public discussions and policy debates continue and are important for resolving whether this technology should be used. Governance frameworks and ethical principles for the responsible use of heritable human genome editing are not in place. Necessary safety and efficacy standards have not been met.'

The guidelines that have caused the current controversy recognise this reality. Section 4.3.2(g) requires researchers to comply with the law when engaging in forms of genetic modification of gametes, zygotes or embryos. 'Researchers must adhere to all relevant laws governing HHGE research. In particular, researchers must adhere to the fourteen-day rule, and must obtain the necessary ministerial permission to conduct research on embryos.'

A draft of the guidelines released for public comment in 2023 did not include text on HHGE. A subsequent draft released early in 2024 included the section on HHGE with a brief window for comment. It is unclear why the National Health Research Ethics Council (NHREC) chose not to consult widely with topic experts to ensure that the text of the guidelines was appropriate, considering the national legal context, ethical concerns and international recommendations and guidelines for HHGE. It is unfortunate that this situation has arisen. The misguided wording in the current guidelines may serve to precipitate a troubling change in opinions in favour of permitting or promoting HHGE in SA.

Consequences

The abovementioned SA research group has used the wording in the current NHREC guidelines to propound their position on the clinical application of HHGE in the country. Its members have consistently advocated for the legalisation of germline/heritable human genome editing in academic publications. For instance, in a 2020 study in the *South African Journal of Science*,[4] members of this team wrote: 'Given its potential to improve the lives of the people of South Africa, human germline editing should be regulated, not banned,' and proposed five guiding principles for HHGE in the country. In a 2023 article in the *South African Journal of Bioethics and Law*, one of the authors furthermore proposed a set of sub-regulations to establish HHGE-specific legal norms to be included in proposed HHGE legislation.[6]

In a deliberative public engagement study on HHGE,[7] this group interrogated SA participants on three major themes, the questions to which were all prefaced with the following statement: 'Provided that it is safe and effective, our country's laws should allow parents to choose to use genome editing before a child's birth to …'. A detailed report followed by a discussion on their findings ensues. First, the question of whether HHGE is safe and effective has not been resolved, and therefore the utilisation of their findings to drive legislative reform cannot be justified. Second, there is no apparent exploration of the participants' understanding of HHGE in the study, which is a serious methodological concern. The concepts of 'genome', 'DNA' and 'gene/genome editing' are poorly understood by a non-specialised audience, as are the terms used to describe unknown consequences of HHGE (such as off-target effects and intergenerational inheritance).

We take no issue with the view of these authors regarding HHGE. However, it is concerning that they are using the changes in the county's research ethics guidelines to advance their position and to create the impression that there is legal certainty where there is none.

In SA, and in most jurisdictions, legal compliance starts with the Constitution as the uppermost form of law that guides the nation. From this, laws are enacted that are supported by regulations and guidelines. A change in guidelines does not have the power to change the law.

It is also concerning that this group has misrepresented the African continent and the principle of *ubuntu* in their writings (see their comments following the Baylis and Hasson article). Regarding the former, they take a defensive stance against the global North, implying that the global view is being forced upon an unwilling continent that wishes to retain its autonomy and make its own decisions. This is misguided, as the principles are applicable globally – as, for instance, Phila Msimang has pointed out in a comment below the original Baylis and Hasson article.[2] Although the disease burden in SA is high, the country's needs are no different to people in other parts of the world when it comes to the potential benefits – and harms – of HHGE. Regarding the principle of *ubuntu*, surely if HHGE results in deleterious consequences that are irreversible and transmitted intergenerationally, which remains a major concern globally, the principle of *ubuntu* would not be well served. The robustness of these authors' engagement with African philosophy has been referred to as 'superficial' and theoretically underdeveloped.[8]

Finally, the notion that HHGE will create a population that is resistant to infectious diseases that are endemic in sub-Saharan Africa, namely HIV and tuberculosis, is misguided. Presumably this comes from the discredited Chinese scientist who in 2018 edited the genomes of three babies to 'protect them from HIV'. Since the outcome in these edited children, for good reason, is not public, it is not clear whether their genomes were successfully edited and, furthermore, it would be unethical to test whether they are immune to HIV.

What should happen next?

Revision of the NHREC guidelines

The NHREC must clarify its view on HHGE. We note the recent press release that was circulated to ethics committees around the country by the chair of the NHREC on 8 November 2024. But this does not sufficiently address nor resolve the controversy, and the press release has no legal standing. The current wording for HHGE for research purposes in the guidelines should be deleted in its entirety. The underlying premise of section 4.3.2 of the guidelines appears to rest on the fact that there will be prospective parents, prospective children and individuals born because of HHGE research interventions specifically, which is problematic and inconsistent with the law. In addition, this current ambiguity in wording blurs the line between HHGE research and clinical application.

Alignment with international standards

Two authors of this editorial (MR and JdV) were members of international committees that considered the permissibility and standards of human genome editing, including HHGE. MR was a member of the International Commission established by the US National Academy of Medicine, the US National Academy of Sciences and the UK's Royal Society, with the participation of academies of sciences and medicine from around the world.[9] De Vries was a member of the Expert Advisory Committee on Human Genome Editing established by the World Health Organization.[10] The reports from both committees concluded that HHGE remains scientifically premature and ethically contentious. These reports also point to the lack of governance and ethical frameworks to support safe, responsible HHGE. The NHREC guidelines, with their section on HHGE, do not fill this gap.

While international debate on HHGE continues, SA must engage the public in meaningful dialogue and involve local and international experts in assessing HHGE's safety and societal implications. HHGE may eventually become permissible, but now is not the time.

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