

# A golden opportunity for South Africa to legislate on human heritable genome editing

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**Background.** South Africa (SA) currently has a golden opportunity to legislate on human heritable genome editing (HHGE), as the country is revising its assisted reproductive technology regulations. A set of sub-regulations that deals with HHGE, which could seamlessly slot into the current regulations, has already been developed. The principles underlying the proposed set of sub-regulations are as follows: HHGE should be regulated to improve the lives of the people and should not be banned; the well-established standard of safety and efficacy should be used in the regulation of HHGE; quality of life is what matters, and not preserving a ‘normal’ genome; parents’ reproductive autonomy must be respected; and equality of access to approved HHGE technology should be promoted.

**Objectives.** To ascertain whether the proposed set of sub-regulations that deals with HHGE is aligned with public opinion in SA, and SA’s Bill of Rights.

**Methods.** Public opinion in SA is determined with reference to a deliberative public engagement study on HHGE conducted among South Africans, and the relevant rights in the Bill of Rights are interpreted with reference to recent case law.

**Results.** This proposed set of sub-regulations that deals with HHGE is aligned with public opinion in SA, and SA’s Bill of Rights.

**Conclusion.** Despite the legal and ethical complexities of HHGE, the proposed set of sub-regulations provides a targeted and effective legislative approach. They fit seamlessly into the country’s existing health law framework, creating specific legal standards for HHGE that align with both public opinion and the country’s Bill of Rights.

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With the Third International Summit on Human Genome Editing having taken place in March 2023, it is time to take stock of progress made with legislative efforts regarding this technology. One challenge is to develop legislation that is aligned with public opinion, but also fits within the boundaries of established legal rights in a given polity. Another challenge is political agenda-setting – human heritable genome editing (HHGE) must make it onto the legislative agenda. South Africa (SA) may currently be in an ideal position to successfully face both these challenges. Firstly, a deliberative public engagement on the governance of HHGE was conducted among South Africans, and the results were published recently.

<sup>[1]</sup> Given the methodology of this public engagement study, which ensured that its participants were properly informed,<sup>[2]</sup> the results provide valuable insight into informed opinions of South Africans. Secondly, the SA government is currently revising the regulations (i.e. subsidiary legislation) relating to the use of assisted reproductive technology (ART).<sup>[3]</sup> Given that HHGE can be viewed as a new ART,<sup>[4]</sup> it can be regulated as such. Regulating HHGE as an ART offers a fast track to the legislative agenda for HHGE. Thirdly, in response to the government’s call for comments from the public on the revision of the ART regulations, a set of sub-regulations for inclusion in the revised ART regulations was formulated by Thaldar and Shoji<sup>[5]</sup> to specifically deal with HHGE. This proposed set of sub-regulations is presented in Fig. 1. If adopted by the SA government, this will be the first HHGE-specific legislation in Africa.

In this article, I discuss the principles that guided the formulation of the proposed HHGE-specific legislation in the light of recent legal developments in SA that clarified the scope of relevant constitutional rights, and the results of the deliberative public engagement study.<sup>[1]</sup> This is followed by remarks on the proposed HHGE-specific legislation itself.

## Principles

The point of departure in formulating the proposed new set of sub-regulations on HHGE for inclusion in the revised ART regulations was the five principles developed by Thaldar *et al.*<sup>[6]</sup> for guiding legal development on HHGE in SA, in line with the country’s Bill of Rights.<sup>[7]</sup>

### Principle 1: HHGE should be regulated, not banned

Given its potential to improve the lives of the people of SA, the clinical use of HHGE should be regulated, not banned. Overwhelming majorities of over 80% of the deliberative public engagement participants supported the use of HHGE (a) to prevent serious disease and disability, and (b) to make persons immune to serious infectious diseases such as tuberculosis (TB) and HIV/AIDS. While support for (a) is roughly similar to the public opinion in countries where opinion polls have been conducted (mostly Western countries), (b) appears to be an outlier. This may be for cultural reasons, but may also be because of the ongoing nature of the TB and HIV/AIDS

epidemics in SA.<sup>[8]</sup> The participants typically framed the deliberations on health-related HHGE as a pragmatic cost-benefit analysis. Not one participant was against HHGE in principle. This finding underscores the principle that instead of banning HHGE, the technology should rather be allowed to operate in a way that is regulated by the law.

But before there can be clinical applications of HHGE, there must first be more *research* into HHGE. In SA, such research would be regulated by a robust system of health research ethics oversight. Interestingly, participants in the deliberative public engagement suggested that the SA government should *encourage research* into HHGE to ensure that SA is a leader in this field, rather than a mere follower.

### Principle 2: Use the well-established standard of safety and efficacy

As with new medicines and medical devices, HHGE clinical applications should be made accessible to the public only if they are proven to be safe and effective. This means that HHGE clinical applications should pass through rigorous preclinical studies, followed by well-powered clinical trials. SA's constitutional commitment to the dignity of the individual would demand no less. Accordingly, all the policy proposals posed to the participants during the deliberative public engagement were explicitly premised on HHGE being found to be safe and effective.

### Principle 3: Using HHGE to modify 'normal' genomes may be permissible

One of the staples in bioethics discourse on HHGE is the idea that there is a morally relevant distinction between using HHGE (*a*) to correct a genetic defect in germ cells, with the aim of the genome-edited individual being born with a 'normal' genome; and (*b*) to modify a normal genome in germ cells, with the aim of the genome-edited individual being born with an 'enhanced' genome. Given that the SA Constitution would recognise persons *qua* persons and protect them irrespective of whether they have a 'normal' genome or a modified ('enhanced') one, this distinction does not appear to hold much sway in the SA legal context. Indeed, the participants in the deliberative public engagement did not give any weight to the distinction between correcting a genetic defect and enhancing a genome. What mattered to them was the anticipated effect on the *quality of life* of the genome-edited individual. Based on this quality-of-life criterion, participants supported allowing HHGE for health-related purposes if the relevant health condition is deemed sufficiently serious.

### Principle 4: Respect parents' reproductive autonomy

The decision on whether to use HHGE in a prospective child should, subject to principles 1, 2 and 3, be left to the prospective parents, and not be made by the state or health practitioners. This principle flows from the right to reproductive autonomy – an enumerated right in the SA Constitution. Accordingly, it was an explicit assumption during the deliberative public engagement that if a specific clinical use of HHGE is allowed by the state, it would be the prospective parents' decision whether to use it. In the context of health-related applications of HHGE, this was not controversial. However, in the context of non-health-related applications of HHGE, participants framed prospective parents' reproductive autonomy as in potential conflict with the autonomy of such parents' prospective children. To use

ethics terminology, participants were concerned about excessive *instrumentalisation* of children by their parents. Consequently, two-thirds of the participants opposed the use of HHGE to influence talents, about 70% opposed allowing the use of HHGE to influence personality traits, such as how aggressive or co-operative a child will be, and about 80% opposed allowing the use of HHGE to influence sexual orientation.

Although these opinions are insightful regarding public opinion, SA is a *constitutional* democracy, meaning that individual rights cannot without reasonable justification be limited by the democratic will of the people. In one of the most consequential judgments for reproductive autonomy in SA's history, the Pretoria High Court in 2022 struck down the statutory prohibition on *non-medical* preimplantation sex selection.<sup>[9]</sup> Importantly, the court held that the right to reproductive autonomy includes within its protective ambit the use of ART, such as preimplantation genetic testing for aneuploidy – even if used for non-health-related purposes, such as non-medical (or 'social') sex selection. After engaging deeply with ethical arguments on both sides, the court held that the impugned prohibition infringes the right to reproductive autonomy and that such infringement is not justified. This decision is a clear vindication of individual reproductive autonomy against the will of society as a collective. The court held that the state may seek to *regulate* parents selecting the sex of their offspring through the use of technology, but that the state *cannot ban* this selection. The same, I suggest, would apply in the case of HHGE for non-health-related purposes – the state can regulate it, but not ban it. But what should be the guiding principle for such regulation?

In a free society, a person's freedom should be limited only to the extent that it could cause harm to another person.<sup>[10]</sup> But, given that gametes and embryos are viewed as legal objects (and private property) in SA law,<sup>[11,12]</sup> can HHGE ever cause harm to a *person*? The answer is 'yes'. This is because the harm-causing act need not happen at the same time as the harm.<sup>[13]</sup> For example, someone might set a time bomb that explodes only days, weeks or even years later. The fact that the harm-causing act (setting the time bomb) and the harm (from the eventual explosion) are removed from each other in time, is irrelevant. In fact, the persons harmed by the explosion need not even exist at the time the time bomb is set. Similarly, HHGE on *germ cells* can eventually cause harm if the *person* who originated from those germ cells is harmed. Accordingly, respecting parents' reproductive autonomy is certainly not a *carte blanche* to perform any kind of editing on their embryos. To determine whether certain (mis) uses of HHGE would constitute *harm* to the eventual genome-edited person, existing standards of civil and criminal wrongs should be extended to HHGE.<sup>[13]</sup> There is no need to invent new standards when there is already much case law on what constitutes *harm* in SA law. I elaborate on this aspect below.

### Principle 5: Promote the achievement of equality of access

Together with dignity and freedom, equality is one of the foundational values of the SA Constitution.<sup>[7]</sup> Equality of access to HHGE was a major issue of concern to the participants during the deliberative public engagement. The general feeling was that the state should – at least in the case of HHGE to avoid serious health conditions – foot the bill to ensure universal access. This is strongly aligned with principle 5.

However, the participants also took this a step further. For many, allowing access to HHGE to avoid *less* serious genetic conditions should be *conditional* on first ensuring that there is sufficient access to HHGE to avoid *serious* health conditions. From a constitutional perspective, setting such a condition is a step too far. In the famous words of Justice Albie Sachs, measures to promote the achievement of equality call for 'equality of the vineyard not the graveyard'.<sup>[14]</sup> In other words, policy that aims to attain equality must do so by levelling everyone up to a level of enjoying the relevant social good, and not levelling everyone down to the same level of inadequate access to the relevant social good. Therefore, making legal access to one health service *conditional* on first reaching actual universal access to another health service would amount to levelling down and would not be constitutionally tenable. The state can set its own healthcare-spending priorities and if, for example, it deems that HHGE to ensure immunity to TB is sufficiently important for public health, it can make it available free of charge. However, unequal access to any specific clinical application of HHGE is not a constitutionally permissible reason to ban such clinical application of HHGE.

The allocation of state funds is not something that is typically dealt with in substantive legislation. Accordingly, this principle is not reflected in the proposed legislation.

## The proposed HHGE legislation Overview

The first two sub-regulations (Fig. 1) establish a temporary moratorium on using HHGE for clinical purposes, while allowing HHGE research and clinical trials. The last two sub-regulations balance parental reproductive autonomy and the interest of

prospective persons not to be harmed. Note that in sub-regulation A4, *recipient* is a legal technical term in SA health law that refers to the woman who intends to become pregnant with the gametes or embryos.<sup>[3,15]</sup>

### A temporary moratorium on using HHGE for clinical purposes, while allowing HHGE research and clinical trials

There is global consensus that HHGE is currently not safe and effective.<sup>[16]</sup> Following principle 2, this justifies a moratorium on the use of HHGE for clinical purposes. However, it does not justify a moratorium on researching this promising technology. Research on HHGE is therefore explicitly allowed. Moreover, a pathway to establish the safety and efficacy of HHGE is made possible by explicitly allowing for clinical trials. Importantly, any HHGE research or clinical trial would need to be ethically approved;<sup>[16]</sup> also, an HHGE clinical trial must be registered with the South African Health Products Regulatory Authority.<sup>[17]</sup>

Importantly, the moratorium on the use of HHGE for clinical purposes in sub-regulation A1 is made subject to a sunset clause in sub-regulation A2. In line with principle 1, this is to ensure that the moratorium does not become an effective ban on this promising technology. After the initial decade, the Minister of Health has a discretion to extend the moratorium 5 years at a time. It should be considered that all executive action in SA, including executive legislation, is subject to the requirements of administrative justice. This would require, among other things, that the Minister of Health's discretion should be rationally exercised, based on scientific evidence at the time.

#### Proposed HHGE legislation<sup>5</sup>

- A1 The genomes of gametes and embryos may be edited only if such an edit is part of a preclinical trial or clinical trial that is:
  - (a) approved by a health research ethics committee registered as such with the National Health Research Ethics Council, and
  - (b) in the event of a clinical trial, registered with the South African Health Products Regulatory Authority.
- A2 Sub-regulation A1 shall cease to have effect after 10 years from the date of promulgation of these regulations, unless the Minister of Health gives notice in the Government Gazette that the effect of the sub-regulation is extended for a specified period not exceeding 5 years.
- A3 The genomes of gametes and embryos may not be edited if such an edit is likely to have an effect on the prospective child that would constitute either a civil or a criminal wrong in law if caused by an act by a parent towards an existing child.
- A4 Subject to sub-regulation A1 and sub-regulation A3, the recipient [i.e. the woman who intends to become pregnant with the gametes or embryos] and, if applicable, the recipient's spouse or life partner, have the right to decide whether to have the genomes of their gametes or embryos edited.

Fig. 1. The proposed human heritable genome editing legislation.<sup>[5]</sup>

## Balancing parents' reproductive autonomy with the interest of prospective persons not to be harmed

Following principle 4, sub-regulation A4 provides that the prospective parent or parents – not the government or health practitioners – have the right to decide whether to use HHGE as ART for their prospective children. This provision is made subject to the moratorium contemplated in sub-regulation A1. In other words, following principle 2, only if HHGE has been established to be safe and effective will the technology enter the post-moratorium space of being used as an ART.

Given the potentially far-reaching power that HHGE may place in the hands of prospective parents, its use is delineated by the interest of prospective persons not to be harmed – the principle of procreative non-maleficence – as expressed in sub-regulation A3. The test for whether an edit to a genome would constitute *harm* is anchored in existing law by comparing the likely effect that the edit in question will have on the prospective child with a similar effect caused by an act directed towards an existing child. If the edit is likely to have an effect on the prospective child that would constitute either a civil or a criminal wrong in law if caused by an act towards an existing child, the edit would be deemed harmful to the prospective child and would hence be prohibited.<sup>[13]</sup> This solution to determine harm is elegant, as it integrates seamlessly with existing law, and is also dynamic, as the law on civil and criminal wrongs is constantly being developed by the courts. Admittedly, not every potential use of HHGE will have a clear precedent in established law. However, in cases of uncertainty, prospective parents can approach the court for a declaratory order. Also, it would be good practice for the Minister of Health to issue guidance notes in step with the development of new applications of HHGE.

## Conclusion

HHGE is a complex legal-ethical topic. However, this does not mean that HHGE legislation should be complex or long-winded. The HHGE legislation proposed by Thaldar and Shoji<sup>[5]</sup> is a single set of sub-regulations in a larger statute, but is sufficient to establish HHGE-specific legal norms. This is possible because the proposed new set of sub-regulations will fit into a comprehensive system of health law in SA – comprising various statutes, common law and case law. Accordingly, a surgical legislative approach is appropriate.

SA currently has a golden opportunity to legislate on HHGE, and to do so in a way that is both responsive to public opinion and aligned with the values of the country's Constitution.

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