Consultation response: developing global standards for governance and oversight of human genome editing

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Submitted to

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

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The PHG Foundation welcomes the WHO's initiative to examine the scientific, ethical, social and legal challenges associated with human genome editing, and to make recommendations for governance mechanisms for both somatic and germline human genome editing. As a health policy think-tank with a mandate to support innovations that might improve population health, we support the evidence based use of human genome editing provided that it can be shown to have demonstrable overall utility.

In our view, this evaluation requires taking account of the high level considerations which are set out in the WHO's draft Governance Framework, but it also requires an assessment of the potential risks and benefits for the individuals who undergo genome editing. This dimension is lacking from the WHO's approach.

Currently the key risks to the individual that are associated with the technology (whether germline or somatic), are the lack of safety in the form of off-target effects arising from genome editing. Some effects from genome editing have been described through clinical trials (such as tumour formation or or unexpected immune reactions) but a key ethical concern is that there is uncertainty about the potential risks and benefits through a lack of sufficiently powered longitudinal trials.

Our view is that the development of a governance framework for human somatic and germline genomic editing should reflect:

- the potential risks and benefits for those individuals being offered genomic editing, in addition to the population or societal risks and benefits
- the nature, scope, scale and quality of evidence concerning risks and benefits to individuals offered the technology
- the nature, scope and scale of current uncertainty, and how this might be mitigated or resolved
- ethical principles governing care and treatment of individuals may be relevant (see question 6 below)

Our work on innovative technologies has included an assessment of various aspects of the potential for somatic genome editing to be used in health care. We have included links to this work in our answers to Q12.

Please provide your opinions on the specific proposals relating to governance of human genome editing specific considerations for good governance in the DRAFT Governance Framework (Part 3)

Values, principles and goals

Box 4 outlines the values, principles and goals specific to human genome editing and which should be entrenched in appropriate policies and practices. These values, principles and goals seem appropriate, and seem a useful starting point for approaching issues of good governance. Although this doesn't claim to be an exhaustive list, and those that are set out are essential for informing governance in this context, other features of good governance and ethical principles used in making treatment decisions could be valid here (depending upon the purpose and scale of change).

One of the most important omissions seem to be the principles which are used to help determine the acceptability of decision-making within contemporary healthcare in countries such as the UK. These include the principles of, autonomy, beneficence and non-maleficence (or promoting well-being). The former is more individual focussed and protects a right to self-determination, and would of course need to be mediated against the other principles. As genome editing is to some extent driven by the desire for genetically related children, including a principle, such as autonomy, which takes into account the value of reproductive freedom as a consideration that needs to be balanced against others, is important. Beneficence and non-maleficence are key to guiding decision making in the context of human health, and support providing benefit and preventing harm to those affected. In doing so it compels consideration for the best interest of individuals who will be receiving treatment.

It is important for the set of values and principles to be as comprehensive as possible here, because they are applied in part 5 to identify questions to be considered when developing governance measures. The omission of these ethical principles, seem significant when combined with the lack of consideration of those factors described in answer to question 5 above.

Proportionality as a balancing principle

The inclusion of the additional ethical principles, virtues, and their legal equivalents means that it is inevitable that these overlap, reinforce one another or conflict, and clearly they cannot be interpreted in isolation. The governance framework should provide more information on how these principles and values should be balanced, the friction between these and how this might be resolved.

One important moderating principle might be that of proportionality. This principle should make us consider whether the action that promotes one principle is proportionate to its associated cost. Are there other less risky options? Is the additional benefit gained proportionate to the risks? Different combinations of variables – strengths of the risks, public interests and benefits – will require different degrees of oversight and sanction. For example, the application of somatic genomic editing might be more clearly justified, offer clinical utility and be associated with fewer risks or uncertainties than the use of germline genomic editing in the short to medium term.

However, the application of genome editing still poses a high degree of uncertainty, not only on a societal level but also for individuals who are at risk of potential harms such as off target effects.

Special challenges: enhancement

Enhancement poses a distinctive set of problems, partly because it seems likely to be interpreted in a highly subjective fashion and is heavily dependent on context.

- Effective governance will need to be flexible enough to adapt to the fact that what is viewed as 'enhancement' will change over time as it relies heavily upon current conceptualisations around what is 'normal'.
- Whilst permitting enhancement applications could lead to social inequality, preventing genome editing on this basis could be regarded as somewhat simplistic, since it would preclude innovation regardless of how they are caused. Indeed, many innovative medical technologies have the potential to perpetuate inequalities. Instead, if there is substantial and proportionate benefit to be derived for some individuals, a suitable strategy for mitigating harms such as inequitable access is key.

Future proofing the governance framework

As new genome editing techniques are developed, it would be desirable to future proof the governance framework, requiring that regulation is directed at an area of activity rather than a specific technique, as inevitably new tools will continue to be developed with the same intended purpose and potential applications. Focusing on current genomic editing technologies exclusively risks developing frameworks that will quickly become out of date.

One approach might be for the WHO to consider drafting two decision trees, one aimed at germline interventions and another at somatic interventions. By distinguishing the two types of intervention by purpose or application, rather than by the overarching technology used, namely genomic editing, these might form a useful guide for the development and use of additional technologies which apply to downstream products beyond the genome.

Indeed, some of these products may be less ethically problematic, but may be able to mitigate against germline defects that might otherwise be disease causing. These technologies include methods which act directly on the RNA, transcriptome or proteins manufactured from the genome itself.

Please comment on the tools, institutions, and processes for human genome editing governance in the DRAFT Governance Framework (Part 4)?

No additional comments.

Please provide your opinions on the scenarios in the DRAFT Governance Framework (Part 5), including whether we have missed any important details?

No additional comments

Please comment on the questions to be considered when developing governance measures (Annex)?

The questions posed surrounding access to the technology focus on market access, and generating the evidence to demonstrate that the technology is safe and effective for a particular patient group for a particular purpose. Even if genome editing treatments are approved and made available, on the individual patient level concerns around resourcing and criteria for accessing treatment require careful consideration. How will we distribute benefits equitably when health systems are unlikely to be able to fund all genome editing treatment for serious disease? Who will decide which treatments are funded, and based on what criteria? Access through private providers is likely to exacerbate inequity.

- To what extent is it necessary to have international consistency in regulatory and governance approaches to genome editing? A lack of consensus could lead to global inequities of access, and result in researchers, corporations and patients operating abroad to avoid regulatory restrictions.
- As mentioned earlier, proportionality may well be a useful moderating principle when attempting to answer the questions that need to be considered when developing governance measures.
- A decision tree would be useful as part of a consistent, systematic approach to navigating these questions as many of them are applicable regardless of application.

What would you want to see in a decision tree to assist those taking governance decisions? (We are currently consider creating a decision tree based on the questions to be considered when developing governance measures (Annex))?

In answer to previous questions we have raised a number of considerations which are important at the level of the individual - such as autonomy, beneficence, non-maleficence and justice. If appropriate, there should be scope to include these considerations when developing governance measures. The need for proportionality and responsible policy development are also overarching considerations. Moreover, it should be emphasised that any considerations raised are likely to depend heavily on context, and that the questions should be viewed as illustrative rather than comprehensive.

Are there additional measures we could include to deter or avoid bad practice around applications of human genome editing (such as rogue clinics or other 'bad actors', inappropriate uses of the technology, etc.)?

No additional comments

What else do you want to tell us about good governance of human genome editing?

At the PHG Foundation, we have explored the applications for somatic genome editing through a series of policy briefings. These briefings provide accessible and informative overviews of the technologies, policy landscape and ethical/regulatory considerations relating to somatic genome editing. These may be of interest to your working group and wider audiences.

Somatic genome editing: an overview - https://www.phgfoundation.org/briefing/somatic-genome-editing-overview

Somatic genome editing: promise and practicalities - https://www.phgfoundation.org/briefing/somatic-genome-editing-promise-practicalities

Somatic genome editing: ethics and regulation - https://www.phgfoundation.org/briefing/somatic-genome-editing-ethics-regulation

Overall, our final policy recommendation is that thought should be given to the most effective means by which the public health and clinical workforce and systems can work together to support better prevention for the UK population.

The forthcoming National Genomics Healthcare Strategy is an excellent opportunity to look at how the significant potential for improved public health and clinical care from genomics can be best utilised, including by non-specialist staff. Genomic data can have quite different implications when considered in healthy citizens and groups compared with those with a specific disease, and new knowledge and understanding of genomics and health continues to emerge, making it a challenge. However, implementation of the strategy could represent a valuable trial for integrating complex data sources in the light of a dynamic knowledge base to underpin intelligent public health and care.

Further reading

Annual report of the Chief Medical Officer 2016: generation genome. Chapter 8, Personalised Prevention. 2017

Health innovation manifesto. PHG Foundation. 2015

What is citizen generated data? PHG Foundation. 2018

Citizen generated data: the ethics of remote patient monitoring. PHG Foundation. 2019

My healthy future: overdiagnosis. PHG Foundation. 2019

Polygenic scores, risk and cardiovascular disease. PHG Foundation 2019

Our healthy future. PHG Foundation. 2019

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PHG Foundation is a health policy think tank with a special focus on how genomics and other emerging health technologies can provide more effective, personalised healthcare

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