Discussion Document for HUGO CELS Workshop (March 2025, Durban)

Balancing Genomic Sovereignty and Common Heritage: Ethical and Legal Frameworks for Population-Specific Reference Genomes

Background and Context

The Human Genome Project (HGP) of the 1990s marked a significant scientific milestone in sequencing the 'human reference genome' [completed in 2003]. There is no one genomic sequence of all of us; and the idea of a single reference genome creates reference biases that limit variant discovery and the accuracy of genetic analyses. In response, the Human Genome Organisation (HUGO) coined the principle that 'the human genome'—specifically the *human reference genome*—should be considered the 'common heritage of humanity', ensuring the benefits of the HGP would remain accessible to all. This principle, formalised in HUGO's 2000 Statement [see further reading], helped shaped ethical and legal approaches to genomics at the time. The ongoing Pangenome Reference Consortium is a collection of genome sequences that captures substantially more diversity in human populations [2023]. Across both sequencing initiatives, data sharing played a prominent role, and 'embedded' numerous legal, ethical, and social issues (ELSI) including genetic privacy; genetic discrimination; and the access, appropriation, and use of genomic data.

While the HGP's reference genome was a landmark achievement, it is predominantly Caucasian, which limits its representation and utility for other populations. The critical concerns about global health justice were addressed under the Pangenome Reference Consortium's initiative to assemble genetically and geographically diverse genomic sequences. The Human Pangenome Reference aims to overcome bias and capture global genomic diversity across 700 haplotypes of 350 individuals. This approach might be in line with the common heritage idea. However, initiatives such as the *Qatar Genome Project* instead aim to address 'single global' reference limitations by developing population-specific reference genomes to advance precision medicine *for specific populations*. A population-specific approach leads to Population Specific Reference Genomes (PSRG), and these potentially challenge the original 'common heritage principle.' Moreover, FAIR principles developed for Open Data initiatives developed for sharing – *Findability, Accessibility, Interoperability, and Reusability* – are not compatible with frameworks developed to protect the rights and interests of communities, groups, or populations. Open access to data is especially harmful to those communities that have not been engaged, and those that have historically been subject to exploitation and oppression. For example, the CARE Principles of Indigenous Data Governance advocating *Collective benefit, Authority to control, Responsibility in use, and Ethics*, create social and physical custody of data under a 'bundle of rights,' allowing data sharing only under conditions, responsibilities, and obligations owed to the community.

This workshop will consider the following questions:

- Are there distinct ethical, legal, and social issues (ELSI) that arise in population-specific sequencing that are distinct from the common heritage approach?

- Should population sequences be considered as common heritage, or are they a subset of common heritage, or are they something different entirely?
- Do population-specific sequencing initiatives require specific governance frameworks?

This workshop will contribute to a new HUGO statement on data sharing. The programme for the workshop is towards the end of this discussion paper.

A Synthesis Framework for ELSI

While the common heritage idea refers to 'a' reference genome, the Pangenome project is representative of a synthesis of reference genomes. Both initiatives are reciprocal in respect to the governance of the collection and use of genomic data to create reference maps and community resources between research laboratories. Both start with access to personal genetic data. Individual genomes may be collected to create a common or sovereign resource. And while personal data is often governed by national and regional laws and policies on genetic privacy and consent in research and medicine, commonality and sovereignty start with the collection of data. Sometimes, this is done without engaging the interests of the community and obtaining their collective consent. In these respects, the principle of genomic sovereignty has emerged as a counterpoint to common heritage. Genomic sovereignty engages with the rights of nations or communities to control access to, and benefit from, their own synthesised genomic data, countering the disproportionate advantages often enjoyed by well-resourced countries accessing globalised sequences. There is no single approach to its implementation at different levels, therefore the notion of national sovereignty over reference genomes may introduce a strong differentiation with the human heritage genome: asserting national jurisdiction protects against bio-exploitation and may ensure public goods flow back to community (Kabata & Thaldar, 2023); in the wrong hands, it may also introduce sociological biases that risks racial and ethnic, or economic, inequity.

For example, Mexico has been explicit in its approach to genomic sovereignty, instituting a state-centric approach to access its genomic data. Other countries, through a series of regulations and guidelines, have claimed genomic sovereignty through the introduction of controls on the sharing and transfer of genetic materials across borders. African nations tend to centralise sovereignty at the national level, reflecting historical and political contexts. Often, there is a recognition of the role of indigenous communities in the sharing of data. Such countries have strong indigenous or First Nations engagement and respect and assert their rights, and recognise the jurisdictional sovereignty of indigenous communities, such as in Canada under OPAC. On a specific level, political, ethical and legal can become entwined: Iceland's national biobank became embroiled in controversy when a private entity became the single holder of proprietary rights over nearly every citizen's DNA under specific 'biobank' legislation. That can be compared with UK Biobank that holds the data of some 500,000 *volunteers* as a steward of a research community's samples and data. The resource is only accessible to *bona fides* researchers whether they be publicly or privately funded, under the condition that the use of data is for the public good. While genomic sovereignty may make international research collaborations challenging where different values are fundament and different policies are used, the aspiration of common heritage of genomic data, has, in practice, been limited by regional and national laws.

This workshop seeks to reconcile the tension between common heritage and genomic sovereignty by analysing the different ethical and legal implications. Using the common heritage and population-specific approaches, we will consider what kinds of governance frameworks are needed to reflect the world's increasing diversification of datasets.

Key Discussion Points for Scientific, Ethical, Legal Pannels

The Relevance of Common Heritage Today

- Does treating PSRGs as *common heritage* perpetuate inequities, given that well-resourced entities are better positioned to utilise shared data?

The Role of Genomic Sovereignty

- Can state-centric approaches to genomic sovereignty balance national interests with global collaboration and benefit-sharing?

Community-Level Governance

- How should sovereignty be applied to communities that do not have nation-state representation? Models such as Canada's recognition of First Nations governance offer potential pathways, but their applicability in other regions remains uncertain.

Potential Solutions for Discussion

Participants are encouraged to explore and critique the following potential governance approaches for PSRGs:

1. Treating PSRGs as Common Heritage

- PSRGs would be freely accessible to all, promoting global benefit-sharing and collaboration.
- *Strengths*: Promotes open science and equality in access.
- *Challenges*: Does not necessarily promote equity in access, and risks perpetuating historical inequities and public capture of goods, where private, well-resourced entities exploit shared genomic data. May not appropriately consider the unique historical stigmatisations of many of these populations.

2. Public-Controlled Governance of PSRGs

- Nation-states where relevant populations reside would control access and use.
- *Strengths*: Ensures national and public interests are prioritised, provides a degree of equity, and encourages solidarity within that specific country.

- *Challenges*: Risks excluding community voices and stifling collaboration with others outside of the borders. Unlikely for there to be a population response, as populations does not conform to national borders.

3. Community-Led Governance of PSRGs

- PSRGs would be controlled by the population group to whom they relate, using recognised governance structures.
- *Strengths*: Respects autonomy and aligns with human rights frameworks.
- *Challenges*: Requires robust governance structures, which may be lacking in some regions.

Note: These are not exhaustive solutions. Participants are encouraged to propose additional frameworks or hybrid approaches to address these tensions.

Workshop Objectives

1. Explore the ethical, legal, and social implications of PSRGs in the current genomic landscape.
2. Critically evaluate the feasibility and limitations of the proposed governance solutions.
3. Identify pathways for global collaboration to develop inclusive governance frameworks for PSRGs.

This document serves as the basis for focused discussions during the workshop, with participants encouraged to contribute their regional and professional perspectives.

Suggested reading

Kabata, F., & Thaldar, D. (2023). Regulating human genomic research in Africa: why a human rights approach is a more promising conceptual framework than genomic sovereignty. *Frontiers in Genetics*, 14, 1208606.

Kabata, F., & Thaldar, D. (2023). The human genome as the common heritage of humanity. *Frontiers in Genetics*, 14, 1282515.

Staunton, C., Barragán, C. A., Canali, S., Ho, C., Leonelli, S., Mayernik, M., ... & Wonkham, A. (2021). Open science, data sharing and solidarity: who benefits? *History and Philosophy of the Life Sciences*, 43(4), 115.

Slabbert, M. N., & Pepper, M. S. (2010). A Room of Our Own: Legal Lacunae Regarding Genomic Sovereignty in South Africa. *Journal of Contemporary Roman-Dutch Law*, 73, 432.

Statement on Benefit Sharing, April 2000. Clinical Genetics 2000;58(5):364-6; *Eubios Journal of Asian and International Bioethics* 10: 70-2. https://www.eubios.info/BENSHARE.htm

Further reading

Capps, B. (2021). Where does Open Science Lead Us During a Pandemic? A Public Good Argument to Prioritise Rights in the Open Commons. *Cambridge Quarterly of Healthcare Ethics* 30(1): 1-14.

HUGO CELS Statement on Bioinformatics and Capturing the Benefits of Genome Sequencing for Society (2019). *Human Genomics* 13, 24 (2019). https://doi.org/10.1186/s40246-019-0208-4

Human Genome Organisation Ethics Committee. (2007). HUGO Statement on Pharmacogenomics (PGx): Solidarity, Equity and Governance. *Genomics, Society and Policy* [*Life Sciences, Society and Policy*] 3: 44 doi: 10.1186/1746-5354-3-1-44

Liao, WW., Asri, M., Ebler, J. et al. (2023).A draft human pangenome reference. *Nature* 617: 312–324 https://doi.org/10.1038/s41586-023-05896-x

Mulvihill, J. Capps, B., Joly, J. Lysaght, T., Zwart, H. and Chadwick, R. The International Human Genome Organisation (HUGO) Committee of Ethics, Law, and Society (CELS). (2017). Ethical Issues of CRISPR Technology and Gene Editing through the Lens of Solidarity. *British Medical Bulletin* 122(1): 109-122.

Glossary

Equity To reduce health inequalities between different populations, and to work towards equal access to care is an important prerequisite for implementing genomic knowledge for the benefit of society (HUGO, 2007).

Genomic sovereignty has been referred to as the ability of a nation, people or state to own and regulate access to and use samples, data and knowledge on human genes (Slabbert and Pepper, 2010). The ideas of commonality and sovereignty here refer to sharing a synthesis of individual genomes at the level of community, population, or country.

Genomic solidarity: The Committee underscored the relationship between solidarity and equity, as solidarity fosters health for connected communities, and is undermined by gross disparities in health, income and access to care. Genomic solidarity encourages participation in worthy initiatives as both sharers and benefactors; it creates obligations to trustworthiness and stewardship and leads to an equitable creation of value. Solidarity provides the framework for working together — researchers, study participants and sponsors — to deliver and share experience and outcomes. It reaffirms reasons for bearing costs and burdens for others, but with acknowledgment or compensation in a reciprocal fashion (Mulvihill, et. al. 2017).

Re-examining the Ethics and Law of Data Sovereignty: Common Human Heritage and Population-Specific Genomic Variation

A HUGO Workshop coordinated by HUGO Committee on Ethics, Law and Society

Human Genome Meeting 2025

March 11th to 14th, 2025

Durban, South Africa

"From Africa to the World: Exploring African diversity through human genomes"

HUGO is a global body that has, over the years, provided guidance statements. These statements balance global framing with national interests. We now need to think about how local reference databases will combine with global genomic diversity. In 2024, the WHO's Guidance for human genome data collection, access, use and sharing was published that aims to "Promote the use of common principles in laws, policies, frameworks and guidelines, within and across countries and contexts." Background to this session includes the HUGO Statement on the Principled Conduct of Genetics Research (1996) that first recognised "the human genome is part of the common heritage of humanity," and the HUGO Ethics Committee statement on benefit sharing (2000):

"Applied to human genetics, [HUGO] maintains that beyond the individual, the family, or the population, there is a common shared interest in the genetic heritage of mankind. Therefore, the Human Genome Project should benefit all humanity."

Each panel will have a short, high-level introduction, followed by open workshop discussion.

Wednesday 12 March

Opening Remarks 9-9.15

Donrich Thaldar, University of KwaZulu-Natal

Historical perspective on the original HUGO statement and its relevance today 9-15-9.30

Benjamin Capps, Dalhousie University

Panel 1: The Science of Population-Specific Genomic Variation 9.30-10.00

Panel includes Michele Ramsay, University of the Witwatersrand; Michael Pepper, University of Pretoria; Karen Miga, University of California Santa Cruz Genomics Institute

Panel 2: Ethical Implications 10.00-10.30

Panel includes Freddy Mnyongani, University of KwaZulu-Natal; Deborah Mascalzoni, Uppsala University and Eurac Research; Ma'n H. Zawati, McGill University

Break 10-30-11.00: Informal Discussion

Panel 3: Policy and Legal Implications 11.00-11.30

Panel includes Paul Ogendi, University of Nairobi; Marietjie Botes, University of Stellenbosch; Ciara Staunton, Eurac Research

The Future Directions: Open Discussion 11.30-12.20

Moderator: Kunal Sanghavi, The Jackson Laboratory

Concluding Remarks 12.20-12.30

Donrich Thaldar, University of KwaZulu-Natal