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Global Alliance for Genomics and Health: Ethics Review Recognition Policy

Preamble

The Global Alliance for Genomics and Health ("GA4GH") is an international, non-profit coalition of individuals and organizations working in healthcare, research, disease advocacy, life sciences, and information technologies dedicated to improving human health by maximizing the potential of genomic medicine through effective and responsible data sharing. Its mission is "to accelerate progress in human health by helping to establish a common framework of harmonized approaches to enable effective and responsible sharing of genomic and clinical data, and by catalyzing data sharing projects that drive and demonstrate the value of data sharing."

In 2014, the GA4GH adopted the *Framework for Responsible Sharing of Genomic and Health-Related Data* (the "*Framework*"), which sets forth a harmonized and human rights approach to responsible data sharing in accordance with Foundational Principles and Core Elements. Elaborating on the general principles and guidance offered in the *Framework*, the GA4GH is committed to creating policies that will provide specific guidance for its application. This Policy on ethics review recognition provides specific guidance to enhance both the "Accessibility" and "Dissemination" Core Elements of the *Framework*. Building on the related work of other organizations, such as the Council for International Organizations of Medical Sciences, the Organisation for Economic Co-operation and Development, and the World Health Organization, the purpose of this Policy is to provide Essential Elements of ethics review recognition for *multi-jurisdictional research projects involving health-related data* (including genomic data and data derived from samples). The two express goals of the Policy are: to both foster recognition of extra-jurisdictional ethics reviews and improve the consistency thereof, as well as to promote efficient and responsible health-related data sharing for human health and wellbeing.

This Policy will be elaborated by subsequent more detailed Practical Guidance on particular ethical and research governance issues. The Policy and subsequent Practical Guidance should be used in projects around the world (whether Global Alliance "inspired" or not) such that they become the tools to turn or refer to for guidance. Recognizing diversity of legal and ethical approaches and being responsive to emerging issues, both this Policy and subsequent Practical Guidance are intended to provide leadership in this domain for wider discussion.

This Policy is intended for research involving health-related data collection, production, access and re-use. It is intended to inspire confidence in the adequacy of an ethics review from another jurisdiction's ethics review jurisdiction on the basis of equivalent requirements that should generate similar quality of the ethics review performed. In turn, this enhances the responsibility of the research enterprise and adds to its credibility and quality. Ethics reviews undertaken in light of this Policy would reflect sufficiently similar procedural approaches to the assessment of the ethical acceptability such that duplicative ethics reviews can be reduced through recognition of the review of another ethics jurisdiction.

I. Context

1. Context. Research ethics committees (RECs) review the ethical acceptability of research involving human participants. Historically, the principal emphases of RECs have been to protect participants from physical harms and to provide assurance as to participants' interests and welfare. The steady growth of internationally collaborative, data-intensive, and population-based research projects has drastically increased the number of ethics reviews undertaken. Yet, there has not been a co-evolution of the ethics review system. This has led to an exacerbation of duplicative ethics reviews. Despite the internationalization and data intensification of research, the same ethics review approach as applies to single-site biomedical studies tends to apply to multi-site data-only studies in multiple countries. Because the jurisdiction of a REC is frequently limited to a single hospital, university, clinic, or local geographic area, multi-jurisdictional research projects are subjected to multiple duplicative ethics reviews. Consequently, these redundant reviews may unduly delay research and use financial resources that should be devoted to enhance scientific knowledge on human health. In addition, replicate reviews have not been shown to improve human subjects' protection.

   Undue inhibition of important low-risk, health-related data research has challenged the ethics review system for decades. Significant advances in genome sciences and technology have exacerbated this situation by shifting health research from the single lab/single investigator paradigm to globally distributed multidisciplinary teams working on large cohort research projects. Duplication of ethics review for health-related data research has become strikingly problematic even though they often raise lower risks and different ethical concerns compared to interventionist research. There is thus an urgent need to build convergence around the establishment of an ethics review recognition framework, which may ultimately lead to convergence around approaches to ethical review recognition.

2. Purpose. The purpose of this Policy is to provide Essential Elements for the ethics review process of multi-jurisdictional research involving health-related data so as to foster recognition of extra-jurisdictional ethics reviews and efficient and responsible health-related data sharing.

   It is hoped that this Policy will be useful to those charged with drafting national, local, and institutional regulations and policies, as well as international, regional, or national accreditation systems, such that the possibility of ethics review recognition between competent RECs can be enhanced.

3. Principles and Statements. This Policy is based on the Foundational Principles set forth in the *Framework*, namely:

   - Respect Individuals, Families and Communities
   - Advance Research and Scientific Knowledge
   - Promote Health, Wellbeing and the Fair Distribution of Benefits
   - Foster Trust, Integrity and Reciprocity

This Policy further affirms the following statements:

- Recognition of extra-jurisdictional ethics reviews can maximize scientific benefits for society without compromising human subjects' protection and wellbeing.
- A variety of organizational approaches (e.g. "REC of Record", mutual recognition, centralized REC) can be used to properly achieve recognition of extra-jurisdictional ethics reviews depending on the legal, institutional, governmental, and factual situation.
- Legal, organizational, and practical issues raised by recognition of extra-jurisdictional ethics reviews can be efficiently managed by specific tools (e.g. reciprocity agreements, reliance agreements, insurance policy riders, cost-sharing, *ad hoc* REC member nomination).
- As norms, policies, and laws may differ between jurisdictions, differences in decisions between RECs may occur. Harmonization and recognition of extra-jurisdictional ethics reviews can help the understanding and managing of those differences.
- The procedural and substantive issues within ethics review are intertwined.

4. Resources. Tools and resources have been developed by the GA4GH to support its Policies. They have been designed to be in accordance with the Foundational Principles of the *Framework*, and are provided to assist with data sharing, interoperability of consent forms, and metadata procedures among RECs. GA4GH resources include the *Data Sharing Lexicon*, the *Consent Tools*, the *Consent Codes*, and the *Automated Discovery and Access Matrix* (*ADA-M*).

   Additionally, in reviewing the ethical acceptability of multi-jurisdictional research involving health-related data, the World Health Organization's *Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants* should be considered.

II. Managing Differences in Ethics Principles, Polices and Norms

Differences in the content or application of ethics principles, policies, or norms between jurisdictions should not be unduly considered as a barrier to achieving ethics review recognition. Such differences impacting on the review of a research application should be identified, and the mandatory or non-mandatory status of the principles, policies, or norms where they originate should be determined.

Mandatory Status

The constraining character of ethics principles, policies, or norms that are mandatory in one jurisdiction should be respected in regard to this jurisdiction. The differences should be managed with inventive solutions to prevent undue exclusion of data that could undermine the research or diminish the value of its results. Innovative solutions to manage these differences could be implemented by many stakeholders (e.g. researchers, RECs, institutions, regulatory authorities, government) at many stages of the process (e.g. research project development, formal

establishment of a recognition system, REC review, etc.). Solutions may include an *ad hoc* harmonization agreement from a competent body or a specific exception applicable to a jurisdiction.

Non-Mandatory Status

Differences in ethics principles, policies, or norms that are not mandatory in one jurisdiction may be formally managed before the ethics review assessment (e.g. through an agreement on recognition). In the absence of such prior formal arrangement, these differences should be managed by RECs in accordance with accepted international ethical principles that protect and promote human dignity and human rights. Management of these differences could involve harmonization for all the jurisdictions involved or a specific exception for one jurisdiction.

Liability

Liability of institutions and individuals arising from ethics review recognition should not be unduly considered as a barrier to implementing recognition. Risk of liability related to recognition should be managed as any comparable liability risk, that is, according to the actual level of risk involved. The level of risk associated with ethics review recognition should be fairly evaluated in the context of all the liability risks usually assumed by the institutions or individuals. Risk management tools should be used, such as regulations, agreements, monitoring, and insurance.

III. Essential Elements of Ethics Review to Foster Recognition

The following Essential Elements establish a common effective baseline of the ethics review process for multi-jurisdictional research involving health-related data. This should ensure trust in the ethics review process followed in another jurisdiction and thereby recognition of the decision rendered by a REC from this jurisdiction. The Essential Elements are intended to complement and build upon existing human rights instruments, laws, regulations, guidelines, and practices. They are not intended to supersede any human rights instruments or national laws and regulations.

All stakeholders (namely researchers and research institutions, research sponsors/funders, governments and other regulatory or quasi-regulatory bodies including managing authorities of RECs, RECs, research participants, and communities) should work together and contribute to achieving each of these Essential Elements in function of their capacity, authority, and responsibility.

Norms, Authority and Independence

- Norms of conduct in the ethics review and continued oversight of the research by REC should be established. These norms should be publicly accessible.
- Adequate authority and independence of the REC should be assured.
- RECs and their members should be free to make decisions on the ethical acceptability of a research application, and must be seen to be free of institutional (public and private), commercial and political influence, as well as conflicts of interest.

Resources

- RECs should be resourced sufficiently such that they can carry out their mandate professionally in respect of the Essential Elements of ethics review recognition.

Competence

- RECs should have professional competence regarding the ethics review of health-related data research, including adequate expertise or experience with such research, and should be well-informed of its specific ethical considerations. The latter may be accomplished through seeking advice from specialist referees. Terms of reference for referees should be established prior to any such consultation.
- Competency standards for REC members and ongoing training to meet these standards should exist. This training should inform members of developments in ethics, science, and technology that are relevant to the ethics review of research involving health-related data.
- Rules and composition of REC membership should be publicly available.

Diligence

- RECs should make their decisions with diligence and communicate with diligence their requests and decisions to researchers, committee members, and other RECs.

Procedures and Forms

- Harmonization of procedures and forms required for ethics review should be promoted to minimize the administrative burden for researchers.
- Information and requirements related to research application submission procedures should be publicly accessible.

Proportionate Scrutiny

- Scrutiny of REC review should be proportionate to the actual and potential scale, benefits, risks, complexity and particularities of each research application under review.

Transparency

- A registry of RECs that operate in a particular legal jurisdiction (i.e. geographic area) should be established and be made publicly accessible and continuously updated.
- Written, clear, reasoned decisions of an unfavourable ethics review opinion or rejection should be provided by RECs to research applicants. All decisions should be kept on file.
- Subject to confidentiality agreements and as the case may be, copies of a REC decision or opinion letter for a multi-jurisdictional research project involving health-related data should be made available to the other RECs involved in reviewing the same project.

Natural Justice and Equity

- In order to maintain confidence in the evaluation and recognition systems, RECs should apply norms of natural justice. RECs should treat applicants equitably and subject them to a fair process of ethics review. This includes the possibility for the applicants:
  - to be heard (e.g. attendance of applicants at REC meetings to provide additional information and to answer questions);
  - to receive a timely, reasoned, ethics-based, and understandable decision; and
  - to ask for a revision of a final decision to the same REC or to appeal to another REC (with appropriate communication between the original REC and the REC receiving the appeal) or competent authority (e.g. managing regulator of RECs, national bioethics council).

Research Oversight

- RECs should maintain risk-adapted and ongoing ethical oversight of the research they approve, such as requiring researchers to submit periodic reports and to publish findings within a reasonable time period following the research project's conclusion.

Accountability of RECs

- RECs should be subject to monitoring of their procedures by competent authorities.
- RECs should publish and make publicly available a summary of their final decisions, whether favourable or otherwise.

Vulnerable Populations

- Ethics review of research with health-related data from vulnerable populations should involve ethics committee member(s) or consultation of specialist referee(s) with specific expertise on research with such populations.

IV. Common Elements of Ethics Review

In reviewing the ethical acceptability of an application for multi-jurisdictional research involving health-related data, due regard should be given to the following:

- Expertise and experience of investigator(s);
- Role of the sponsor(s);
- Research protocol (e.g. study design; dissemination of findings/feedback to participants; documentation issues);
- Prior ethics review;
- Study context and site(s) information;
- Specific health-related data research issues (e.g. relevant regulatory approvals);
- Conflict of interest (e.g. financial, organizational, personal);

- Consent process (e.g. participant identification and solicitation, information provided, type of consent used – written, explicit, broad, etc.; assent in cases of minors or adults with incapacity; withdrawal);
- Potential risks and harms for participants, communities, and society;
- Potential benefits for participants, communities, and society;
- Adequate assessment of the scientific value;
- Privacy and confidentiality (e.g. protection, access, control, security, retention, disposal of the data; at the stage of publication; compliance with relevant privacy/data protection regulations);
- Considerations for vulnerable populations;
- Funding (e.g. participant compensation; researcher compensation/benefit; sufficiency and source of funding);
- Evidence of training, education, or experience about the ethical conduct of research involving health-related data;
- Legacy of the project-generated data, i.e. a plan for how the data generated by the project will be stored, archived, and become accessible for new research; and
- Where relevant regulatory information is recorded in the form of metadata, the interoperability of the metadata.

V. Implementation Mechanisms and Amendments

1. Attention should be paid to the interrelation of this Policy with other GA4GH Policies (e.g. Consent Policy, Privacy and Security Policy, Accountability Policy) and the Data Sharing Lexicon.

2. Any entity or individual may propose an amendment to the present Policy by communicating with the GA4GH's Regulatory and Ethics Working Group (REWG). The REWG shall circulate such amendments for comments and evaluate its possible inclusion in this Policy.

3. The REWG, in collaboration with GA4GH members and other GA4GH Working Groups, will track the adoption of this Policy and its application. The REWG will also routinely review the Policy's provisions, be aware of scientific and information technology advances and ethical developments, and attempt to ensure that this Policy is fit for purpose.

Acknowledgements

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Policy Revision History

Policy Number/Version	Date Effective	Summary of Revisions
POL 004 / v. 1.0	XXX	Original document