Documentation of Background Information for The Public Meeting on The Future of Genetic Research in India

This document has been prepared to provide participants of the Focus Group Discussion to be held on 07 December, 2019 some background information on the topic of genetic research. In that, it provides insight into,

1. Key definitions in the field of genetic research
2. A general overview of genetic research in India
3. Regulations governing genetic research
4. Moving towards a people centred approach

It must also be remembered that this information is not inclusive of all the nuances of genetic research, but only those facets that are essential to the agenda of the discussion. However, relevant citations are provided if participants wish to further explore any of the points addressed in this reading.

Definitions

1. Genetic Test:
   A type of medical test that identifies changes in chromosomes, genes, or proteins. The results of a genetic test can confirm or rule out a suspected genetic condition or help determine a person's chance of developing or passing on a genetic disorder. (NIH[1])

2. Biobanking:
   An organized collection of resources that can be accessed to retrieve human biological material and data for research purposes. Repository activities involve three components: collection of biospecimens and/or data; storage of biospecimens and data including its management; and retrieval and disbursement to researchers. (ICMR[2])

3. Genetic Information:
   Genetic information can be defined as,
   - An individual's genetic tests (including genetic tests done as part of a research study);
   - Genetic tests of an individual's family members (defined as dependents and up to and including 4th degree relatives);
   - Genetic tests of any fetus of an individual or family member who is a pregnant woman, and genetic tests of any embryo legally held by an individual or family member utilizing assisted reproductive technology;
   - The manifestation of a disease or disorder in an individual's family members (family history); or

[1] https://ghr.nlm.nih.gov/primer/testing/genetictesting

[2] https://www.icmr.nic.in/sites/default/files/guidelines/ICMR_Ethical_Guidelines_2017.pdf

- Any request for, or receipt of, genetic services or participation in clinical research that includes genetic services (genetic testing, counseling, or education) by an individual or an individual's family members.

Genetic information does not include age or sex related information. (GINA[3])

4. Genomic Research:
   The study of genes which code for a protein, enzyme, or a transporter in a particular individual, and to find out if there is any mutation, single nucleotide polymorphism, or copy number variations which may determine the susceptibility of the individual to a disease or the response to drugs[4].

General Overview

Genetic research is paving the way for new insights within the biomedical field - particularly in the areas of personalised medicine and public health. The role of genetic research is coming to be seen as indispensable in the diagnosis and treatment of genetic disorders, infectious diseases and non communicable diseases[5]. The collection of biological samples to conduct genetic testing and the publishing/sharing of data collected thus become essential to the progression of the field of genetic research.

However, with the advent of genetic research there are several ethical concerns that have come to light. These include: consent, including consent options, waiver of consent and re-consent for secondary or extended use of the sample; trust and ownership; privacy and confidentiality; disclosure of findings; transfer of samples; and benefit sharing. Subsequently, issues such as genetic privacy, genetic confidentiality and "genetic exceptionalism" (arising from the uniqueness of one's genes) give rise to complexities that are greater than in other kinds of research[6], necessitating specialised governance[7]. There are

[3] https://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-genetic-information-nondiscrimination-act/index.html

[4] Chandrasekaran, A., Mathaiyan, J., & Davis, S. Ethics of Genomic Research. Perspectives in Clinical Research. 2013; 4(1)

[5] https://www.who.int/genomics/research/en/

[6] Cambon-Thomsen A. The social and ethical issues of post-genomic human biobanks. Nat Rev Genet. 2004;5(11):866–73
Palsson G, Hardardottir KE. For whom the cell tolls: debates about biomedicine. Current Anthropology. 2002;43(2):271–301
Boverberg JA. Towards an international system of ethics and governance of biobanks: a 'special status' for genetic data? Critical Public Health.2005;15(4):369–83. doi: 10.1080/09581590500523400

[7] Scholtes VPW, de Vries JPPM, de Kleijn DPV, Moll FL, de Borst GJ, Pasterkamp G. Biobanking in atherosclerotic disease, opportunities and pitfalls. Curr Cardiol Rev. 2011;7(1):9–14. doi: 10.2174/157340311795677707
De Souza YG, Greenspan JS. Biobanking past, present and future: responsibilities and benefits. AIDS. 2013;27(3):303–312. doi:10.1097/QAD.0b013e32835c1244

also issues related to the individual and to the entire community from where samples were received and in the case of archived data, whether and how recontact with the individuals or communities for re-consent is possible and/or ethical[8]. Typically, in biobanking, there is a shift from the individual to the collective, as human biological material collections and research is sought to be done on genetically isolated populations, those with a common genetic mutation, those with a favourable trait, those with a rare or orphan disease, among others[9].

Having said that, the attractiveness of biobanking and genetic research has not escaped India, as is apparent with the number of biobanks (mostly of stem cells, cord blood and 'waste tissue') that have been set up mostly for research[10]. But in India, till around 2013 there has been relatively little discourse on potential bioethical issues related to biobanking. Further, while the 2017 ICMR Guidelines addresses the gap of its 2006 predecessor - devoting a new section to Biological materials, Biobanking and Data sets - challenges remain in converting these broad guidelines into practices which are implementable, people-centred, and uphold the ethical principles of respect, protection of public interest, privacy, confidentiality and reciprocity. Since there is no statutory requirement to formally register biobanks with a regulatory authority, there is no official data available on their numbers or locations in India.

Regulations

Genetic research, in particular the advancement and the reduced costs of sequencing of the human genome, has opened the way for far-reaching medical research and biomedical applications. Genetic data can be used for medical diagnosis, disease prevention and population genetics studies. As the number of genetic bio/data banks is rising, protection of participants involved in such research has become a priority.

Caulfield T, et al. Research ethics recommendations for whole-genome research: consensus statement. PLoS Biol 2008; 6(3): e73. doi:10.1371/journal.pbio.0060073

Vaz M, Sridhar TS, Pai SA. The ethics of research on stored biological samples: outcomes of a workshop. Indian J Med Ethics. 2016 Apr-Jun;1(2) 118-22

Bull, Susan, Roberts N, Parker M. Views of Ethical Best Practices in Sharing Individual-Level Data from Medical and Public Health Research: A Systematic Scoping Review. Journal of Empirical Research on Human Research Ethics. 2015; 10(3): 225–38. doi:10.1177/1556264615594767

[8]Vaz M, Vaz M, Srinivasan K. Ethical challenges in biobanking: moving the agenda forward in India. Indian J Med Ethics. 2014;11(2):79–88. Available from: http://ijme.in/index.php/ijme/article/ view/1932/4197

[9]Blasimme, A. & Vayena, E. BMC Med Ethics (2016) 17: 67. https://doi.org/10.1186/s12910-016-0149-6

[10]Limaye N. "Pharmacogenomics, Theranostics and Personalized Medicine – The Complexities of Clinical Trials: Challenges in the Developing World. Appl Transl Genom. 2013;17-21

These are some of the key regulations in the global context:

1. International:
    a) *International Declaration on Human Genetic Data*[11] *published by the United Nations Education, Scientific and Cultural Organisation (UNESCO)*
    The UNESCO Declaration on Human Genetic Data urges that, States may consider establishing a framework for the monitoring and management of human genetic data, human proteomic data and biological samples based on the principles of independence, multidisciplinarity, pluralism and transparency, as well as the principles set out in the Declaration.

    b) *The 'International Ethical Guidelines for Health-related Research Involving Humans*[12]*' prepared by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO).*
    The CIOMS document is a key milestone in the development of people centred guidelines for conducting biomedical research involving human participants. Further the guidelines also identifies the existence of variations in socio-cultural across communities, and states the need to ground scientific research within local cultural values and beliefs, through various modes of community engagement.

2. Europe:
    a) *The European Union guidelines as the recommendation [Rec(2006)4*[13]*] of the Committee of Ministers to member states on research on biological materials of human origin*
    The document provides a general rule for the use of biological samples which states: Research on biological materials should only be undertaken if it is within the scope of the consent given by the person concerned. The person concerned may place restrictions on the use of his or her biological materials.

3. USA:
    a) *'The Common Rule' ie. the U.S. Department of Health and Human Services Title 45 CFR 46 (Public Welfare) Subparts A, B, C and D*[14]
    The Common Rule is a regulation of ethics regarding biomedical and behavioral research involving human subjects in the United States. It comprises of a set of requirements that ensure protection for human subjects

[11] http://portal.unesco.org/en/ev.php-URL_ID=17720&URL_DO=DO_TOPIC&URL_SECTION=201.html
[12] https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMS-EthicalGuidelines.pdf

[13] https://search.coe.int/cm/Pages/result_details.aspx?ObjectID=09000016805d84f0

[14] https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=&SID=83cd09e1c0f5c6937cd9d7513160fc3f&pitd=20180719&n=pt45.1.46&r=PART&ty=HTML#_top

involved in research. Further, it details requirements in special cases for research involving prisoners, children and pregnant women, human fetuses and neonates. Some of the key features of the basic policy are,

- The Common Rule requires informed consent, where an investigator must provide to each potential research participant a clear summary of the research study, including any risks to participants, and where each individual then needs to consent to permit the researcher to include them in the study.
- The Common Rule also requires that federally-funded human subjects research studies are overseen by an Institutional Review Board (IRB) to ensure the safety of research participants.

b) *The Genetic Information Nondiscrimination Act (GINA)*[15]

GINA, is an Act of Congress in the United States designed to prohibit some types of genetic discrimination. The act prohibits health insurers or health plan administrators from requesting or requiring genetic information of an individual or an individual's family members, or using such information for decisions regarding coverage, rates, or preexisting conditions. GINA also prohibits employers from using genetic information for hiring, firing, or promotion decisions, and for any decisions regarding terms of employment. However, GINA does not extend to life insurance, disability insurance, or long-term care insurance.

c) *Health Insurance Portability and Accountability Act (HIPAA)*[16]

HIPAA is a United States legislation that provides data privacy and security provisions for safeguarding medical information. Every individual is granted the following rights under HIPAA,

- Ask to see and get a copy of your health records
- Have corrections added to your health information
- Receive a notice that tells you how your health information may be used and shared
- Decide if you want to give your permission before your health information can be used or shared for certain purposes, such as for marketing
- Get a report on when and why your health information was shared for certain purposes
- If you believe your rights are being denied or your health information isn't being protected, you can

[15] https://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-genetic-information-nondiscrimination-act/index.html

[16] https://www.hhs.gov/hipaa/for-individuals/guidance-materials-for-consumers/index.html

- File a complaint with your provider or health insurer
- File a complaint with HHS

Within the Indian context, regulations governing biomedical research are published by the Department of BioTechnology (DBT) and the Indian Council for Medical Research (ICMR).

1. DBT:
    a) *The Human DNA Profiling Bill*[17] *[erstwhile]*

    b) *The DNA Technology (Use and Application) Regulation Bill*[18]
    The bill sets up the regulations for the use of DNA technology for establishing the identity of certain persons. It includes provisions for:
        - Collection and use of DNA data
        - Establishment of a National DNA Databank
        - Establishment and functioning of a DNA Regulatory Board
        - Considerations for DNA laboratories

(The DNA Profiling bill subsequently became the DNA Technology Regulation bill. However neither were or have been passed as an act by parliament)

2. ICMR:
    a) *National Ethical Guidelines for Biomedical and Health Research Involving Human Participants*[19]
    The 2017 ICMR Guidelines addresses the gap of the 2006 Guidelines by devoting a new section to Biological materials, Biobanking and Data sets. It covers issues such as the definition of biological materials, biobanking and data sets; storage including safety requirements and quality maintenance; sample typology based on identity linkage and related confidentiality concerns, ethical aspects of consent, including consent options, waiver of consent and re-consent for secondary or extended use of the sample; ownership; transfer of samples; and benefit sharing.

A final point to address regarding regulations is that with respect to data generated as an outcome of research. The development/usage of large datasets in genetic research is inevitable. Presently, data protection in India is primarily governed by the Information Technology Act, 2000, and the Information Technology (Reasonable Security Practices and Sensitive Personal Data or Information) Rules, 2011. However, there have been several debates which note that these laws are not adequate for the protection of individual interests.

[17] http://lawcommissionofindia.nic.in/reports/Report271.pdf

[18] http://prsindia.org/billtrack/dna-technology-use-and-application-regulation-bill-2019

[19] http://ethics.ncdirindia.org/asset/pdf/Handbook_on_ICMR_Ethical_Guidelines.pdf

In 2018, to overcome these setbacks, a draft of the Personal Data Protection Bill[20] was announced - which is yet to be tabled in the parliament. The bill also draws heavily from the European Union's General Data Protection Regulation[21]. Some of the salient features of highlighted in the bill are,

1. The right to know where your data is being stored
2. The right to limit/minimize personal data being collected
3. The right to be forgotten
4. The right to access (and correct) your data

Apart from collection and collation involved in the use of data, genetic research also employs data sharing practices, to further its progression. In this regard, the mechanisms established by the NIH Genomic Data Sharing policy[22] are often cited as a hallmark. Within India, data sharing practices are informed by the Department of Science and Technology's National Data Sharing and Accessibility Policy[23].

People Centred Governance

Over the last decade, genetic research has seen a noticeable shift towards more people centric approaches. Introduced by Graeme Laurie, the Ethics+ approach is defined by a set of continuous reflective and deliberative processes, rather than just procedural relevance, when it comes to understanding the ethical concerns related to genetic research[24]. Even for data sharing governance, stakeholder consultations have shown that the need for community engagement, oversight groups, consultative processes are necessary mechanisms for data access across researchers and across countries[25]. There is a need for research governance policies and regulations to support this. A good example of these approaches finding their way into practice can be seen in the development of the guidance documents and governance mechanisms for the The Human Heredity and Health in Africa (H3Africa) consortium[26]. This

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[20] https://meity.gov.in/writereaddata/files/Personal_Data_Protection_Bill,2018.pdf
[21] https://gdpr-info.eu/

[22] https://www.genome.gov/about-nhgri/Policies-Guidance/Genomic-Data-Sharing/data-standards

[23] https://data.gov.in/sites/default/files/NDSAP.pdf
https://data.gov.in/sites/default/files/NDSAP%20Implementation%20Guidelines%202.4.pdf

[24] https://www.research.ed.ac.uk/portal/files/48288589/Laurie2017ABRWhatDoesItMeanToTake.pdf

[25] Jao, I., Kombe, F., Mwalukore, S., Bull, S., Parker, M., Kamuya, D., … Marsh, V. (2015). Involving Research Stakeholders in Developing Policy on Sharing Public Health Research Data in Kenya: Views on Fair Process for Informed Consent, Access Oversight, and Community Engagement. *Journal of empirical research on human research ethics : JERHRE*, *10*(3), 264–277. doi:10.1177/1556264615592385

[26] Tindana P, Campbell M, Marshall P, et al. Developing the science and methods of community engagement for genomic research and biobanking in Africa. Glob Health Epidemiol Genom. 2017;2:e13. Published 2017 Sep 4. doi:10.1017/gheg.2017.9
http://www.health.uct.ac.za/sites/default/files/image_tool/images/116/documents/research/H3Africa%20CE%20Guidelines_Final.pdf

offers a clearer picture for developing countries, like India, on how to incorporate people centric mechanisms to govern genetic research, despite the vast diversity that exists both in terms of populations and opinions.

https://h3africa.org/wp-content/uploads/2018/05/App-D-H3Africa-Data-and-Biospecimen-Access-Committee-Guidelines-final-10-July-2017.pdf