Laws and Regulation on Biobanks : Present Status and Future Directions

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P3G

HumGen International

PROMOTING HARMONISATION OF PHOEBE EPIDEMIOLOGICAL BIOBANKS IN EUROPE

Outline of Presentation

- Introduction
- Ethical and Legal Frameworks
- Governance Structures and Mechanisms
  - International Guidelines
  - National Biobank Laws
  - Other Related Practices
- Future Directions for Laws and Regulations

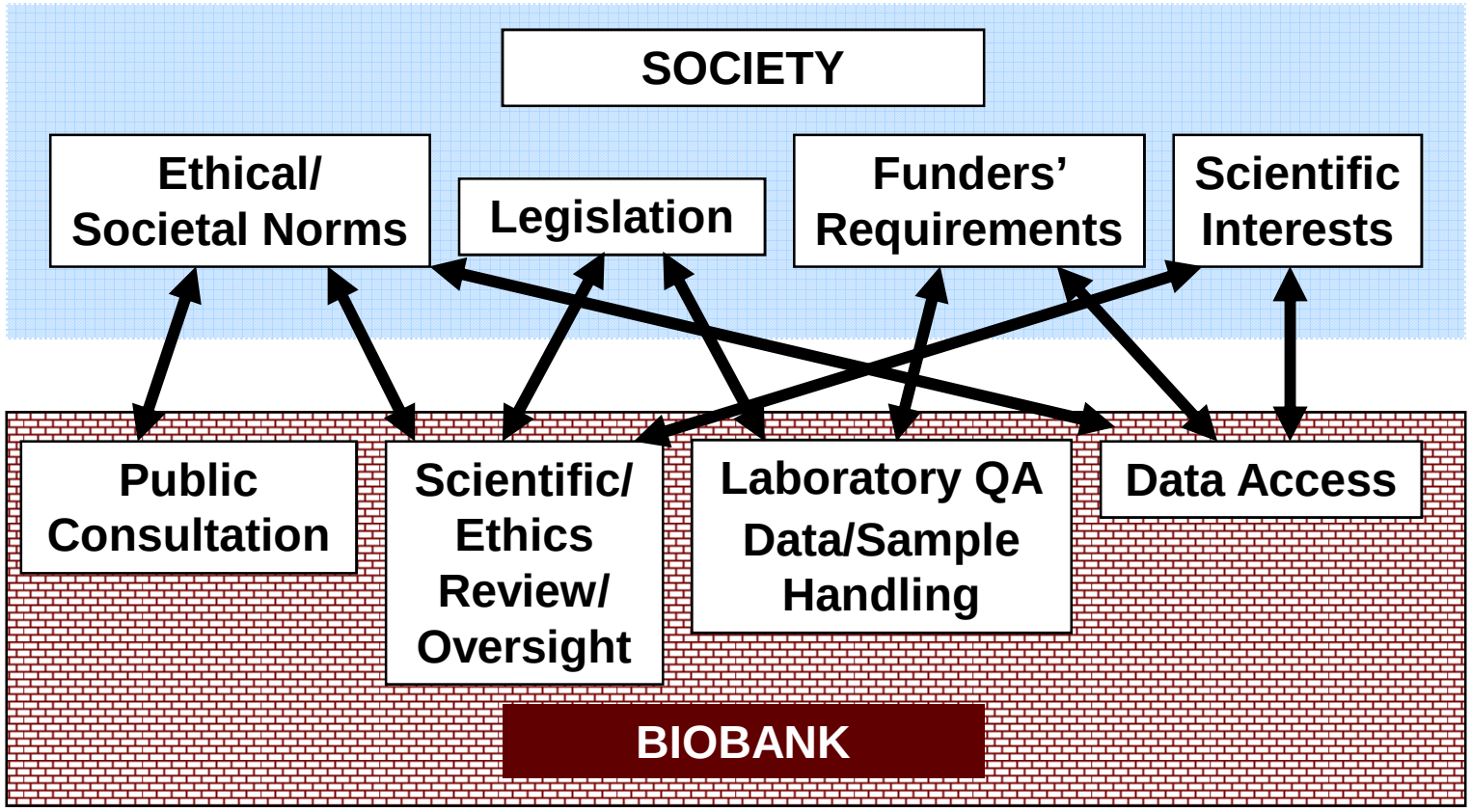
Appropriate Ethical and Legal Frameworks

- Protection of participants
- Need for ethical/legal guidelines for the particular context of biobank harmonization
  - Long term use
  - Research questions not pre-defined
  - Data/samples sharing between studies/countries
- Protection of eventual intellectual property
- Higher degree of data security

Appropriate Ethical and Legal Frameworks

- Public support is needed to ensure the successful creation, running and financing of a biobank
- Participants must trust that:
  - The biobank will have an appropriate and effective governance structure
  - The research will be conducted ethically and will be beneficial for society
  - Their personal information will be protected

Interaction of Biobank with Society



Governance

- “The process of policy orientation and management that guides and regulates research under ethical and scientific norms so that the results can be used for the benefit and improvement of the health of the population.”

P3G/PHOEBE Lexicon, online:

<http://www.p3gobservatory.org/lexicon/list.htm>

Governance Structures

- "…the agreements, procedures, conventions or policies that define who gets power, how decisions are taken and how accountability is rendered".

Institute on Governance, online: <http://www.iog.ca./publications/policybrief15.pdf>

Governance Mechanisms

1. International Guidelines
2. Legislation specific to biobanks
3. Other general related practices

International Guidelines

- Human Genome Organization (HUGO)
- International Bioethics Committee (IBC) of UNESCO
- Organisation for Economic Co-operation and Development (OECD)
- International Council on Harmonisation (ICH)
- Council of International Organizations of Medical Services (CIOMS)

Human Genome Organization (HUGO)

- Statement on the Principled Conduct of Genetic Research (1996)
- Statement on DNA Sampling: Control and Access (1998)
- Statement on Human Genomic Databases (2002)

HUGO Ethics Committee

Statement on Human Genomic Databases (2002)

Recognizing:

- The potential global good arising from genetic research;
- The scientific and clinical uses of genomic databases;
- The potential for conflicts between the free flow of
- information that is crucial to research advances and the
- legitimate rights to return from research expenditure;
- The potential risk of misusing genetic data;
- The need to rapidly place primary genomic sequences in the public domain.

HUGO Ethics Committee

Statement on Human Genomic Databases (2002) (cont.)

<u>Recommendations:</u>

1. Human genomic databases are global public goods
   a) Knowledge useful to human health belongs to humanity
   b) Human genomic databases are a public resource
   c) All humans should share in and have access to the benefits of databases [...]

International Bioethics Committee (IBC) of UNESCO

- Universal Declaration on the Human Genome and Human Rights (1997)
- International Declaration on Human Genetic Data (2003)

IBC International Declaration on Human Genetic Data (2003)

- "Where appropriate, ethics committees at national level should be consulted with regard to the establishment of standards, regulations and guidelines for the collection, processing, use and storage of human genetic data, human proteomic data and biological samples. They should also be consulted concerning matters where there is no domestic law." **Article 6(b)**

IBC International Declaration on Human Genetic Data (2003) (cont.)

- "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 this Declaration. This framework could also deal with the nature and purpose of the storage of these data." **Article 20**

Organisation for Economic Co-operation and Development (OECD)

- OECD Best Practice Guidelines for Biological Resources Centres
- OECD Draft Guidelines on Human Biobank and Genetic Research Databases (HBGRDs) (2008)

OECD Draft Governance, Management, and Oversight Principles for HBGRDs

- 3.A … governed by the principles of transparency and accountability.
- 3.B … clearly formulate the governance structure and management responsibilities applicable to the HBGRD and should make available information to participants, stakeholders and the general public.
- 3.C [a]…governance structure should ensure that the rights and well-being of the participant prevail over the research interests of the initiators and users of the HBGRD.
- 3.D … should have a mechanism to review applications for access to the human biological materials and/or data.
- 3.E … ensure that all HBGRD activities are carried out in accordance with the highest legal norms and ethical principles.
- Specific roles and chains of responsibilities … should be clearly delineated.

OECD Draft Governance, Management, and Oversight Principles for HBGRDs (cont.)

- 3.F … oversight mechanisms to ensure that the governance, management and operation of the HBGRD comply with applicable domestic and international ethical, financial, and regulatory legislation, policy and frameworks.
- 3.G … individuals involved in the oversight procedure should be drawn from diverse relevant areas of expertise, including the scientific, legal, and ethical fields.
- 3.H Participants should have access to an independent means of recourse for redressing breaches of the ethical, financial, and regulatory legislation, policy and frameworks.
- 3.I … anticipate that over its lifespan the need to modify its policies, protocols and procedures will arise.
- 3.J …have in place an independent audit mechanism to review uses of the human biological materials and data for consistency with the research uses agreed to by a participant during the informed consent process.

P3G Guidelines Comparison Chart

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Guidelines Comparison Chart

For each guideline the table addresses biobanking development steps in either of the following three detail levels:

- mentioned or
- guidelines (detailed enough to dress a protocol/ model), or
- protocols/ model ready to be followed, to be used)

Author(s)/organization		OECD	ISBER	IARC, WHO	NCI, NIH, HHS	ABN	EHRM	RAND	INSERM, AFNOR
Publication date		2007	2005	2007	2007	2007	2002	2003	2008
Title		OECD Best practices guidelines for Biological Resource Centres	Best Practices for Repositories I: Collection, Storage and Retrieval of Human Biological Materials for Research	Common Minimum Technical Standards and Protocols for Biological Resources Centres Dedicated to Cancer Research	National Cancer Institute Best Practices for Biospecimen Resources	Australasian Biospecimen Network Biorepository Protocols	European Health Risk Monitoring (EHRM) Recommendation for indicators, international collaboration, protocol and manual of operations for chronic diseases risk factor	Case Studies of Existing Human Tissue Repositories 'Best Practices' for a Biospecimen Resource for the Genomic and Proteomic Era	Management system of a BRC and quality of biological resources from human or micro-organism origin
County		International (28 countries)	International Forum based in United States	Worwide Directors of National Cancer Centres	United States	Australia	Finland	United States	France
URL		http://www.oecd.org/home/0,987,en	http://www.isber.org	http://www.iarc.fr/	http://www.cancer.gov	http://www.abrn.net/	http://www.ktl.fi/ehrm/	http://www.rand.org/publications/	
Sample type(s)		wide: Human, animal and plant, and micro-organism	Human: Blood, urine saliva, nails, breast milk, tissues, etc	Human: blood (plasma, serum, white blood cells, buffycoat, urine, buccal cells, saliva, bronchoalveolar lavage, bone marrow aspirate, fine needle aspirate, cerebrospinal fluid, semen, cervical and urethral swabs, hair, nail	Human: blood and solic tissue mentioned bet not extensively	Human: Blood (serum, plasma, white blood cells, buffy coat), Urine, buccal cells, bone marrow	Human: Blood	Human: blood, serum, tumor, tissues	wide: Human
Steps/ areas covered	Infrastructure/ Apparatus	guidelines (apparus maintenance)	protocols (ventilation temperature, lighting etc.)	protocols (temperature for devices)			guidelines		guidelines
	Biosafety	guidelines	guidelines	guidelines	guidelines		guidelines		
	Staff training	guidelines	guidelines	mentionned	guidelines				guidelines
	Ethics	guidelines	guidelines (privacy rules, consent form, IRB)	mentionned	guidelines (consent form, privacy protection)	Model (consent form)	guidelines	guideines	
	Intellectual Property			mentionned	guidelines			guideines	
	Clinics Data Management			protocols	guidelines	guidelines	model oliquestionnaire protocols for anthropometric measures		
	Sample Traceability/ Labelling	mentionned	guidelines	guidelines	guidelines		guidelines	guideines	
	Sample type choice		discussion (advantage-inconvenient balance)	discussion (advantage-inconvenient balance)	discussion (advantage-inconvenient balance)	discussion (advantage-inconvenient balance)			
	Sample Collection and Processing	mentionned	guidelines (sample type-dependent)	protocols (sample type-dependent)	guidelines	protocols (sample type-dependent)	protocols	guideines	mentionned
	Sample-derived data management	recommended data set: MDS and RDS)	guidelines	guidelines (minimum information)	guidelines		guidelines	guideines	guidelines
	Sample Storage	guidelines (sample type-dependent)	guidelines (aliquoting)	protocols (sample type-dependent)	guidelines	protocols (sample type-dependent)	protocols	guideines	mentionned
	Quality Control	guidelines (methods validation; sample quality)	guidelines	guidelines	guidelines	guidelines (materials and sample type-dependent), protocols (RNA)	guidelines	guideines	protocols (on all topics)
	Transportation/ shipping	mentionned	guidelines	protocols	guidelines	guidelines (sample type-dependent)			mentionned
	Fundy Sustainability	mentionned		mentionned				guideines	
	Access to data/ Transfert	mentionned		guidelines	Model (materia transfert agreement)	guidelines	guidelines	guideines	guidelines
	Informatics support	guidelines	mentionned	mentionned	guidelines (caBIG system)			guideines	guidelines
	Other	Recapitulative tables on requirement for each topics (sample type-dependent: maintenance, storage, ethics etc..	Sources websites for every topics (biosafety, shipping, processing protocols etc..)	table mentionning 16 other biorepository guidelines (ISBER, ABN, OECD, NCI, WHO, RAND, etc...)		protocols for RNA and genomic DNA isolation and stable cell lines generation Laboratory suppliers suggestion (for reagent and apparatus) Sugestion of the sample future use depending on the sample type	Useful guidelines to build a study/biobank: Indicators for risk factors that could be used for background, Sample size discussion, target population, recruitment procedures, duration of surveys, questionnaire administation etc..	Evaluation and comparison of tissues and processes from 12 tissue repositories in USA, Comparison table for all 12 biobanks	Table that lists of all documents required to assess good quality at each step Table comparing ISO 9001:2000 norms and BRC standards
certification-oriented?		Yes (3 phases)						RAND evaluation	Yes ISO 9001

National Biobank Laws

- 4 examples of national legislation on biobanks

Country	Scope and Purpose	Organisation or Establishment of a biobank	Conditions of closure	Condition of storage	Condition of access and scope of research	Consent and rights of donors
Norway	X	X	X	X	X	X
Estonia	X	X		X	X	X
Sweden	X	X	X	X	X	X
Spain	X	X	X	X	X	X

National Biobank Laws

Country	Controls, appeals and penalties	Confidentiality and coding	Commercialisation, IP and licensing	Discrimination
Norway	X	X		
Estonia	X	X	X	X
Sweden	X	X	X	
Spain	X	X		

Details about Scope and Purpose

- What is the purpose of the legislation?

  Different approaches:

  - some are specific to one biobank,
  - some relate to any biobank in the country, and
  - others have a broader scope and only discuss biobank in a chapter within the law.

Details about Scope and Purpose

1)Ex. **Estonia**: Specific legislation for the Gene Bank

- «The objective of this Act is to regulate the establishment and maintenance of a Gene Bank, to organise the genetic research necessary…» *Human Gene Research Act, Ch. 1. Art. 1 (2000)*

2)Ex. **Spain**: General legislation covering biomedical research, but including a chapter on Biobanks.

- «The object of this law is the regulation of biomedical research, and in particular: d. The storage and movement of biological samples. E. Biobanks. » *Law 14/2007, of July 3 on Biomedical Research, Title 1, art. 1*

Consent and Rights of Donors

- They all have to a certain extent used a broad consent approach with the same general principles:
  - Free informed consent
  - Right to withdraw

1) Ex. **Norway**: free informed consent

  - «Documentation of consent shall be available, and it shall be based on information on purpose, methods, risks, discomfort, consequences and any other information of significance for the validity of the consent.» *Act Relating to Biobanks, Ch.3, art.12, (2003).*

Consent and Rights of Donors

2) Ex. **Sweden**: Right to withdraw

- «A person who has granted consent for the use of a tissue sample may withdraw the consent at any time. If the withdrawal of consent refers to all uses, the tissue sample shall be immediately destroyed or depersonalised». *Biobanks in Medical Care Act, Ch.3 section 6, (2003).*

Specific provisions to each biobank laws

- In addition to their common articles, the biobank laws also have specific provisions:
  1. Estonia: discrimination
  2. Norway: transfer to another country
  3. Sweden: release of tissue sample from a biobank

Estonia: Prohibition on Discrimination

- «Employers are prohibited from collecting genetic data on employees or job applicants and from requiring employees or job applicants to provide tissue samples or descriptions of DNA». Ch. 5. Art. 26.1

- «Insurers are prohibited from establishing different insurance conditions for people with different genetic risks and from establishing preferential tariff rates and determining insured events restrictively». Ch.6. Art. 27.2

Norway: Transfer to another country

- « A biobank or parts of a biobank may only be transferred to another country with the approval of the Ministry and in accordance with the consent given by the donor of the material. » Ch. 2 Art. 10.

- «The Ministry may lay down regulation relating to the use of material from other countries for research purpose in Norway». Ch.2 Art. 10

Sweden: Release of tissue sample from a biobank

- «If tissue samples in a biobank are to be released to a recipient in another country for research purposes, a Swedish research institution must submit an application. If this application is approved, a condition shall be placed on the recipient in the foreign country that the specimens are to be returned or destroyed when they are no longer needed for the purpose for which they were released». Ch.4. Section 3.

Summary

- **Common principles**:
  - consent
  - right of the donor to withdraw
  - conditions of storage
- **Diverse approaches:**
  - access by researchers
  - scope of the law
  - organisation
  - Extent of protection and oversight

How can we promote harmonisation?

Issues

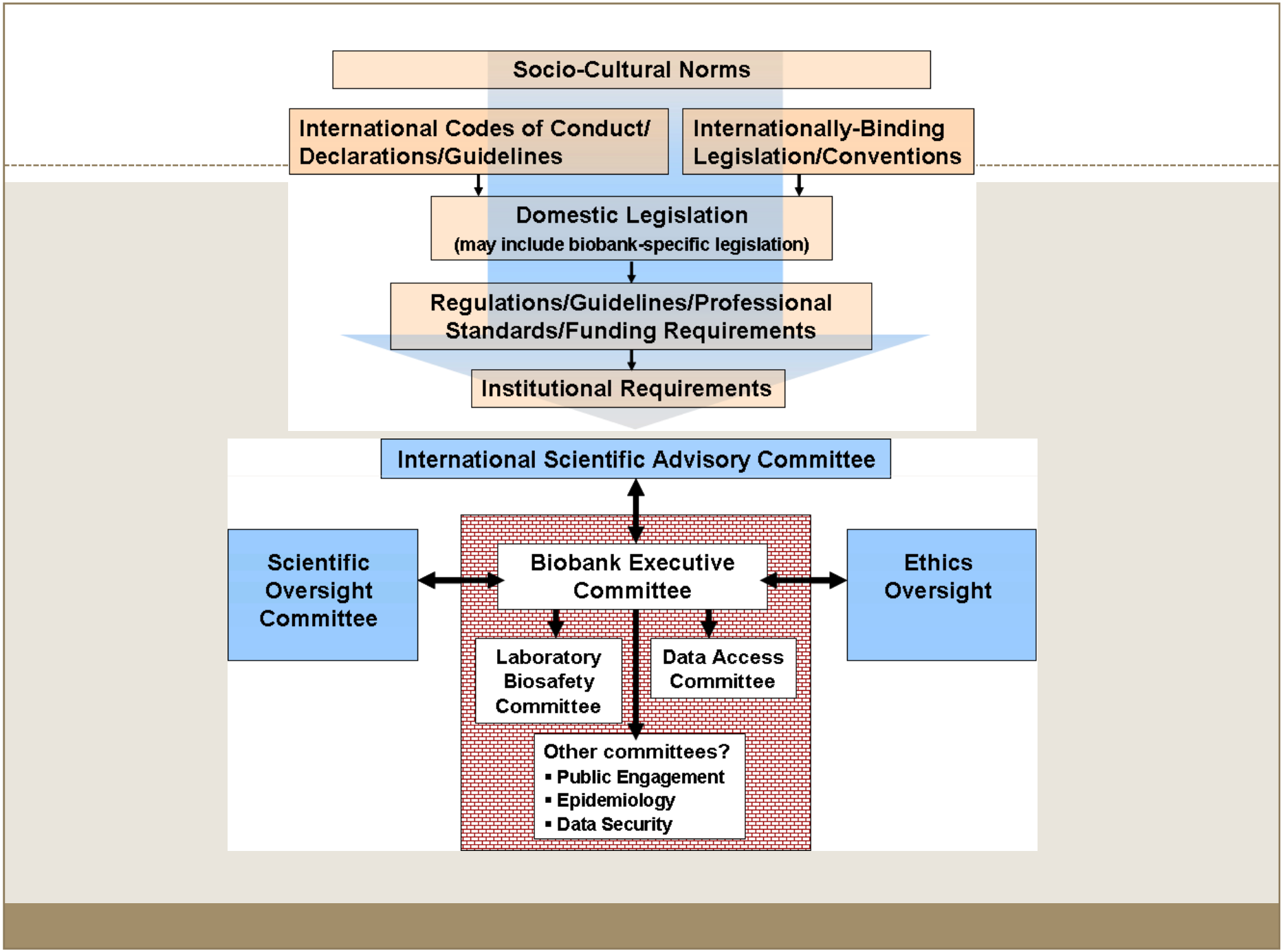
- Are the laws on biobanks too narrow to adapt to the pace of science?
- Are they useful for the protection of participants?
- Are they answering a need? If yes, what is that need? Perhaps some control over the creation to these structures is needed?

Biobank Legislation or Existing Governance Mechanisms?

- No consensus as to whether specific biobank-related legislation is beneficial or a detriment to scientific research in this area
- Is it more efficient for a country to have specific biobank legislation or to rely on other governance mechanisms found in biomedical research guidelines or laws generally?

Other Related Practices

- Applicable legislation/regulations and standards
  - Human rights; data protection; health and safety; statistics; use of human tissue; blood and other biomaterials; protection of humans involved in research
- Scientific and ethics review
- Professional and institutional guidelines


Socio-Cultural Norms
International Codes of Conduct/ Declarations/Guidelines
Internationally-Binding Legislation/Conventions
Domestic Legislation
(may include biobank-specific legislation)
Regulations/Guidelines/Professional Standards/Funding Requirements
Institutional Requirements
International Scientific Advisory Committee
Scientific Oversight Committee
Biobank Executive Committee
Ethics Oversight
Laboratory Biosafety Committee
Data Access Committee
Other committees?
Public Engagement
Epidemiology
Data Security

Conclusions

- No one governance framework can apply to all biobanks
- Frameworks must be context-driven
- However, frameworks should ensure certain aspects

- *Scientific Aspects:*
  - The research conducted will advance science and benefit the population and individuals in the future.
  - The resource's procedures and activities will receive regular independent scientific review.

- *Ethical aspects*:
  - The confidentiality of personal information will be protected.
  - The resource's procedures and activities will receive regular independent ethics review.
  - All requests for access to data and samples will be reviewed at some level.
  - The resource will comply with all relevant legislation, guidelines and standards.

- *Expertise:*
  - There will be expert representation on all governance and oversight committees as appropriate (i.e., epidemiologists, bioinformaticians, sociologists, geneticists, etc.)

- *Communications:*
  - The population will be kept generally informed of the research conducted using their data and samples.
  - Participants will be able to register their comments, queries and complaints with the resource, with the assurance that any complaints will be addressed.

Future Directions for Laws and Regulations on Biobanks

- Reframe the rights of donors to withdraw in the context of international use and sharing of samples and data?
- Make provisions for the closure of a biobank
- Provide re-contact/general communication models
- Facilitate access for researchers without compromising confidentiality and quality of the research

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