RNATIONAL SUMMER SCHOO

disease and orphan drug registries

The need for data sharing in rare diseases research: ethical, legal and social issues

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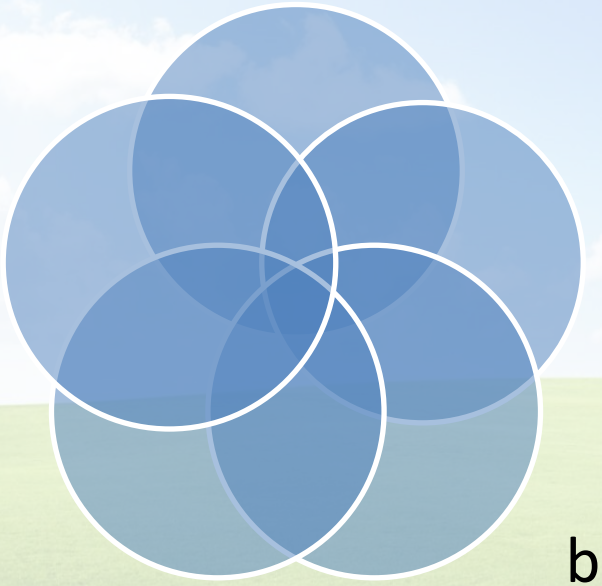
Values at stake in RD research

integrity

wellbeing

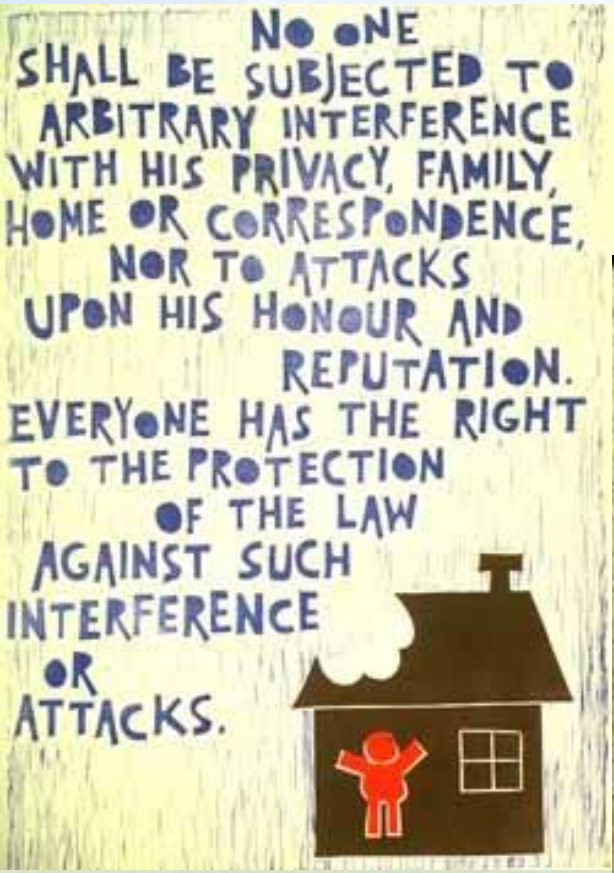


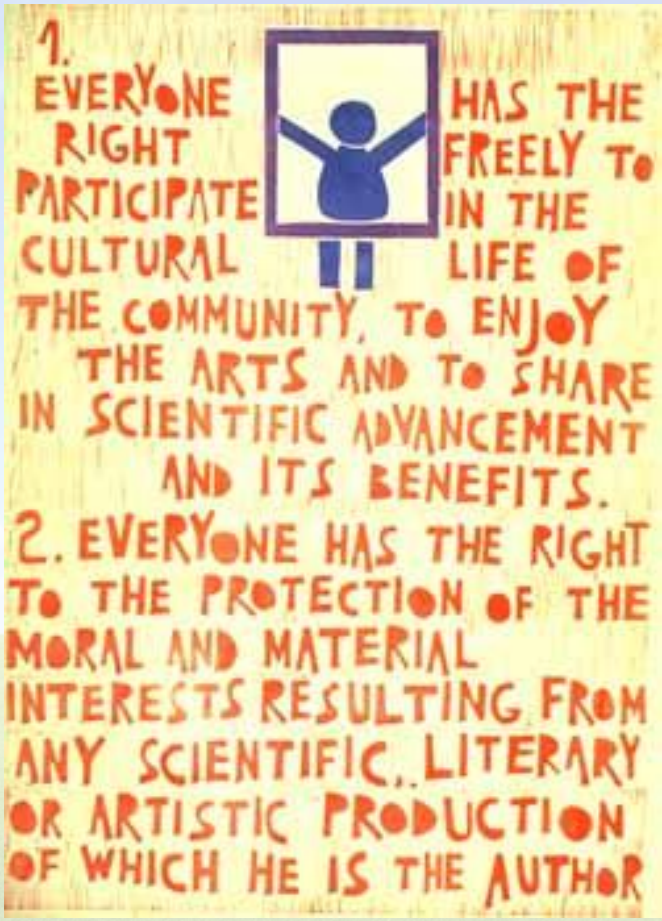
privacy

solidarity

...right to benefit from research?

The Universal Declaration of Human Rights





Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine

- **Article 3 – Equitable access to health care**

Parties (…) shall take appropriate measures with a view to providing, equitable access to health care of appropriate quality.

- **Article 10 – Private life and right to information**

Everyone has the right to respect for private life in relation to information about his or her health.

- (…)
- (…)restrictions may be placed by law on the exercise of the rights contained in paragraph 2 in the interests of the patient.

CHARTER OF FUNDAMENTAL RIGHTS OF THE EUROPEAN UNION

(2010/C 83/02)

European Commission

Article 8

Protection of personal data

1. Everyone has the right to the protection of personal data concerning him or her.

Article 35

Health care

Everyone has the right of access to preventive health care and the right to benefit from medical treatment under the conditions established by national laws and practices. A high level of human health protection shall be ensured in the definition and implementation of all the Union's policies and activities.

United Nations Educational, Scientific and Cultural Organization

Universal Declaration on the Human Genome and Human Rights

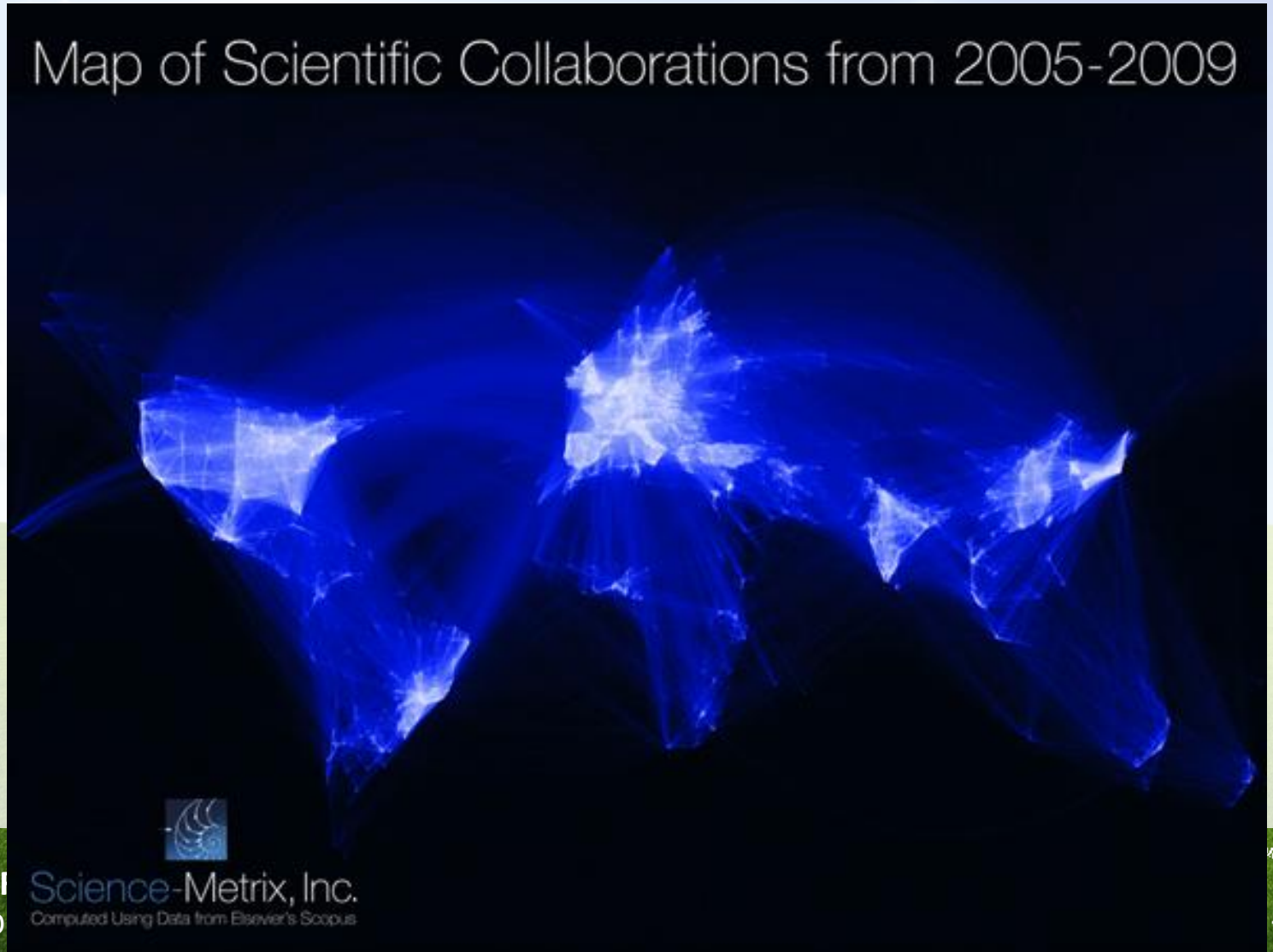
11 November 1997

Article 12

(a) Benefits from advances in biology, genetics and medicine, concerning the human genome, shall be made available to all, with due regard for the dignity and human rights of each individual.

(b) Freedom of research, which is necessary for the progress of knowledge, is part of freedom of thought. The applications of research, including applications in biology, genetics and medicine, concerning the human genome, shall seek to offer relief from suffering and improve the health of individuals and humankind as a whole.

An age of collaboration: global data and global research



Data sharing: 3 key benefits

- Faster progress in improving health
- Better value for money
- Higher quality science

- **A necessity in the field of RD research!**

Data sharing: main advantages

- Independent scrutiny: re-analysis of data to verify results;
- New discoveries in old data sets
- long-term preservation, data integrity;
- Re-collection of data minimized, use of resources optimized;
- Safeguards against misconduct related to data fabrication and falsification;
- Replication studies as training tools

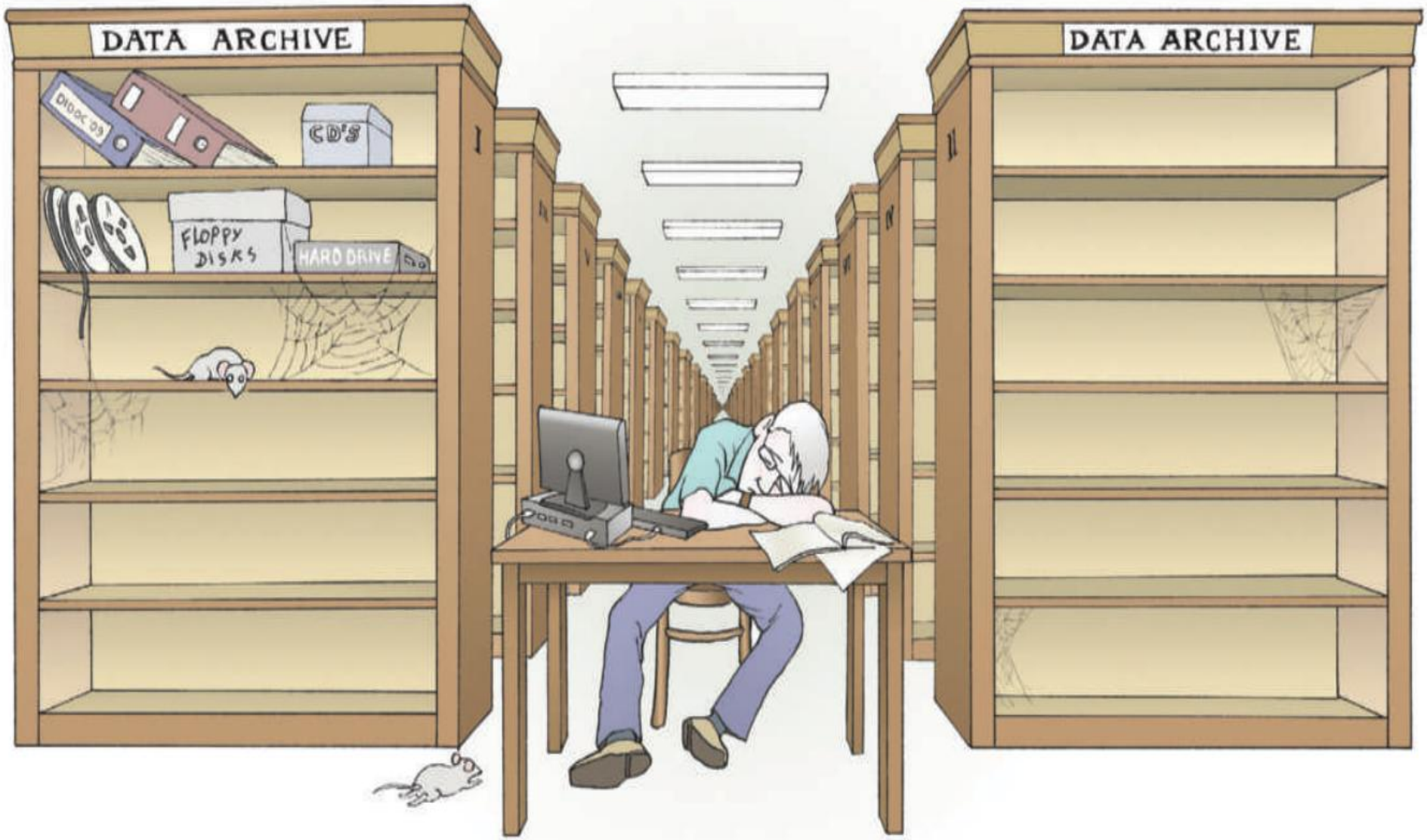
Data sharing by scientists: practices and perceptions. Tenopir et al. Plos One 2011;6(6):e21101

Table 12. Reasons for not making data electronically available.

	Responses	Percent
Insufficient Time	603	53.6%
Lack of Funding	445	39.6%
Do not Have Rights to Make Data Public	271	24.1%
No Place to Put Data	264	23.5%
Lack of Standards	222	19.8%
Sponsor does not Require	196	17.4%
Do not Need Data	169	15.0%
Other Reasons For Data Not Available	164	14.6%
Should not be Available	162	14.4%

doi:10.1371/journal.pone.0021101.t012

Empty archives



Empty archives

- Data lying isolated and forgotten on personal hard drives and CDs.
- Researchers fail to develop clear, well-annotated datasets to accompany their research (i.e., metadata), and may lose access and understanding of the original dataset over time.

- Savage CJ, Vickers AJ (2009) Empirical study of data sharing by authors publishing in PLoS journals. PLoS ONE 4: e7078. doi: 10.1371/journal. pone.0007078.
- 15. Campbell EG, Bendavid E (2003) Data-sharing and data-withholding in genetics and the life sciences: Results of a national survey of technology transfer officers. J of Health Care Law Policy 6: 241–255.

Unless we address these issues soon, the likely outcome will be a mix of balkanized data storage systems, creating a barrier to ever gaining the benefits of data aggregation.

(B. Knoppers, Communication at ISS meeting 28-1-2014)

The role of key stakeholders

- Funding agencies can demand data sharing in return for support;
- Scientific societies can establish it as a precedent;
- Journals, can make sharing a condition of publication.

National Science Foundation

The U.S. National Science Foundation (NSF) recently took action by announcing that all proposals to NSF involving data collection must include a data management plan so that ‘‘digital data are routinely deposited in well-documented form, are regularly and easily consulted and analyzed by specialist and nonspecialist alike, are openly accessible while suitably protected, and are reliably preserved’’.

IRDiRC

INTERNATIONAL
RARE DISEASES RESEARCH
CONSORTIUM

MEMBERSHIP

- Any research funding body or group of funders spending over 10 million USD over 5 years for rare diseases
- Government, academia, industry, patient organizations
- Currently over 39 members from 4 continents

IRDiRC POLICIES AND GUIDELINES

Researchers are expected to comply with the following:

- RD research to be collaborative
- Quick release of data for public use
- Data deposited in public databases
- Contribution to a well-curated list of RD
- Interoperability and harmonization of data repositories
- Sharing of data while respecting IP
- Publication of negative results
- Involvement of patients in all relevant aspects of research
- Acknowledgement of the use of infrastructures: biobanks and registries

Global Alliance for Genomics & Health

Mission: 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 to catalyze data sharing projects that drive and demonstrate the value of data sharing.

Framework for Responsible Sharing of Genomic and Health-Related Data

Published: September 12, 2014 | **Last updated:** September 10, 2014

Foundational Principles for Responsible Sharing of Genomic and Health-Related Data

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

The privacy barrier

- The need to re-consent as a main obstacle – time consuming, possible drop outs
- RECs preparedness on evaluate registries and biobank studies
- Impossibility to re-use data and samples: unethical in RD research?

Much research data about people—even sensitive data—can be shared ethically and legally if researchers employ:

- strategies of informed consent
- anonymisation
- controlling access to data

Informed consent: paradigm shift

- 1995 - Statement on Human Genomic Databases of the Human Genome Organization's Ethics Committee

- more broad and flexible interpretation of consent
- from the principle of respect for autonomy and self determination to the values of beneficence, solidarity, justice, reciprocity, mutuality, citizenry and universality

Knoppers BM, Chadwick R. Human genetic research: emerging trends in ethics. Nat Rev Genet 2005 Jan;6(1):75-9.

Broad consent

- At the time of data/samples collection, their future specific use may be described in very broad general terms, e.g. for cancer research, rare disease research or medical research.
- In broad consent, an individual gives consent to widely specified research, which allows for many future uses of tissue and data
- Broad time frame

Secondary use(s)

- Using data or samples in a way that differs from the original purpose

Broad consent: is it acceptable?

- Proper on-going ethical and legal oversight are in place (e.g. approval by a research ethics committees for new projects).
- There is a right to withdraw (?)
- There are mechanisms to update research participants on the use of their data/samples.

Different situations

- new research projects (biobanks and registries) for which the information sheets and consent templates can be created ex-novo
- Secondary uses of old data/collections obtained with / without informed consent, where data sharing is not addressed or even specifically excluded

Traditional elements for the informed consent of biobanks and regsitries

- General (name of the PI, Institution, funding, duration, oversight, contact persons)
- Aims, research uses of data (e.g cancer research, RD research)
- Voluntariness of participation and possibility to withdraw
- Procedures involved in participation, including interviews, blood taking, etc.
- kinds of samples and data that will be collected;
- Potential physical, psychological and social risks
- Potential benefits
- Description of the coding system
- Protections in place locally to ensure the confidentiality of data/samples
- Access to data/samples for research purposes: who will have access who should control and what the procedures in place (data access committee)
- Access to data/samples for purposes such as validation, quality control, etc.
- Study oversight
- Compensation/reimbursement
- Custodianship of data/samples
- Study dissemination

New elements for data sharing platforms

- Hosting of the data in an open access database
- Access by industry if foreseen
- Possible linkage to different data (registries, medical records, etc)
- Possibility of large scale genome sequencing techniques
- Possibility of data sharing across research groups and national borders
- Return of incidental findings
- Withdrawal procedures, such as sample retrieval and/or destruction
- Prospects for third-party commercialization and intellectual property procedures;

Withdrawal, anonymisation... still possible?

- Impossibility to retract the data once released
- Re-identification for the individual
- Genetic information is shared among a same family or group

Informed consent

- Donors should be informed that the confidentiality of their information will be protected through secure technology and strict coding measures, but that there is no guarantee of complete confidentiality due to the evolving variety of techniques and technology advances in genome and gene sequencing that may lead to the potential identification of the individual.

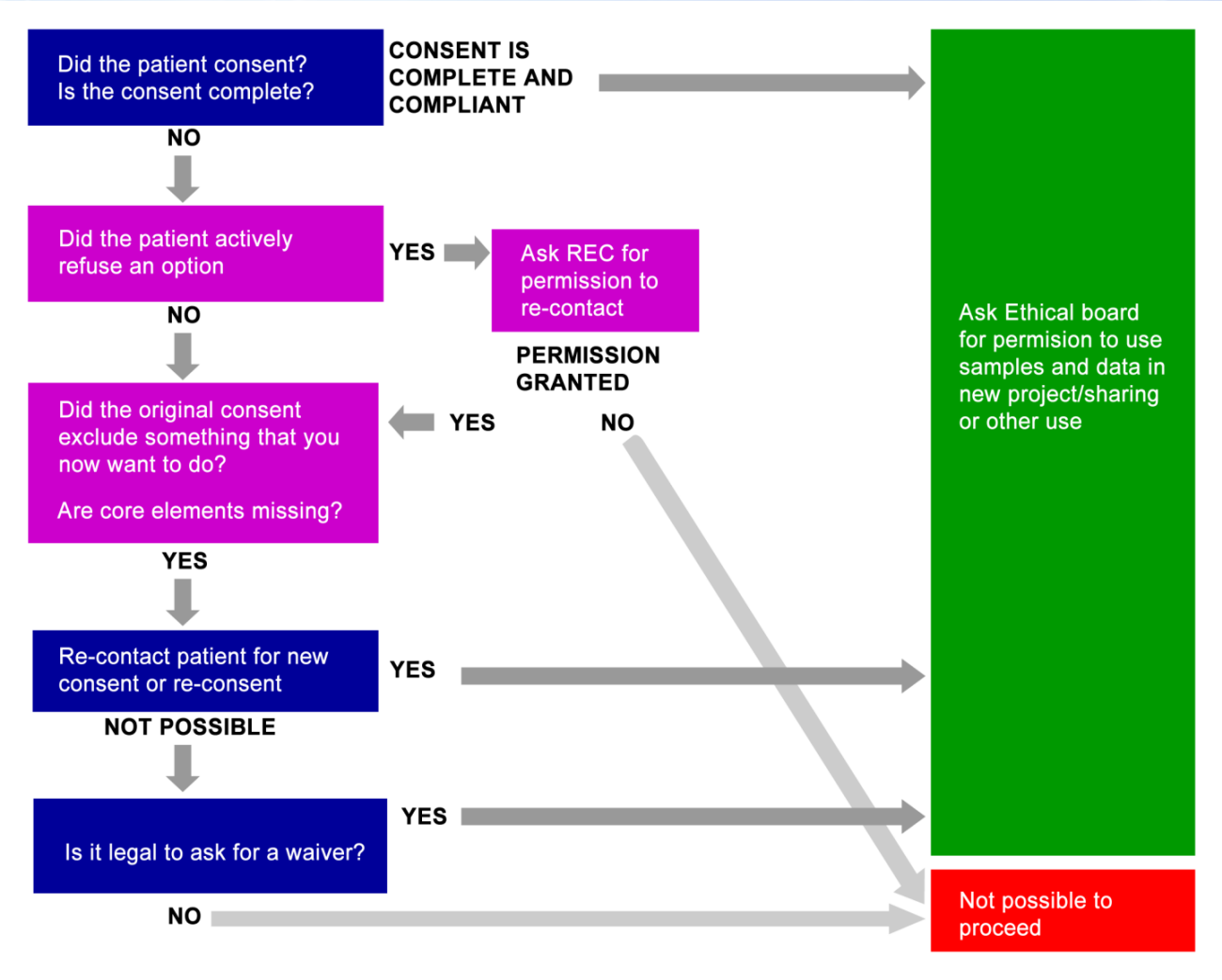
Data ownership, exchange and proprietary rights

- Free access to data for the benefit of science – public benefit
- Use of data for commercial gain

Informed consent in secondary use(s)

- re-contact and re-consent
- notification with opt-out schemes
- where re-contact of patients is unfeasible and disproportionate to benefits (very old collections) a waiver for re-consent can be granted by a research ethics committee/ethics review board.
- "moral endorsement" of patient organizations may be sought in order to ensure that the patient community agrees with certain uses of data

Informed consent in RD-Connect



Dynamic Consent

- Dynamic Consent is a new approach for engaging individuals about the use of their personal information. It is also an interactive personalised interface that allows participants to engage as much or as little as they choose and to alter their consent choices in real time.

Jane Kaye et al. Dynamic consent: a patient interface for twenty-first century research networks. European Journal of Human Genetics (2014), 1–6

What makes Dynamic Consent 'dynamic'?

- It allows the same samples/information to be (re)used with the knowledge and consent of the individual.
- It enables individuals to give and revoke consent to the use of their samples and information in response to their changing circumstances.
- It provides a record of all transactions and interactions in one place.
- It allows people to be approached for different kinds of consent or to obtain their opinions as new research projects are started and new ethical questions arise.
- Consent preferences can be modified over time.

Data access, custodianship and governance framework

- Good governance underpins a system of data sharing that depends on trust.
- Public trust is increasingly translated through broad consents, counterbalanced by both security systems and governance.

NIH Genomic Data Sharing (GDS)

Policy Oversight

NIH Data Access Committees and Chairs

NIH Data Access Committees (DACs) review and approve or disapprove all requests from the research community for access to datasets within the database of Genotypes and Phenotypes (dbGaP). Decisions to grant access are made based on whether the request conforms to the specifications within the GDS Policy and program specific requirements or procedures (if any). In particular, all data uses proposed for dbGaP data must be consistent with the data use limitations proscribed for the dataset by the submitting institution and identified on the public website for dbGaP. DACs also review and approve or disapprove all requests for access to dbGaP data for programmatic oversight by NIH employees.

DACs are composed of senior Federal employees with appropriate scientific, bioethics, and human subjects' research expertise. Members may be appointed for a specified term as defined by the convening Institute. Consultants with specific expertise may be invited to meetings or to provide written consultation. Consultants may be Federal or non-Federal employees, and are not voting members of the DAC. Timelines for responding to requests for access to dbGaP data will vary, but all NIH DACs will strive to provide decisions or feedback to requesting investigators in a timely manner.

European Genome-phenome Archive

EGA home | About | Studies | Datasets | Data access committees | Data providers | Submit to EGA | Co

Data Access Committees

For each dataset that requires access control, there is a corresponding Data Access Committee (DAC) who determine access permissions. Data access is not the responsibility of the EGA. The pages describing each DAC includes contact details or links to an external website, where you can find more information on how to request access. DAC details can also be found on each Dataset description page.

Total number of data access committees: 169
Displaying 1 - 169

- **Data Transfer Agreement (DTA)/Material Transfer Agreement (MTA): DTAs and MTAs should always be used to govern data/material transfer between parties.**
- DTAs and MTAs are legal contracts that help ensure that the parties signing the agreement will comply with a set of rules defined by the involved parties. These documents state the scope of the use of data or bio-specimens, the limits posed by the informed consent used for the original collection, special limitations, duration of sharing and use, and other special conditions including donors' expectations, etc.

Data access agreements

- Access agreements must be drafted clearly, so that researchers and their institutions are aware not only of their obligations, but also that “the border between acceptable and unacceptable conduct be clearly delineated and predictable.
- Explicit sanctions are important in order to respond effectively to any breach. These sanctions must be balanced—harsh enough to deter abuse by researchers and yet not to discourage access.

Building trust

- Trust needs to be relational, with contracts serving as a way to punctuate what has already been agreed to rather than the sum total of how a relationship will work.
- Trust is more common where people share core values and interests or are committed to a common cause.

Registry transition and/or termination

Is there a need for research ethics committee review?

- If the purpose of the registry is unchanged and no new data are being collected, IRB/EC review may not be required.
- REC approval may be required if new data will be collected through contact with patients, if the new data include identifiable personal information, or if the data will be used in a different manner than previously communicated to patients.

Will any changes be required in the informed consent process?

Re-consenting may be needed, ifthe registry transition will result in

- (1) longer followup than what was originally agreed
- (2) direct contact with patients to obtain new data,
- (3) collection of biological samples
- (4) use of data from deceased participants
- (5) linkage of the participant's data to other databases.

Other relevant cases

- Collection of biological samples
- National to international registries
- Data ownership and licensing
- Policies for data access

General Data Protection Regulation

Draft Report, released by the rapporteur for the LIBE committee, Jan Philipp Albrecht (Germany), whose position is clarified by the disconcerting justification that “Processing of sensitive data for historical, statistical and scientific research purposes is not as urgent or compelling as public health or social protection. Consequently, there is no need to introduce an exception which would put them on the same level as the other listed justifications.”(Justification to Amendment 27).

EUROPEAN·COMMISSION¶

MEMO¶

Strasbourg,·12·March·2014¶

Progress· on· EU· data· protection· reform· now· irreversible· following·European·Parliament·vote¶

http://www.epirare.eu/petition.html

orphanet Inserm

EPIRARE European Platform for Rare Disease Registries

EURORDIS Rare Diseases Europe

ESHG EUROPEAN SOCIETY OF HUMAN GENETICS

TREAT-NMD Neuromuscular Network

RD Connect

Genetic Alliance

STATEMENT ON THE EP REPORT ON

THE PROTECTION OF PERSONAL DATA

EURenOmics

II INTERNATI

Organise

Thank you for your attention!