Promoting the use of biobank resources: the challenges of exchanges and openness policies

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Biobanks: Introduction and Next Steps

Specific questions

- Is large scale biobanking and genome analysis methods modifying the picture of use and exchanges, from the point of view of ethics?
- Is ethics promoting or preventing sharing of bioresources and data?
- Is there an optimal model for sharing data?

Controversial and evolving ethical issues

- Informed consent - (withdrawal, secondary uses)
- Confidentiality - (degree of identifiability; selection/discrimination - issues in use of genetic testing)
- Sharing of data and results - (the right to know and not to know, general vs individual results, public release, incidental findings)

Cambon-Thomsen *et al.* Trends in ethical and legal frameworks for the use of human biobanks. Eur Respir J 2007 ; 30 : 373-382

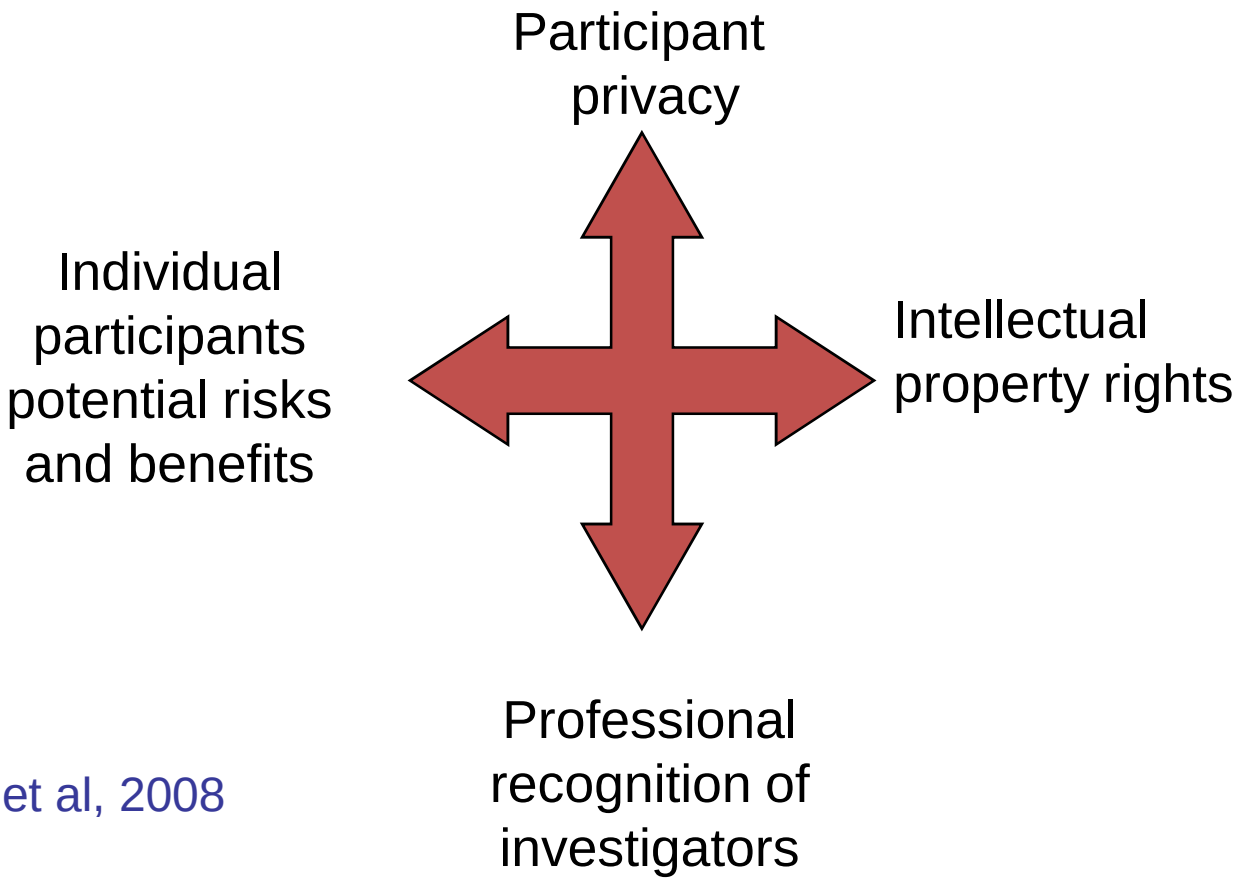
New developments, new issues

- Research developments bring new questions or challenge the existing frameworks
  - GWAS and Whole genome studies
    - Caulfield T et al. Research ethics recommendations for whole-genome research: consensus statement. PLoS Biol. 2008 Mar 25;6(3):e73.
  - Specific issues :
    - consent,
    - withdrawal from research,
    - return of research results,
    - sharing & public data release

Policy for “using” and “sharing” as a component of strategic plan for biobanking

- Human biobanks are set up to be used
- An assessment of this use is needed, based on defined criteria and quantitative indexes
- The optimization of this use is one of the challenges faced by institutions and biobank managers
- One way to achieve such optimization is through exchanges and sharing of samples & data, and networking activities
- Thus exchanging and sharing policies are central in a strategic plan for biobanking

Values in tension and policies for sharing samples and data



Rial-Sebbag et al, 2008

Who has a say on the use of biobanks ?

- Institutions setting up biobanks
- Governments and funders
- Patients and individuals whose samples and data are included in biobanks
- Researchers, clinicians and industrials using them
- The public
- Others

What are the blocking factors of the use of biobanks

- Technical ones (quality etc.)
- Institutional ones
  - No exchange, sharing or access policy
  - No practical help
  - Cost
- Intellectual property ones
- Information ones
  - No easily available information on content
  - Restricted use to pre-defined professional circles
- No obvious positive spin off : incentives?

What are the needs for assessing the use of biobanks ?

- For institutions: need to justify their use to
  - Patients
  - Funders
  - Users
- For researchers/practitioners: need of documented long term recognition of the effort of quality biobanking
- For individuals donating: need to be reassured that this is used, in reality
- For the public: need to be sure that the major investment is justified and has an impact at society level

The need for an explicit sample/data access policy

- Part of a governance model
- Transparency
- Value based, not opportunistic
- Adapted to the context and aims of the biobank:
  - No “one size fits all”
- Taking into account all stakeholders views:
  - Incentives needed to implement the policy
- Assessment of the use of biobanks organised, in accordance with the sharing policy

Different models of data access policy

- Strong restriction of access : who decides?
- Open access : question of pressure, quality?
- Sharing, collaboration : what incentives?

Evolution :

“My data, samples, families”….

“My very used collection”

“The collection I collaborated to…that is widely used”

Large scale pushes to collaboration; but what in society pushes to sharing? Is open access THE solution?

Issues in data access following large scale genetic studies: promoting data sharing and protecting individuals, contradictory requirements?

- GWAS are usually performed on a large number of cases and controls, using huge number of genetic markers thanks to technological platforms.
- The recently published Policy for Sharing of Data obtained in NIH supported Genome-Wide Association Studies (GWAS) has triggered a debate in the genetics research community and among other stakeholders.
- Notices posted on August 28, 2007 in the Federal Register (http://edocket.access.gpo.gov/2007/pdf/E7-17030.pdf).

NIH policy for GWAS data access when NIH funding

- Public funds use result in public data produced
- The proposed NIH policy relies on
  - a central repository,
  - A 12 months limited period of data embargo,
  - de-identified individual data made accessible to users
  - users declaration that they will protect personal data and to describe their protocol (no external committee approval).
- It is usually accepted that GWAS genotype data can never be completely de-identified, since genotypes are themselves identifiers.
- In such a context a number of conflicting interests must be carefully balanced
  - participant privacy
  - potential risks and benefits for individual participants
  - provision of methodological guidance for interpretation and use of data
  - professional recognition of investigators
  - intellectual property rights
  - characteristics of a centralized NIH or other kind of data repository

NIH GWAS data sharing policy challenged by scientific advances

- A research team, led by David W. Craig, Ph.D. at the Translational Genomics Research Institute (TGen) in Phoenix AZ, has developed *a new bioinformatics method that allows the detection of a single person's SNP profile in a mixture of 1,000 or more individual DNA samples*
- *Homer et al.,* PLoS Genet 2008 4(8): e1000167. doi:10.1371/journal.pgen.1000167 *:* "Resolving Individuals Contributing Trace Amounts of DNA to Highly Complex Mixtures Using High-Density SNP Genotyping Microarrays."
- In other words, bioinformatics techniques have progressed to the point that with enough genomic data on an individual from another source, it is now possible to determine whether that individual participated in a study by analyzing only the pooled summary data.

Adaptation

- This discovery, however, has important policy implications for the way the scientific community shares such pooled sets of genetic data.
- Because individual SNP profiles can now be detected within aggregate data, the NIH has moved quickly to assure continued protection of research participant privacy in genomics studies by controlling access to pooled datasets.
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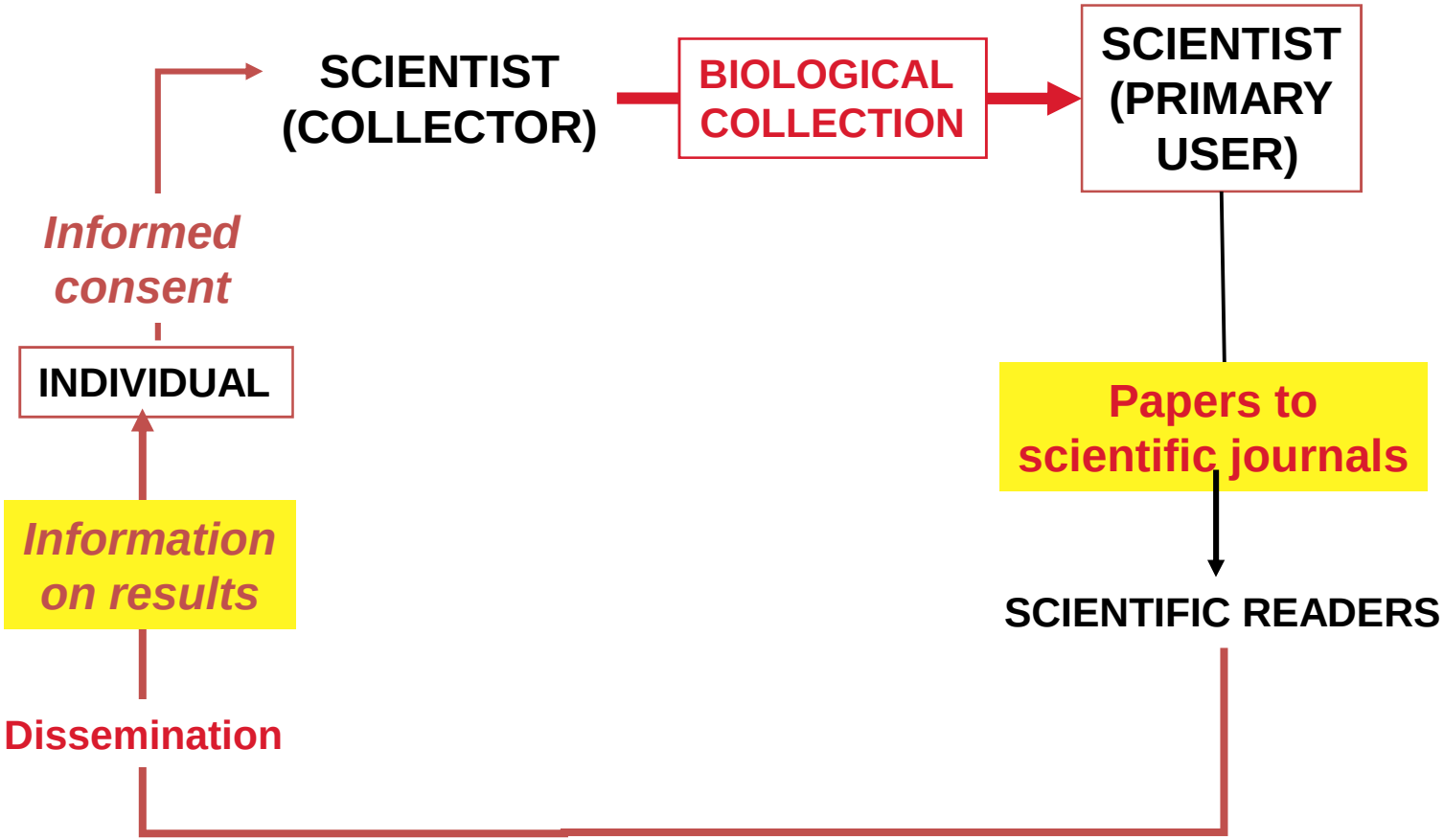
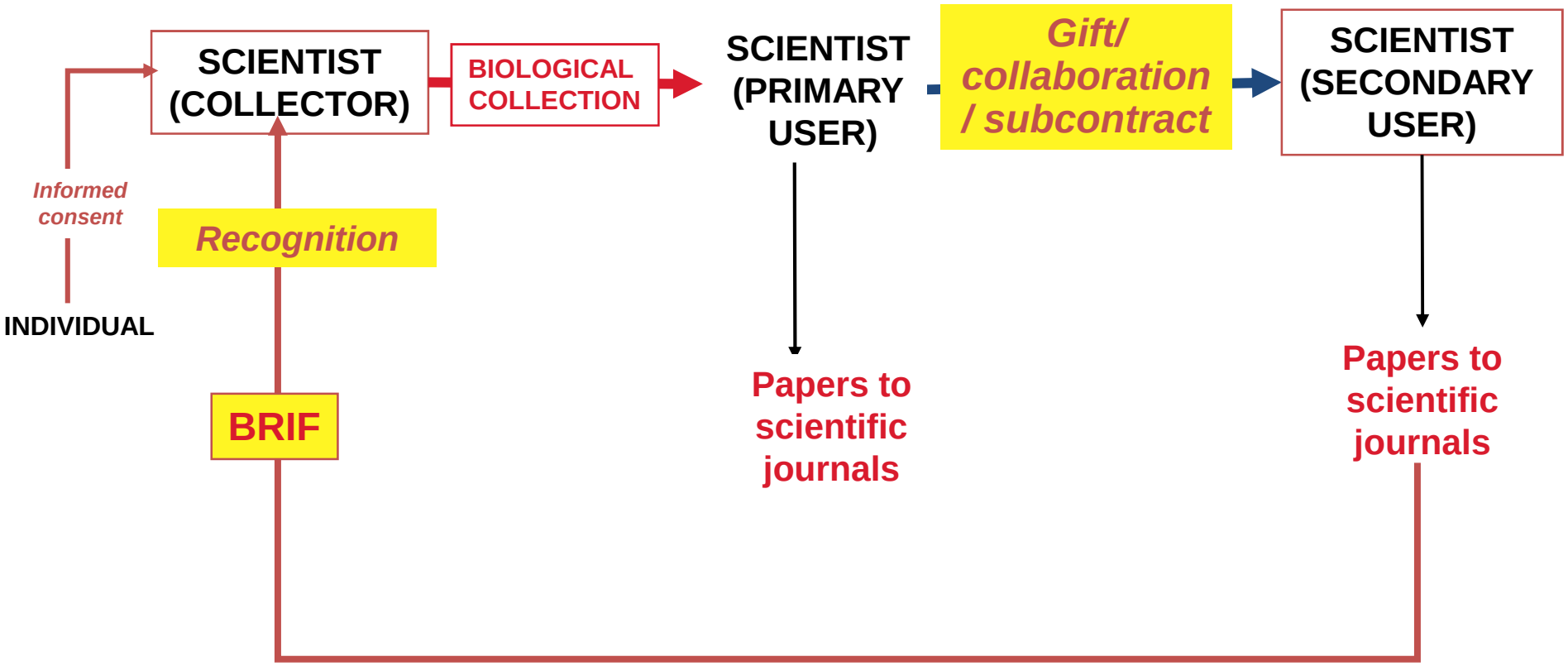
Examples of different levels of tools to promote use and exchange

- Indexes to measure impact in relation to use and exchange (BRIF)
- Unique identifyer to follow the life and uses of a collection (biobank) (Number)
- Web based tool to simplify access to legal provisions to exchange samples (HSERN)


SCIENTIST (COLLECTOR)
BIOLOGICAL COLLECTION
SCIENTIST (PRIMARY USER)
Informed consent
INDIVIDUAL
Papers to scientific journals
Information on results
SCIENTIFIC READERS
Dissemination



BRIF : Biological Resssource Impact Factor; Sharing models;

Cambon-Thomsen A, Nat Gen 2003; 34:25-6

Milanovic F et al. 2007, *Genomics, Soc. Policy*. 2007, 3, (1) 17–30

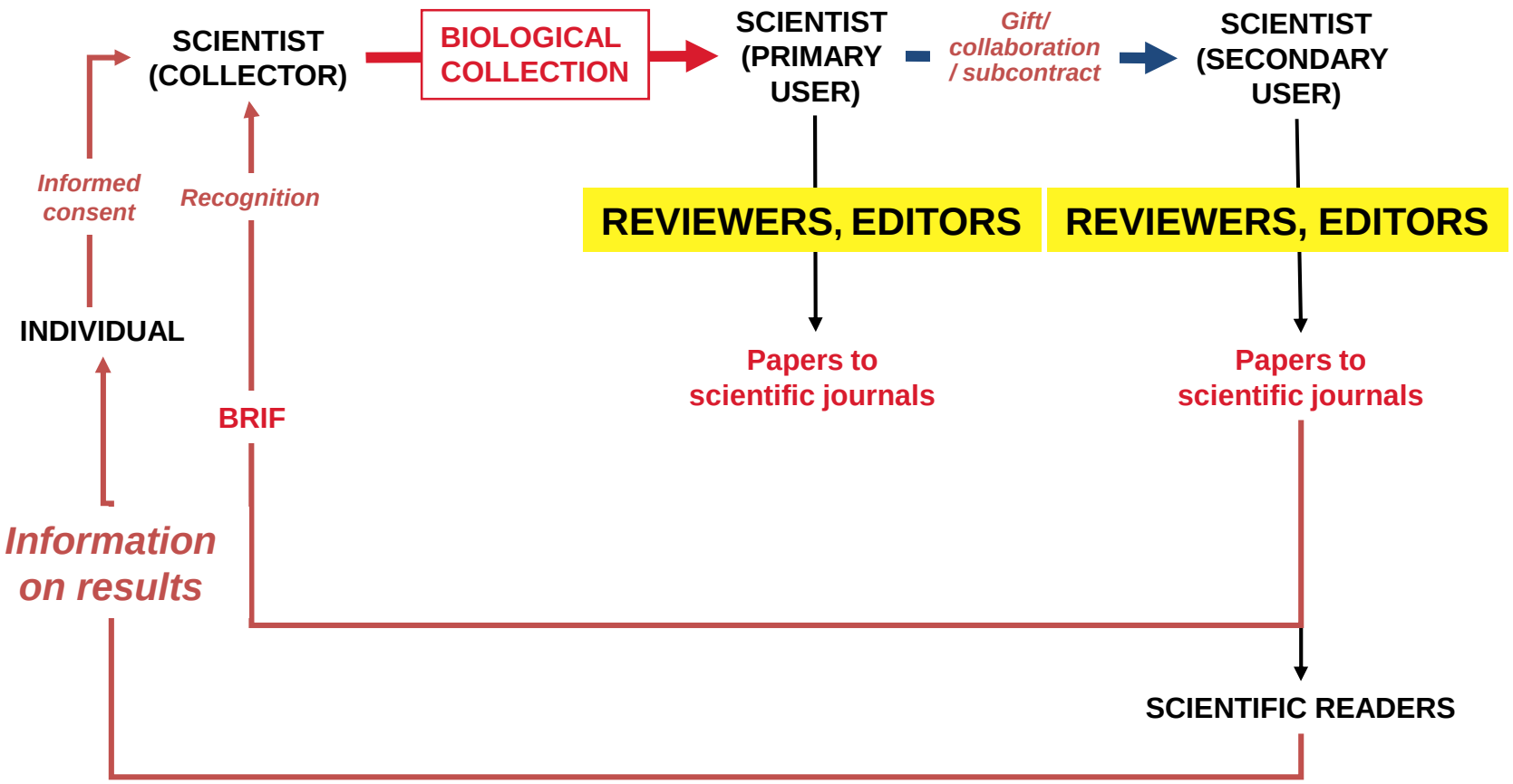
Assessing the use of biobanks

CAMBON-THOMSEN A, ***Nat Genet***, 2003, 34, (1): 25 - 26

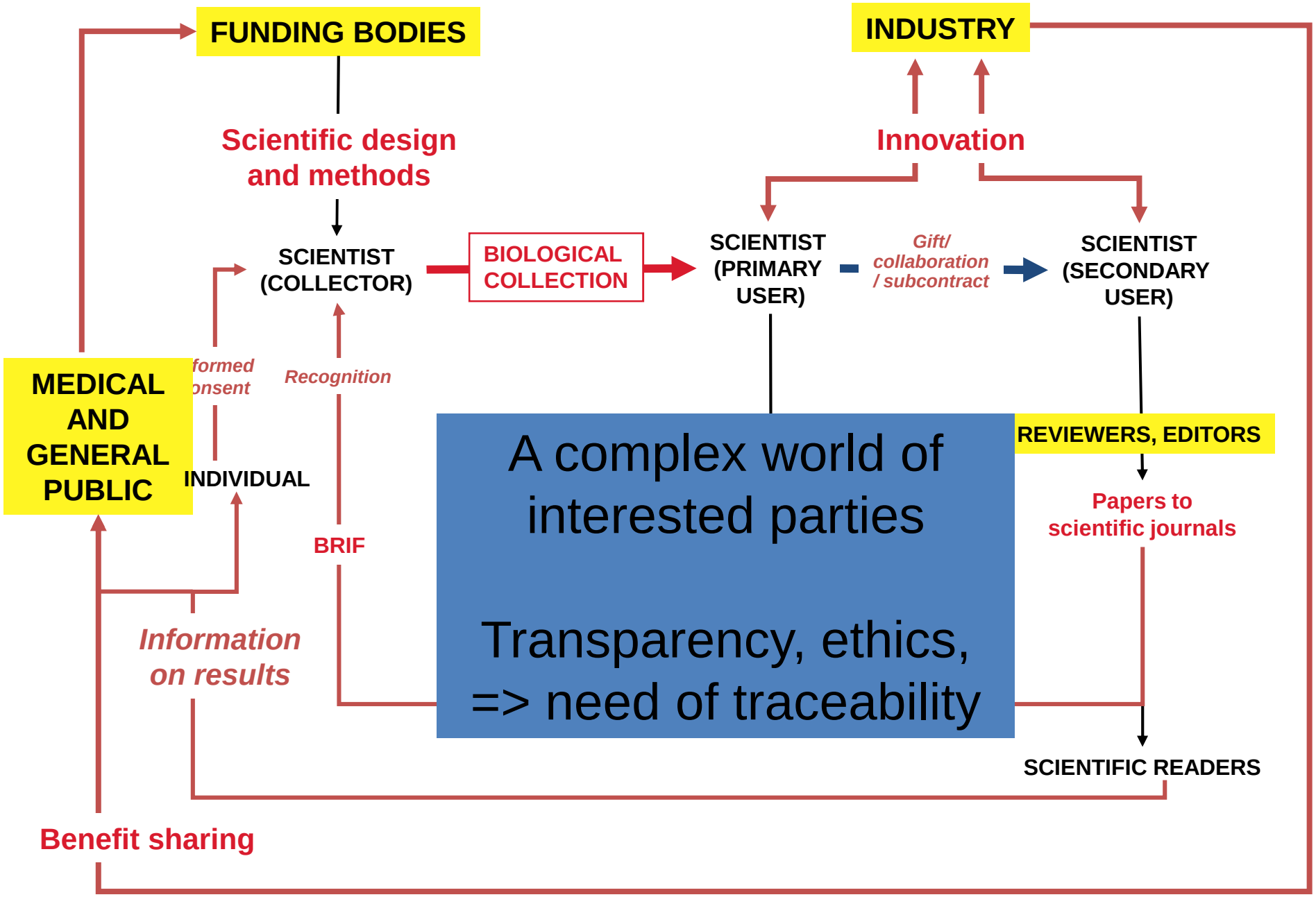
- BRIF : BioResource Impact Factor. Why?
  - Need of long term recognition
  - Need of sharing resources outside specialised circles
  - Need of connecting the use of biobanks with the results and impact on research
  - Need to find and justify resources for biobanking
  - Presently no quantitative parameter
- How?
  - Standardise way of citation of biobanks used, in publication
  - Tracking by ISI
  - Choose parameters very carefully

Assessing the use of biobanks: BRIF as a tool?

- Over time BRIF would become a more rational measure of the impact than « reputation »
- It would allow a longitudinal view on the use
- It could be a tool for monitoring the use of the biobanks
- It might become an incentive to increase use and sharing of bioresources
- A working group on BRIF to be set up ?

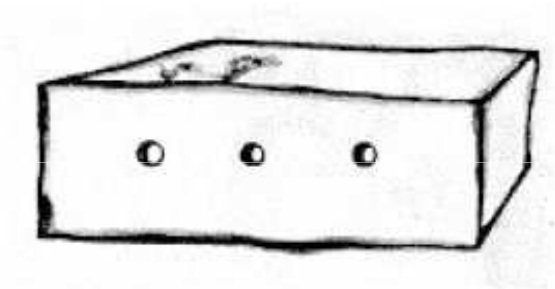


Microattribution: Nat Genet., 2008, M Axton
http://blogs.nature.com/ng/freeassociation/2008/03/microattribution_for_community_1.html


FUNDING BODIES
INDUSTRY
Scientific design and methods
Innovation
SCIENTIST (COLLECTOR)
BIOLOGICAL COLLECTION
SCIENTIST (PRIMARY USER)
Gift/ collaboration / subcontract
SCIENTIST (SECONDARY USER)
MEDICAL AND GENERAL PUBLIC
formed onsent
Recognition
INDIVIDUAL
BRIF
A complex world of interested parties
Transparency, ethics, => need of traceability
REVIEWERS, EDITORS
Papers to scientific journals
Information on results
SCIENTIFIC READERS
Benefit sharing

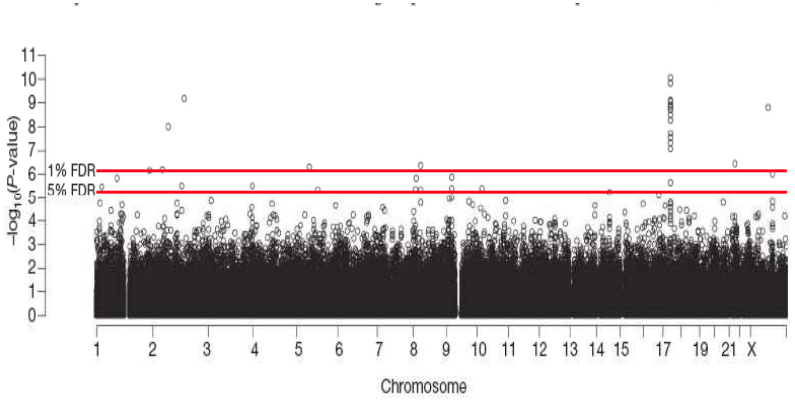
Googling

- ISBN 2070408507



Le Petit Prince
A de Saint Exupéry
Gallimard

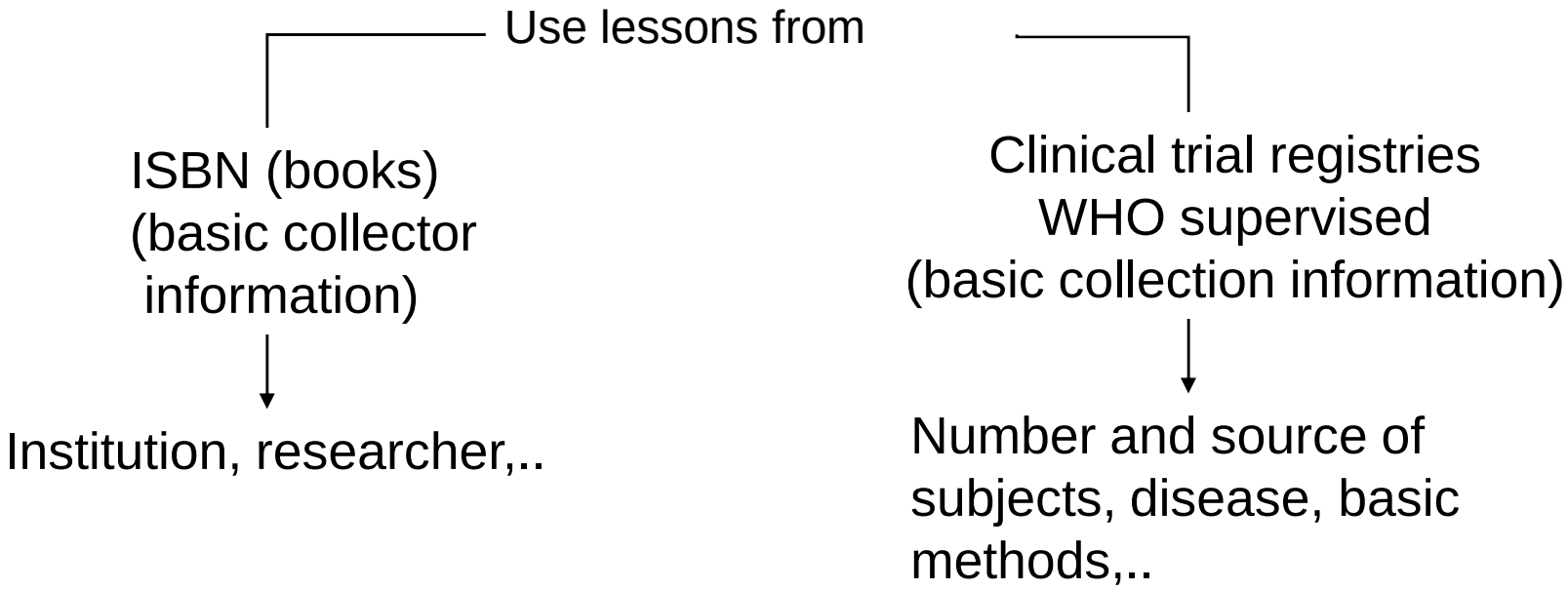
- PMID: 17611496



Moffatt MF *et al.*
Nature 2007; 448:470-3

=> But no identifier for biobanks

Tracing all collections with a universal identifier



Then put that identifier on all products of the collections, such as methods descriptions, published papers, web site, etc.. => transparency and access to all parties.

Lots of other works on « unique identifyers » especially among bioinformaticians

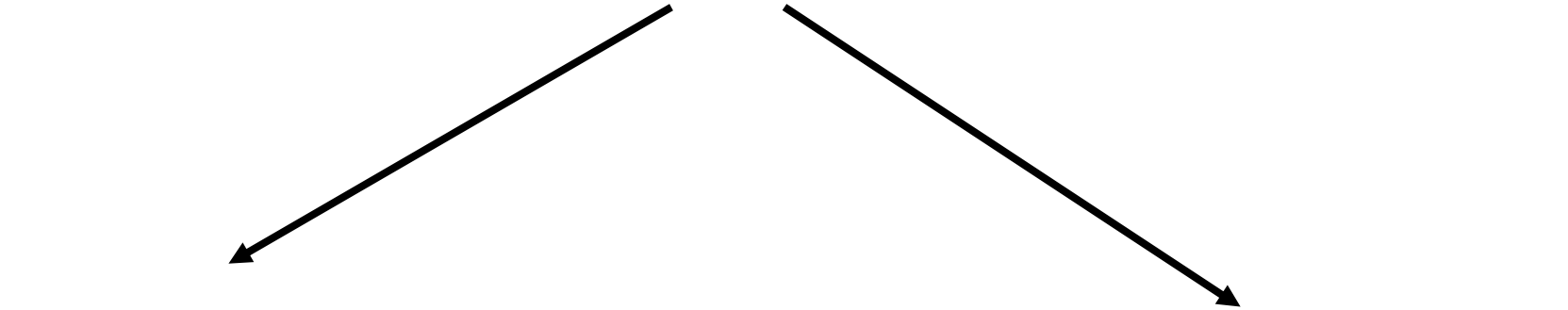
Kauffmann F, Cambon-Thomsen A.
Tracing biological collections: between books and clinical trials.
JAMA 2008 ;299:2316-8.

But some other kind of tools

- To promote the actual sharing and exchange
- A tool to help researchers in regulatory issues regarding importing/exporting human biological samples

Why such a tool?

- New methodologies in Genetic Research Using Biobanks



More samples are needed

Increase exchange of samples cross-borders

Lack of researchers' knowledge concerning legal provisions

Human Samples Exchange Regulation Navigator (hSERN)

- Allows addressing practically a series of relevant requests, for different countries, on the issue of regulatory aspects of exchanging human biological samples across borders.
- This tool is under construction and validation steps (not yet publicly open)
- It will permit every registered person to get information on theoretical as well practical legal aspects, for exchanges of human biological samples for research purposes.

METHODOLOGY (1)

- IDENTIFY FREQUENT QUESTIONS POSED BY RESEARCHERS:
- “I am in country A, want to send samples xxx to country B for use yyyy : what do I (and my collaborator in country B) have to do to respect legal/regulatory provisions?
- Practical aspects of import/export addressed by researchers
  - Documents to be produced?
  - What kind of forms?
  - To which authority?
  - Consent form issue?

METHODOLOGY (2)

- IDENTIFICATION OF THE LEGAL RELEVANT TEXTS IN THE COUNTRIES
  - Ga2len project partners, as a start
  - Proof of concept with 2 countries (France and UK) to be extended to 2 others (Poland and Spain)
  - Research made by jurists from the Genetic and Society Platform
- IDENTIFICATION OF LEGAL EXPERTS
  - To validate the information

METHODOLOGY (3)

- Competencies needed
  - Lawyers, interested not only in theoretical legal aspects but understanding the issue at stake from the researcher point of view and being tool oriented
  - Strong collaboration with computer scientist
    - To construct the data base
    - To design the website
    - To organise the queries : “researcher friendly”
    - To make the updating of the database “lawyer friendly”

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Sample Exchange Regulation Navigator

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Welcome on SERN,

SERN permits every registered person to get informations on the legal aspects, as well theoretical as practical, for exchanges of biological samples for research purposes. The knowledge base is developed in a structured way starting with France and UK, then extending to other countries partners of GA²LEN, starting with Spain and Poland. This updated Database is constituted to fill out the tool with international and national legal instruments related to such issue. Furthermore, after having selected your country of departure and your country of arrival for your exchanges of biological samples, four categories of informations are available:

- Overview: provides a general comment related to the selected countries on such issue.
- Theory: provides an easy access to different legal notions and an access to the implemented legal texts.
- Practice: provides an access to the legal or administrative forms and to the actions to undertake.
- Problems: makes available a questioning on related problems and found articles which are relevant.

N.B: The three last categories, Theory, Practice and Problems, are organized in the same manner: the legal notions are dealt in the same order.

SERN's latest news

▶ News 1

GA²LEN (Global Allergy and Asthma European Network), is a consortium of

Navigator

From France To France Submit

France
Poland
Spain
United Kingdom

Search o

Keywords Search Advanced search

What is GA²LEN ?

GA²LEN (Global Allergy and Asthma European Network), is a consortium of leading European research centers addressing the growing public health concern of allergic disease. This project was funded by the European Union under the 6th framework programme and started on February the 1st, 2004 for 60 months. The workpackage 2.9 "Genetics, genomics and post-genomics", led by Francine Kaufmann from the "French National Institute of Medical Research and Public Health" INSERM, focuses on methodological and organizational aspects to favour collaborations between researchers.

A general lack of knowledge regarding the legal aspects of biological samples' exchange for research was noticed: very few partners were using material transfer agreement forms when shipping biological samples in another laboratory/country. Several researchers could be out of law when they exchange samples because they are not aware of the legal aspects of such issue. Indeed, the legal frameworks are very variable within Europe.

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Sample Exchange Regulation Navigator

SEND SAMPLE FROM **FRANCE** TO **UNITED KINGDOM** :

FROM FRANCE :

- **Overview**
- **Theory**
- **Practice**
- **Problems**

TO UNITED KINGDOM :

- **Overview**
- **Theory**
- **Practice**
- **Problems**

FROM FRANCE :

OVERVIEW

France has a specific framework to organise import/export of human biological samples for research. It consists of law and other regulations. They indicate the French agency delivering an authorisation and the different requirements to be fulfilled.

THEORY

To exchange tissues, cells and their elements including DNA (except stem cells of foetal or embryonic origin)

Challenges

- Access to the legal information in other countries
  - Extend
  - Validate
  - Update
- Technical
  - Adapted to researcher views for the queries
  - Adapted to lawyers views and way of working for data base updating
  - Legal Language to be implemented in the tool
- Extend to data exchange

Overview

- Ethics as a major player in biobanking strategy
- Sharing policy central to it
- Different models exist at national and international level for their regulation
- Some international trends towards consensus
- Focus on tools and monitoring aspects of the use of biobanks
- Biobanks as a central focus for research and for therapeutic applications in public health context.

Conclusion : Ethics concern all parties

- Ethical research means research with good data, samples and power => collaborations
- Do not be naive about consequences of work => safeguards
- Be open to share data, explicit roles, recognize the input of all parties in research (data collector, phenotyper, environmentalist, genotyper, statistics specialist, writer and ethics gate keeper...)
- Accept to participate on research on the ethical aspects of practice at all levels

=> Need of interdisciplinary teams

A multidisciplinary team on Genomics, health and society

A number of members involved in biobank/genetic research related issues

Equipe: “Génomique et santé publique”
Inserm U 558:
Epidémiologie et analyses en santé publique
Faculté de médecine, 37 allées Jules Guesde, Toulouse

A societal platform in the Genopole Toulouse

Responsable : Anne Cambon-Thomsen, cambon@cict.fr
Contact : Emmanuelle Rial-Sebbag, rialseb@cict.fr

BBMRI
Biobanking and Biomolecular Resources Research Infrastructure

WWW. BBMRI.eu

GEN2PHEN

PROMOTING HARMONISATION OF PHOEBE EPIDEMIOLOGICAL

GA²LEN
Global Allergy and Asthma European Network
Network of Excellence

Collaboration with

GenPoS
www.genpos.org

Bilateral programme France UK: ALLIANCE

geno toul

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Université Paul Sabatier
TOULOUSE III

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Some relevant publications from the speaker's team

- Cambon-Thomsen et al. Mapping genetic epidemiology designs and ethics (In preparation)
- *Kauffmann F & Cambon-Thomsen A.JAMA*, 2008;299(19): 2316-8
- *Ria-Sebbag E. Rev Générale Droit Médical*, 2008, 27, 63-73
- *Milanovic et al. Genomics, Soc. Policy*. 2007, 3, (1) 17–30 on line
- *Cambon-Thomsen A et al. Eur Respir J.* 2007; 30: 373-382
- *Ducournau P* New Genet Soc, 2007; 26, 1, 105-115
- *Ria-Sebbag E Médecine/Sciences, 2006, vol 22.. 8-14*
- *Cambon-Thomsen A et al. GenEdit 2005; 3(1):1-13* (on line)
- *Cambon-Thomsen A Nat Rev Genet, 2004, 5, 866-873*
- *Cambon-Thomsen A Nat Genet, 2003,* 34, (1): 25 - 26
- *Cambon-Thomsen A Obs. Génét, 2003, N°10, (on line)*
- *Cambon-Thomsen A et al.* Comp. Funct Genomics, 2003 *4 : 628-34*