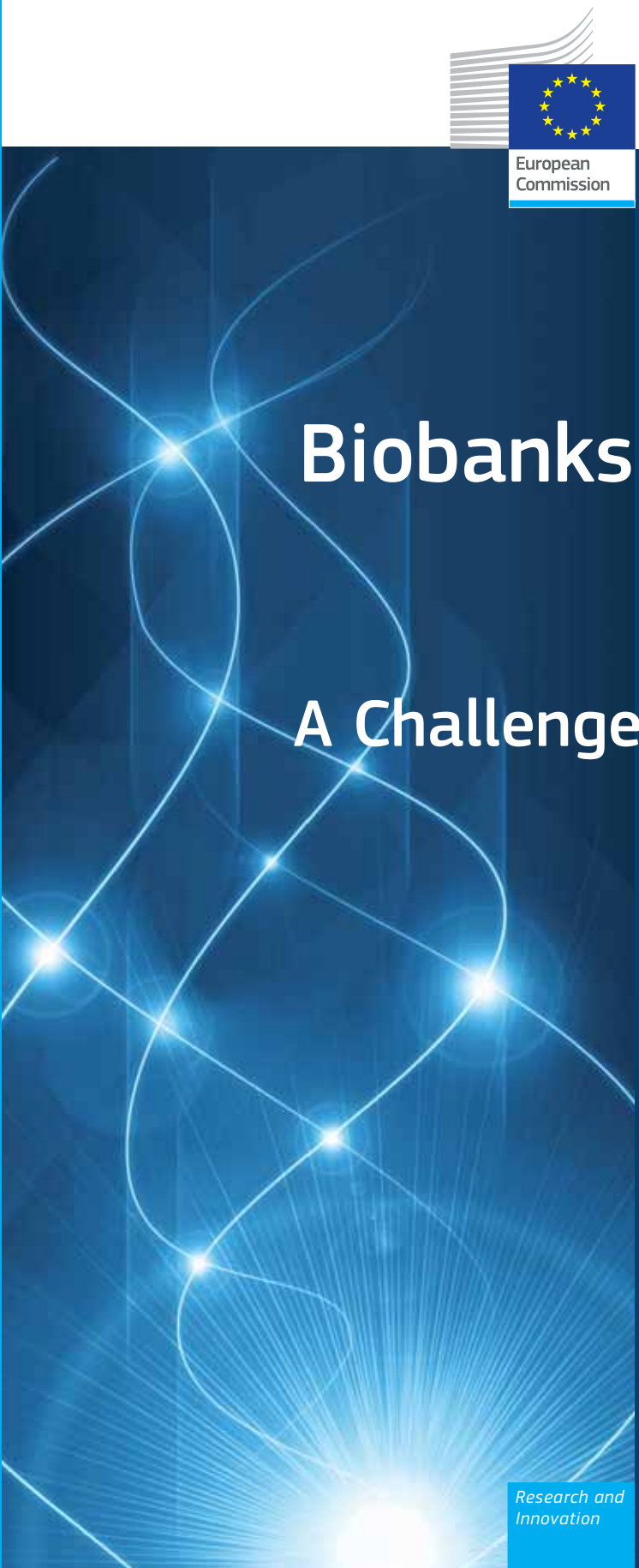

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Biobanks for Europe

A Challenge for Governance

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EUROPEAN COMMISSION

Biobanks for Europe

A challenge for governance

Report of the Expert Group on Dealing with Ethical and Regulatory Challenges of International Biobank Research

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Executive summary

The member states of the European Union are world leaders in the development of biobanking infrastructure to support research, making huge investments each year to support such initiatives. Biobanks collect biological samples and associated data for medical-scientific research and diagnostic purposes and organise these in a systematic way for use by others. The vision within Europe is to link biobanks together as part of a pan-European infrastructure to support medical research and health care. The long-term growth of the medical field of the life sciences within Europe will depend and be accelerated by this investment, which has the potential to lead to innovation in medical research, drug development and health care delivery. However, the governance framework for biobanking needs to be strengthened to adequately support this new infrastructure development.

A known challenge in this field is that the implementation of relevant ethical guidelines and legal instruments, such as the EU Data Protection Directive (Directive 95/46/EC), differs significantly from country to country, which impedes international collaboration and exchange of information. As an action under the 2011 Science in Society Work Programme of the Seventh Framework Programme (FP7), an interdisciplinary expert group was established to reflect on the ethical and regulatory challenges of international biobank research, and to identify options for addressing these challenges. This report presents the outcomes of the expert group's reflection.

Chapter 1 introduces biobanks. Over the past decade the scale of biobanking activities, both in terms of the quantity of samples and data, as well as the range of disease areas and institutions involved in biobanking have increased considerably. Furthermore, biobanks are embedded in complex networks of research collaborations that span regions, countries and the globe. However, most Europeans have never heard about biobanks, and the legal and regulatory frameworks that apply to this area are fragmented.

Chapter 2 explains the umbrella term 'governance' and how it can be distinguished from regulation which in contrast only applies to the laws and formal oversight bodies provided by the state. In the biobanking field, governance consists of both formal and informal oversight mechanisms. Therefore, both formally-constituted regulatory bodies, statutes and other legal instruments, as well as informal mechanisms such as advisory boards, professional guidance, biobank policies and professional values and culture help to guide decision-making, compliance and policy development in this field.

Chapter 3 presents an overview of the developments in the science of biobanking. It points out that contemporary medicine is moving from "reactive approaches" centered on disease therapy to personalized, predictive, preventive and participatory medicine ("P4 Medicine") which focuses on the maintenance of health. This transition is fostered by advances derived from sequencing of the human genome and rapid improvements in bioinformatics and analytical laboratory technologies. Biobanks have the potential to become important tools and instruments for helping to drive this change in healthcare delivery.

Chapter 4 continues with a description of some of the main international biobanking activities in Europe, with as one of the main initiatives being the 'Biobanking and Biomolecular Resources Research Infrastructure' (BBMRI). Biobanking in Europe faces a number of other important challenges, with regard to informatics, cross-border exchange of samples and (security of) data transfers, as well as to secure the long-term financial sustainability of biobanks.

Chapter 5 reviews public perceptions of biobanks in Europe. Drawing on the findings of the Eurobarometer survey, it shows there is a lack of public awareness about biobanks and that many citizens appear to be reluctant to participate in biobank research, let alone give broad consent for the use of their samples and data in biobank research. Furthermore, citizens are concerned that biobank research eventually might turn against them, through the violation of their privacy rights or by being disadvantageous to them in other ways (e.g. profiling with regard to insurance and employment). It concludes that public trust, to be achieved through transparent governance and public engagement, is key to the long-term success of biobank research in Europe.

Chapter 6 gives an overview of the regulation of biobanks in Europe. There is a diversity of legal requirements for biobanking activities across Europe but also at national levels, as there is no one binding instrument that applies specifically to biobanks. The chapter reviews the key relevant international legal instruments and guidance, such as the 1997 Council of Europe Oviedo Convention and the EU Clinical Trials Directive and the Data Protection Directive. It furthermore discusses national law and points out that the different approaches reflect different national styles in addressing regulatory challenges, and that there is no 'one size that fits all'. This complexity could, however, put researchers at risk of operating unlawfully if they share research data and samples across borders where different laws are in force – and they do not exercise due diligence. The chapter also describes the role of the main bodies responsible for oversight of biobanks: research ethics committees and data protection authorities. It argues that better coordination and collaboration between these national oversight bodies would help mitigate concerns about differences in opinions between national bodies.

Chapter 7 describes the main challenges for the governance of biobanks, involving oversight, privacy and data protection, informed consent and public engagement and makes the following recommendations:

Recommendation 1: Member states and European institutions should develop a consistent and coherent legal framework for biobanking that should protect participants' fundamental rights, in particular in the areas of privacy, data protection and the use of human tissue in research.

Recommendation 2: There should be better coordination and collaboration between national oversight bodies (e.g. data protection authorities and ethics committees) as well as mutual recognition of decision-making to eliminate unnecessary duplication of oversight and compliance requirements, with training to support this.

Recommendation 3: For European biobanks to operate successfully there need to be sustainable governance mechanisms to involve and engage the public, and in doing so ensure their continual participation, trust and support.

Recommendation 4: Sustainable governance mechanisms for creating a relationship of reciprocity between biobanks and European society need to be encouraged so that Europeans can understand and obtain the benefits from biobank research.

Chapter 8 looks into new governance mechanisms that have been proposed in response to the governance challenges. It discusses the option of linking a dedicated advisory body to a biobank and furthermore discussed some specific initiatives currently being undertaken. For example, on the European level, the European Research Infrastructure Consortium (ERIC) allows biobank research activities to be undertaken under a common legal structure, as to ensure that a biobank research infrastructure is in conformity with all relevant regulation. On the national level, the 'CuraRata' model, implemented in the Netherlands, aims to better embed biobank research within the healthcare infrastructure. Furthermore, it points to new ways of protection privacy and data with new ICT technology that enables data analysis without individual-level data being transferred abroad (DataSHIELD). Finally, it discusses recent experiences with patient involvement in biobank research, for example via stakeholder forums, and what principles should underpin such involvement. This review of new governance mechanisms brings the group to another five recommendations:

Recommendation 5: The new governance bodies that have emerged specifically for biobanks should be integrated into the existing governance system to help to develop a meta-governance system for biobanking within Europe.

Recommendation 6: To ensure their sustainability, biobanks need to become embedded in the public healthcare structure as valuable resources that can be used for clinical care, personalized medicine and translational research.

Recommendation 7: Greater investment should be made in the development of e-governance tools to embed "ELSI by design" solutions, which can be used to augment existing governance structures and facilitate the sharing of samples and information between biobanks and researchers at a meta-level.

Recommendation 8: The potential to use web 2.0 technologies to involve patients, research participants and the wider public, in the governance of biobanks should be supported to ensure that Europeans can have trust in biobank research and those organizations that establish and maintain biobanks.

Recommendation 9: New accreditation systems need to be developed to reward and acknowledge the effort of scientists who establish and build biobanks.

In conclusion, chapter 9 summarises the main conclusion and lists all the recommendations made in the report.

1• Introduction

Biobanks collect biological samples and associated data for medical-scientific research and diagnostic purposes and organise these in a systematic way for use by others. The collection of samples and data for research purposes has a long history in the educational and medical systems. In the past, biorepositories were relatively uncontroversial, residing largely in the seclusion of pathology institutes. With recent technological advances, the potential to open up these existing collections for new uses is starting to be realized, but also new biobanks are being established. Innovations in information technology enable the systematic collection, linkage and tracking of samples and data but also provide the tools for analysis across vast sample and datasets. What distinguishes the present from the past is that the general scientific context has changed, and the scale of biobanking activities, both in terms of the quantity of samples and data, as well as the range of disease areas and institutions now involved in biobanking have increased considerably.[1] The other significant change is that these collections are being configured so that they can be used as a resource for the whole scientific community.

Advances in bioinformatics and computing technology have enabled scientific research to be organised and carried out in new ways. Scientific practice 'has become increasingly interdisciplinary, with the rapid formation of flexible and dynamic research collaborations around the world'.[2] Research projects are frequently global in nature, involving teams with different types of expertise, such as clinicians, laboratory staff and researchers, bioinformaticians, statisticians and other data analysts. Biobanks are embedded in these complex networks of research collaborations that span regions, countries and the globe. As a result there are many different types of biobanks that have been built for a range of different purposes and reasons[3]. The longer term vision for biobanks within Europe is to facilitate the linkage of different biobanks as part of a meta-level infrastructure across Europe. The expected impacts on medical research, drug development and health care for Europe are anticipated to be significant as such infrastructure will enable new scientific questions to be rapidly addressed with increasing efficiency.

But there is a problem with biobanks in Europe: Most Europeans have never heard about biobanks, and many citizens appear to be reluctant to participate in biobank research, either as donors to biobanks or as participants in cohort studies. At the same time, there are concerns among European citizens that eventually biobank research might turn against them, through the violation of their privacy rights or by being disadvantageous to them in terms of insurance and employment discrimination. In addition, the legal and regulatory frameworks that apply to this area are fragmented, with variation of practice across different areas of medical research. Biobanks test our regulatory

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1 Knoppers B.M., Zawati, M.H., Kirby E.S. Sampling Populations of Humans Across the World: ELSI Issues *Annu. Rev. Genomics Hum. Genet.* 2012. 13:1.1–1.19

2 Kaye J, Heeney C, Hawkins N, de Vries J, Boddington P. Data sharing in genomics – re-shaping scientific practice'. *Nat. Rev. Gene.* 2009. Vol. 10, pp. 331-335

3 Gottweis H, Petersen A. Biobanks: Governance in Comparative Perspective. 2008 London and New York, Routledge.

frameworks and the principles for medical research but also raise a number of complex issues for society[4]. Thus, we hold that the development of biobank research in Europe is not only a matter of scientific excellence, financial investments and the build-up of much needed infrastructures, but also, and in particular, a matter of developing robust biobank governance.

We will argue that the development of an appropriate system of biobank governance has made substantial progress over the last decade, but that the further shaping of a coherent and comprehensive approach towards biobank governance within Europe still is a pressing need. An essential element of this governance approach is to involve and engage European citizens in biobank development, and to communicate about biobank research openly and transparently. The central goal of biobank governance must be to enable European citizens to benefit from the rapid progress in biobank research, while at the same time protecting them from possibly adverse impacts of this line of research. An effective governance system must also address and be tailored to the new challenges that building a biobank infrastructure present. The main benefit of establishing appropriate and comprehensive mechanisms for biobank governance will be to create trust in biobanking, without which biobanks in Europe cannot further develop.

This report will document the rapid transformations that are occurring in the scientific context and the implications this has for biobanking, as well as recent findings about European citizens' attitudes to biobanking. It will provide a picture of the complex regulatory framework that applies to biobanking within Europe. It will go on to describe the specific governance challenges that biobanking has presented for European medical research governance. Finally it will report on some of the innovations that have been developed in biobanking governance and make a number of recommendations on the issues that need to be addressed if we are to develop an infrastructure to support European medical research as the 21st century progresses.

4 Rial-Sebbag E, Cambon-Thomsen A. The Emergence of Biobanks in the Legal Landscape: Towards a New Model of Governance, *J. of Law and Soc.* 2012. Vol 39, No 1, pp. 113–130

2• What is Governance?

The term 'governance' is understood in different ways and there are many definitions of this concept, depending upon the context in which it is used. Governance in its broadest sense can be described as 'the intentional activity of attempting to control, order or influence the behaviour of others'[5]. Governance and regulation are terms that are often used to cover and explain the same activities. The scope of activities that they cover can be narrowly or broadly defined. For the purposes of this report, we have defined regulation as being narrower in scope than governance and applying just to the formal structures of law and legally constituted regulatory bodies. 'Governance' in contrast to regulation, is an overarching concept that includes regulation but also less formally constructed mechanisms that dictate behavioural norms. In the biobanking field, governance can consist of formally-constituted regulatory bodies, statute and other legal instruments, as well as informal mechanisms such as advisory boards, professional guidance, biobank policies and professional values and culture that help to guide decision-making. The component elements of governance are therefore people (individual decision-makers as well as institutions), procedures, policies and everyday practice.

BOX 1 The difference between governance and regulation

Definitions of 'regulation' and 'governance' vary depending upon the field that is being discussed. In the field of biobanking, Kaye et.al have defined and articulated the differences between these terms. They define governance as being '[a] multifaceted compound situation of institutions, systems, structures, processes, procedures, practices, relationships and leadership behaviour in the exercise of social, political, economic, and managerial/administrative authority in the running of public or private affairs.' This encapsulates laws and government institutions as well as the professional culture and guidelines that guide biobanking practice that are not necessarily written down but become 'the way we do things'. In contrast, regulation can be seen as being narrower in scope, applying just to the formal structures of law and legally-constituted regulatory bodies that play a role in regulating biomedical research[6].

5 Black J. Critical reflections on regulation *Aus. J. of Leg Philos.* 2000. Vol. 21, pp. 1–35.

6 Kaye J, Gibbons SM, Heeney C, Parker M, Smart A. Governing Biobanks – Understanding the Interplay between Law and Practice; Hart 2012.

The benefit of a relevant and appropriate governance system in tune with social expectations is that:

> 'it promotes certainty and efficiency as people know what the rules are, what happens, and when. It can ensure uniformity and equality—that things are done in a uniform way with everyone and the same issues being treated the same. Such a system enables problems to be anticipated as there are mechanisms to deal with the routine issues but unanticipated situations can also be resolved efficiently. Having a governance system in place ensures that ethical and lawful research is supported through accountable and transparent decision making. This not only protects the integrity of the research community but also has the effect of promoting public confidence and trust.'[7]

Governance structures and mechanisms are built up over time and each successive innovation can test, alter and refine the governance mechanisms at play in a given situation. This can challenge existing governance systems and the principles and practices that they are based on. This can sometimes result in inappropriate 'legacy' governance systems being applied to new types of research. Sometimes, innovations in scientific practice can be accommodated within existing governance structures without the need for considerable reform. However, this is not always the case and there may need to be an evaluation of existing governance systems to see how they should be modified, adapted or improved to accommodate new scientific practice. In chapter 7 and 8, we will review the governance challenges for biobanking and the innovations that have been developed to improve governance in the field of biobanking.

7 Kaye J. From single biobanks to international networks: developing e-governance. *Hum. Genet.* 2011. Vol. 130, No. 3, pp. 377-382.

3• The Science of Biobanking

Contemporary medicine is moving from "reactive approaches" centered on disease therapy to personalized, predictive, preventive and participatory medicine ("P4 Medicine") which focuses on the maintenance of health[8,9]. This transition is fostered by advances derived from sequencing of the human genome and rapid improvements in bioinformatics and analytical laboratory technologies[8,10]. Biobanks have the potential to become important tools and instruments for helping to drive this change in healthcare delivery.

Given the immense complexity of human biology, medical research has traditionally been utilizing a so called "reductionist strategy" [9,11]. This strategy, used in current medical research and practice, is based on the assumption that itemization of complex biological phenomena into smaller "research issues" makes them more easily amenable to our current technical possibilities and to human reason/logic-based examinations[7,10]. Although this research strategy has been very successful, it is now reaching its intangible limits. With few exceptions, it is becoming evident that complex diseases cannot be ascribed to disturbances of individual biological entities, e.g. merely mutated genes[9,11,12].

In order to address the substantial complexities of biology and medicine, interdisciplinary fields of systems biology/systems medicine have been established. In these young scientific disciplines interactions of individual biological elements are studied by advanced mathematical and statistics strategies. Systems biology can not only retrospectively analyses biological parameters, but also can model *in silico* different interactions. Thus, systems biology research combines "wet laboratory" experimentation with "dry laboratory" predictions of biological processes, and vice versa.[8,9,10] All these developments, which started to accelerate approximately a decade ago, have led to the rapid establishment of organized biobanking[13,14].

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8 Hood L, Rowen L, Galas DJ, Aitchison JD., Systems biology at the Institute for Systems Biology, *Briefings in Functional Genomics and Proteomics* 2008 ,Vol. 7, pp.239-248.

9 Loscalzo J, Barabasi AL., ´Systems biology and the future of medicine´, *Wiley Interdisciplinary Review of Systems Biology Medicine*, 2011, Vol. 3, No. 6, pp.619-627.

10 Ginsburg GS, Willard HF, Genomic and personalized medicine: foundations and applications. *Translational Research*, 2009, Vol.154, No. 6, pp. 277-287.

11 Sobradillo P, Pozo F, Agustí A., P4 medicine: the future around the corner, *Archivos de Bronconeumologia*. 2011, Vol. 47, No. 1, pp.35-40.

12 Venter JC, Adams MD, Myers EW, Li PW, Mural RJ, Sutton GG, et al. The sequence of the human genome, *Science*, 2001, Vol.291, pp. 1304-1351.

13 Asslaber M, Zatloukal K., Biobanks: transnational, European and global networks, *Briefings in Functional Genomics and Proteomics.* 2007, Vol. 6, No. 3, p. 193-201.

14 Riegman PH, Morente MM, Betsou F, de Blasio P, Geary P, Biobanking for better healthcare and the Marble Arch International Working Group on Biobanking for Biomedical Research, *Molecular Oncology.* 2008, Vol. 2, No. 3, pp.213-222.

3.1• What is a Biobank?

Biobanks typically: (a) collect and store biological materials that are annotated not only with medical, but often also epidemiological data (e.g. environmental exposures, lifestyle/occupational information); (b) are not static "projects", since biological materials and data are usually collected on a continuous or long-term basis; (c) are associated with current (defined) and/or future (not yet specified) research projects at the time of biospecimen collection; (d) apply coding or anonymisation to assure donor privacy but have, under specific conditions, provisions that participants remain re-identifiable in order to provide clinically relevant information back to the donor[13,14,15]; and (e) include established governance structures (e.g. ethics review committees) and procedures (e.g. consent) that serve to protect donors' rights and stakeholder interests[16].

Notwithstanding some shared features, the field of biobanking is, generally speaking, very heterogeneous[13,14,15]. Although it is difficult to exhaustively list all distinguishing characteristics of biobanks, there are some that can be used to characterize different types of biobanks. These are size, research design, the types of biological samples collected, the method of sample collection, processing and storage, and the disease/research focus. These characteristics will influence the scope of biobank activities, such as the recruitment of donors, the consent procedures, the scale of informatics support needed, the governance structures, and the potential for commercial exploitation. Until recently, terminology denoting organized collections in medicine has not been consistent. A number of terms such as "human genetic research databases (HGRDs)", "population genetic databases", "biorepositories", or "tissue banks" have been used to refer to activities involving biobanks/biobanking. However, "biobank" is now the over-arching term that is most commonly used. An example of a European legal definition of a biobank is found in the Council of Europe Recommendation on research on biological materials of human origin (2006)[17] which also refers explicitly to biobanks (BOX 2). This could also be applied to other types of biobanks.

BOX 2 Legal definition of a population biobank[17]

Article 17

1. A population biobank is a collection of biological materials that has the following characteristics:

i. the collection has a population basis;

ii. it is established, or has been converted, to supply biological materials or data derived therefrom for multiple future research projects;

iii. it contains biological materials and associated personal data, which may include or be linked to genealogical, medical and lifestyle data and which may be regularly updated;

iv. it receives and supplies materials in an organised manner.

3. Member states should consider applying the provisions of this chapter to collections that have some, but not all, of the characteristics specified in paragraph 1.

15 http://www.austlii.edu.au/au/journals/JlLawInfoSci/2010/5.html

16 Yuille M, Dixon K, Platt A, Pullum S, Lewis D, Hall A, Ollier W., The UK DNA banking network: a "fair access" biobank, *Cell and Tissue Banking.*, 2010, Vol. 11, No. 3, pp. 241-251.

17 https://wcd.coe.int/ViewDoc.jsp?id=977859 (This Recommendation is currently under re-examination)

The key factor that distinguishes a biobank from a research collection is that a biobank has established governance mechanisms in place to allow access to the resource in a systematic way to outsiders.[3]

3.2• Biobank designs

Sample size is a characteristic that can be used to distinguish different kinds of biobanking activities. Large-scale biobanks are generally used for prospective and longitudinal molecular epidemiology research projects, while smaller scale biobanks are established for specific research projects, such as case-control studies[13,14]. Within the European context large-scale biobanks include the UK Biobank (BOX 3)[18], deCode-associated Icelandic Biobank[19], the Estonian Biobank[20], and the Genome Austria Tissue Bank (GATiB) projects[21]. While large-scale biobanks are relatively recent, small collections established for specific research projects have been more the norm. The majority of these biobanks comprise comparatively small collections of up to several thousand samples. Despite their different research foci and their often limited statistical power, these smaller scale projects represent an indispensable scientific resource complementary to large-scale biobanks[13,14,15]. For this reason, more organisations are seeking to link their clinical research collections under one biobank[22].

BOX 3 The UK Biobank[18]

This is a large scale prospective cohort biobanking project that started more than a half a decade ago and which operates on a nationwide basis. Its multisource funding is provided by institutions such as the Wellcome Trust, the UK Medical Research Council, the Department of Health and the Scottish Executive. The UK Biobank is one of the largest biobanks in Europe and has already recruited over 500,000 participants. Donors are ascertained within routine medical settings and provide comprehensive medical and lifestyle data. Their samples are cryopreserved at a fully automated facility. This biobank was opened for access by researchers in 2012.

18 http://www.ukbiobank.ac.uk

19 http://www.decode.com

20 http://www.geenivaramu.ee/en/

21 Asslaber M, Abuja PM, Stark K, Eder J, Gottweis H, Trauner M, Samonigg H, Mischinger HJ, Schippinger W, Berghold A, Denk H, Zatloukal K. The Genome Austria Tissue Bank (GATiB). *Pathobiology.* 2007, Vol. 74, No. 4, pp. 251-258.

22 For example, the Oxford Radcliffe Biobank links existing collections within the University of Oxford and the Oxford Radcliffe Hospitals NHS Trust; http://wyvern.ndcls.ox.ac.uk/orb/about_overview.html

Within the context of medical research there are multiple biobank formats which can be differentiated based on their design and scientific target. However, all biobank formats are interlinked and to a certain degree represent a continuum within the infrastructure supporting all gradual steps of the biomedical research "pipeline" [13,14,15].

3.2.1• Population-based biobanks

The main research objective of population-based biobanks is generally to discover biomarkers for disease susceptibility within a specific population through prospective molecular epidemiology research strategies. These types of biobanks typically recruit healthy donors who are representative of a region, country, or specific ethnic group. One of the most commonly stored biospecimen is germline-DNA isolated from venous blood. Associated data comprise not only medical history but also physical measures and epidemiological information (e.g.: life habits, socioeconomic status)[13,14,15]. The specifics of population-based biobanks are compiled and analyzed by the Public Population Project in Genomics[23] (BOX 4) in its internet resources.

BOX 4 Public Population Project in Genomics

The Public Population Project in Genomics (P³G)[23] *represents an international, non-profit consortium which is promoting collaboration between all stakeholders in the field of population genomics. The P³G Consortium provides resources and a unique platform for international exchange of expertise and knowledge in this field. Tools such as "comparison charts" of existing biobanking guidelines, operational procedures, websites and instruments are available on the P³G website[24].*

3.2.2• Disease-oriented biobanks

Compared to population-based biobanking initiatives, disease-oriented biobanks store a much more heterogeneous collection of biological materials, which are mainly collected within the context of clinical care. Biological materials found in such biobanks are usually collected from patients, and can lead to eventual re-sampling at follow up visits in the course of their disease treatment. A number of different disease-oriented biobank subtypes exist[13,14,15].

3.2.3• Case-control biobanks

Case-control biobanks can offer distinct advantages to some of the resource-intensive large-scale cohort studies. The prerequisite for meaningful case-control studies is collection of matched (age and sex as a minimum) individuals presenting a given disease with compatible healthy controls.

23 http://www.p3g.org

24 http://www.p3gobservatory.org/repository/comparisonCharts.htm

Epidemiological case-control studies may be designed to serve as biobanks, nested case-control can be generated from population-based biobanks (cases and controls extracted from biobank participants), or patients from case-only biobanks can, under certain conditions, be matched to controls recruited from population-based biobanks[13,14,15].

3.2.4• Tissue banks

Tissue banks represent extremely diverse collections of tissue specimens. These are generally cryopreserved at hospital pathology departments following their usual mode of sampling by invasive medical procedures, thereby representing residual "bioptic material". These samples are associated with detailed information on the nature of the underlying disease for which these were sampled. Following patient consent, hospital information systems may allow further annotation of a given bioptate with longitudinal follow-up clinical records, response to treatment and eventually final disease outcome. A specific form of tissue banks is represented by formalin-fixed paraffin embedded (FFPE) specimen collections[13,14,15].

3.2.5• Biobanking within the context of clinical trials

Biobanking has been going on in tandem with many clinical trials[25] performed by various clinical research organizations and/or investigator-driven clinical trials in Europe, and elsewhere. During the time-line of a trial, these organizations compile not only complex clinical and laboratory monitoring data, but also examine samples (e.g. blood, urine of trial subjects/controls), which can in turn be integrated into a biobank and used for research. The major aim of clinical trial related biobanking is to identify disease/trial-associated biomarkers.

3.2.6• Other specific biobanking formats: Guthrie cards, cord blood, stem cells

Remaining archived blood spots collected through routine nationwide neonatal screening programs ("Guthrie cards") could also be utilized in medical research. The best known example of a biobank storing neonatal blood spots is the Swedish PKU Biobank that has collected several million Guthrie cards from nationwide neonatal screening programs and which operates within a national framework.[26]

In the area of cord blood biobanking the UK Cord Blood Bank Ltd[27] could serve as an illustrative example. This biobank is financed privately and its range of operations also includes continental European countries. Due to their in depth experience with cell cultures of pluri-potent cells, most cord blood biobanks are now expanding their operations to stem cells derived from other tissues. The UK Stem

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25 Halim SA, Newby LK, Ohman EM. Biomarkers in cardiovascular clinical trials: past, present, future. *Clinical Chemistry.* 2012, Vol. 58, No. 1, pp.45-53.

26 http://www.biobanks.se/

27 http://www.cordbloodbank.co.uk/

Cell Bank[28] was established as a dedicated repository of human embryonic, fetal and adult stem cells, including the storage of human embryos for research under defined conditions. This facility is now ready to generate "clinical grade" cell lines for future regenerative therapies, for instance.

3.3• The potential of personalized medicine

There is the potential for biobanks to be key tools in enabling personalized medicine and for this to become a common approach within Europe. Personalized Medicine or 'P4 Medicine' involves the following characteristics [8,9,11,29]:

1. "*personalization*" which reflects the individual "digital genome";
2. "*predictivness*" which is due to the ability to predict the risk of certain diseases based on "personal genome" information in combination with lifestyle data, age, sex, occupation etc.;
3. "*preventiveness*" that is based on individualized risk prediction,
4. this requires an active "*participation*" of the individual concerned in proactively maintaining their health.

Such a paradigm shift in medical practice will empower individuals to undertake informed decisions about their health future. But before the vision of personalized medicine is widely accepted, vast amounts of digitalized personal medical data must be collected, analyzed and properly integrated.[30] Genomics studies are one of the initial inroads into the entire complexity of biology of health and disease. It is expected that in the near future developments in informatics, nanotechnologies and microelectronics will enable transition from the current evidence-based, but still population-centered personalized (i.e. stratified) medicine, to the ultimate level of the individual patient.[31] This will represent a major paradigm shift in health care provision, public health[32], reimbursement[30,33], and also open novel avenues of research in the area of social sciences and medical ethics[34].

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28 http://www.ukstemcellbank.org.uk

29 Khoury MJ et.al Centers for Disease Control and Prevention. The Scientific Foundation for personal genomics: recommendations from a National Institutes of Health-Centers for Disease Control and Prevention multidisciplinary workshop. *Genet Med.* 2009, Vol. 11, No. 8, pp.559-567

30 Lehrach H, Subrak R, Boyle P et al. ITFoM-the IT Future of Medicine. *Procedia Comput Sci* 2011, Vol. 7, pp.26-29.

31 Bereczki, D. Personalized medicine: a competitor or an upgrade of evidence-based medicine? *Personalized Medicine* 2012, Vol. 9, No. 2, pp. 211-221

32 Cesuroglu, T; van Ommen, B; Malats, N; Sudbrak, R; Lehrach, H; Brand, A. Public health perspective: from personalized medicine to personal health. *Personalized Medicine* 2012, Vol. 9, No.2 pp 115-119

33 Canestaro, WJ; Martell, LA; Wassman, ER; Schatzberg, R. Healthcare payers: a gate or translational bridge to personalized medicine? *Personalized Medicine* 2012, Vol. 9, No. 1, pp. 73-84

34 Hogarth, S; Hopkins, M; Faulkner, A. Personalized medicine: renewing the social science research agenda. *Personalized Medicine* 2012, Vol. 9, No.2 pp. 121-126.

There are several important initiatives that together have the potential to move medicine towards the individual patient. The Public Heath Genomics European Network II project[35] aims to establish best practice guidelines for the use of genome-based information and technologies. The European Flagship Future and Emerging Technologies initiative[36] and the "IT Future of Medicine" (ITFoM)[37] pilot project also will help the personalized medicine agenda to advance. Such initiatives will help address the transition from personalized medicine to personal health from the data-integration and modeling perspective points of view. While the concept of personalized medicine and the role that biobanks can play in that vision is gaining momentum in the scientific field, it is not clear that the general public are aware of, or support such developments.

35 http://www.phgen.eu

36 http://cordis.europa.eu/fp7/ict/programme/fet/flagship/

37 http://www.itfom.eu

4• Biobanking in Europe

In many European countries, high quality population-based and disease-oriented biobanks have been established. Major financial and scientific investments have been committed and millions of citizens have voluntarily contributed data and bio-specimens to such biobanks. These investments have permitted major progress in the comprehension of specific risk factors of complex diseases. The potential to further strengthen pan-European and global collaborations are now one way the research community can ensure the optimal leveraging of the scientific potential of current and future biobanks. Increasing data compatibility is crucial to enable valid comparison across countries or jurisdictions and to permit integration (or pooling) of data across biobanks. This integration is essential to obtain the large numbers of participants and samples necessary to conduct research investigating, for example, the interplay between genetic, lifestyle, environmental, and social factors that determine health and (complex) diseases. Nonetheless, cross-border biobank cooperation within the context of heterogeneous ethical and legal national and/or regional frameworks faces important challenges for the European Union[38].

4.1• Prospects for harmonisation and networking in Europe

In 2010, the European Institute for Prospective Technological studies (IPTS) of the European Commission´s Joint Research Centre[39] in collaboration with the European Science and Technology Observatory (ESTO)[40] published results from a comprehensive survey of biobanks (Biobanks in Europe: Prospects for Harmonisation and Networking; 2010)[41]. The main objectives of this project were to survey biobanking in Europe and identify challenges for networking and harmonisation. The overarching message from this survey was the variation and fragmentation of biobanking practices and activity within Europe. On the basis of this evidence, the report recommended the creation of an international umbrella or network organisation that would foster harmonisation and standardisation of biobank practices (see Annex 1 for more details).

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38 Yuille, M., van Ommen, G.J., Brechot, C., Cambon-Thomsen, A., Dagher, G., Landegren, U., Litton, J.E., Pasterk, M., Peltonen, L., Taussig, M., Wichmann, H.E., Zatloukal, K., 'Biobanking for Europe'. *Briefings in Bioinformatics.*, 2008, Vol. 9, pp. 14–24.

39 http://ipts.jrc.ec.europa.eu

40 http://ipts.jrc.ec.europa.eu/ataglance/networks.cfm

41 Zika E, Paci D, Schulte in den Bäumen T, Braun A, RijKers-Defrasne S, Deschênes M, Fortier I, Laage-Hellman J, Scerri C.A., Ibarreta D., 'Biobanks in Europe: Prospects for Harmonisation and Networking', European Commission Joint Research Centre, Institute for Prospective Technological Studies (EUR 24361 EN; ISBN 978-92-79-15783-7; ISSN 1018-5593)

Biobank networking and harmonization have become key issues in the biobanking field. In order to ensure meaningful collaborative research and overcome heterogeneity of biobanking in Europe, the development of common guidelines, standard operating procedures (SOPs), and harmonization methodologies (see BOX 5) is crucial[13,14,15].

BOX 5 The difference between standardization and harmonization

'Rather than demanding complete uniformity among biobanks, harmonization is a more flexible approach aimed at ensuring the effective interchange of valid information and samples. One critical task of the harmonisation process is to articulate those situations when true harmonisation is required. Standardisation requires that precisely the same protocols/standard operation procedures are used by all biobanks. For example, if data are to be passed between biobank databases then there needs to be agreement on standard ontologies and exchange formats. Likewise, comparison of high-throughput-technology derived data requires that platforms and operational details be identical. Harmonisation is context-specific and pertains to the compatibility of methodologies and approaches to facilitate synergistic work. It thereby relates to the critical areas of generating, sharing, pooling and analyzing data and biological samples to allow combining resources and comparing results from different biobanks.'[42]

To answer to this need, a number of major international networking initiatives have emerged. These include the Biomedical Informatics Grid[43] and European Prospective Investigation into Cancer and Nutrition[44] (cancer); Public Population Project in Genomics (BOX 4); and PHOEBE[45] (population biobanks); EuroBioBank (rare diseases)[46]; GenomeEUtwin[47] (sibling and twin cohorts); TuBaFrost[48] (frozen human tissue bank); and NUGENOB[49] (nutrition and obesity). In addition, the Organisation for Economic Co-operation and Development (OECD)[50,51], the US National Cancer Institute (NCI)[52], and the International Society of Biological and Environmental Repositories

42 Harris JR, Burton P, Knoppers BM, Lindpainter K et.al. 'Towards a Global Roadmap in Global Biobanking for Health'; *European Journal of Human Genetics* 2012 (in press)

43 http://cabig.nci.nih.gov

44 http://epic.iarc.fr/ centers/iarc.php

45 http://www.phoebe-eu.org

46 http://www.eurobiobank.org/

47 http://www.genomeutwin.org/

48 http://www.tubafrost.org

49 http://www.nugenob.org

50 OECD (Ed.), 2007. OECD Best Practice Guidelines for Biological Resource Centers – General Best Practice Guidelines. OECD, Paris http://www.oecd.org/dataoecd/7/13/38777417.pdf.

51 OECD Organization for Economic Cooperation and Development. OECD guidelines on human biobanks and genetic research databases. *Eur J Health Law.* 2010, Vol.17, No. 2:191-204.

52 NCI, 2007. NCI Best Practices for Specimen Resources. NCI, Bethesda. Available from: http://biospecimens.cancer.gov/ global/pdfs/NCI_Best_Practices_060507.pdf.

(ISBER)[53] have established guidelines and recommendations for biobanking. Finally, the European Commission has supported several collaborative projects within the last EU Framework 7 Programs. The preparatory phase Biobanking and Biomolecular Resources Research Infrastructure (BBMRI)[54] (BOX 6), the TISS.EU project (Evaluation of legislation and related guidelines on the procurement, storage and transfer of human tissues and cells in the European Union;[55]) and the BioSHARE-EU project (Biobank Standardization and Harmonization for Research Excellence in the European Union[56]) are examples of such EU-funded initiatives.

BOX 6 BBMRI

BBMRI[54] – *Biobanking and Biomolecular Research infrastructure Preparatory Phase (BBMRI-PP) aims to prepare the construction of a pan-European infrastructure for biomedical and biological research in Europe and worldwide, building on existing infrastructures, resources and technologies, specifically complemented with innovative components and properly embedded into European ethical, legal and societal frameworks.*

4.2• Infrastructural and health care provision-related developments relevant to biobanking

More than a decade ago the European Commission established the "European Strategy Forum on Research Infrastructures[57] (ESFRI), whose ultimate aim is to overcome fragmentation of European biomedical facilities by development of integrative policies ("Roadmaps"), which are continuously updated with new partners and scientific domains. The associated Community legal framework for a European Research Infrastructure Consortium (ERIC)[58] entered into force at the end of August 2009. This specific legal structure was designed to facilitate the establishment and joint operation of respective research infrastructures within ESFRI. This will allow biobanks across Europe that become part of the ERIC to operate under a common legal structure.

4.3• Biobanking challenges in Europe

In addition to major harmonization issues, the current practice of biobanking and biomedical research in Europe faces a number of other important challenges. While networks and consor-

53 International Society for Biological and Environmental Repositories (ISBER). 'Best practices for repositories: collection, storage, retrieval and distribution of biological materials for research'. *Cell Preserv. Technol.*, 2008, Vol. 6, pp. 3–58; http://www.isber.org/Pubs/BestPractices2008.pdf.

54 http://www.bbmri.eu

55 http:// www.tisseu.uni-hannover.de

56 http://www.bioshare.eu

57 http://ec.europa.eu/research/infrastructures/index_en.cfm?pg=esfri

58 http://ec.europa.eu/research/infrastructures/index_en.cfm?pg=eric

tia are increasing, there are still serious issues that need to be addressed with regard to cross-border exchange of samples and data transfers.[59,60] In addition, informatics challenges in medical biobanking are immense. For instance, there are major challenges associated with the integration of various forms of data such as text (clinical information); numeric values (laboratory data, age); categorical (staging, grading, scoring); image (histology, röntgenology, magnetic resonance); array (genomic data); composite (DNA signatures, mutations, variants, transcription factor interactions); and/or hierarchic (pedigrees)[13,14,15]. Moreover, there exist a number of data security and confidentiality concerns related to the exchange of sensitive patient data[61].

There are also financial challenges associated with the long-term sustainability of individual biobanks as well as biobank networks and infrastructures. As ongoing financial support is uncertain, quite often biobanks must seek out multi-source financing whether they are based in the public or private sectors[62]. The biobanking "business cycle" is comparatively long and thus requires durable investment strategies[63]. In this respect networking grants or research grants, which are usually given to establish a biobank, do not assure long-term operational financing. Financial sustainability of biobanks strongly depends on background support from host partners such as academic hospitals (e.g. by offering free services and/or discounts for their own affiliates). For these reasons there have been calls to embed biobanks within healthcare structures so that they can fulfill a dual purpose of clinical care and research use.[32,64,65]

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59 Goebel JW, Pickardt T, Bedau M, Fuchs M et.al. Legal and ethical consequences of international biobanking from a national perspective: the German BMB-EUCoop project. *European Journal of Human Genetics*, 2010, Vol. 18, No. 5, pp. 522-525

60 Bellazzi R, Diomidous M, Sarkar IN, Takabayashi K, et.al. Data analysis and data mining: current issues in biomedical informatics. *Methods Inf Med*. 2011 Vol. 50, No. 6, pp:536-544.

61 Schwarz E, Leweke FM, Bahn S, Liò P. Clinical bioinformatics for complex disorders: a schizophrenia case study. *BMC Bioinformatics*. 2009, Vol. 10 Suppl 12, pp. S6.

62 Rogers J, Carolin T, Vaught J, Compton C. Biobankonomics: a taxonomy for evaluating the economic benefits of standardized centralized human biobanking for translational research. *J Natl Cancer Inst Monogr*. 2011; Vol. 2011, No. 42, pp. 32-38.

63 Vaught J, Rogers J, Carolin T, Compton C. Biobankonomics: developing a sustainable business model approach for the formation of a human tissue biobank. *J Natl Cancer Inst Monogr*. 2011; Vol. 2011, No. 42, pp.24-31.

64 Kaye J. Embedding biobanks as tools for personalised medicine. *Norsk Epidemiologi* 2012; Vol. 21, No. 2, pp. 169-175

65 Murtagh MJ, Demir I, Harris JR, Burton P. Realizing the promise of population biobanks: a new model for translation, *Human Genetics* 2011; Vol. 130, pp. 333-345

5• Public Attitudes Towards Biobanking

As we have shown in the last section, the development of biobank infrastructure and the use of this as a basis for personalised medicine has become a central strategic goal in the fields of European biotechnology, genomics, and international politics. However, this new way of doing science and potentially this new way of delivering healthcare is challenging as it raises a number of multifaceted medical-ethical issues as well as more general socio-political issues, such as the perception and the acceptance of biobanks in society. Controversial projects, such as the Icelandic[66] and Tongan[67] population biobanks have shown that not all biobank projects are warmly received by all groups in society. Biobanks are dependent not only on donors but also on continued societal and political support to remain operational. There is also the possibility that ambitious projects such as these may fail due to political pressure. Therefore, public attitudes towards biobanks are of great importance and will considerably influence the development and future success of biobanks. In this respect, the political-cultural context of any biobank project is essential and needs to be carefully considered.

The continued success of the biobanking infrastructure strategy and the vision for personalized medicine is strongly dependent upon public support – to provide not only the long-term funding for such endeavors, but also to be actively involved as donors of samples and data (BOX 7) but also as participants in the evolution of healthcare provision towards personalized medicine based on genomics. But what do Europeans expect from biobanks? What do they know about them, and how do they want biobanks to operate? Where are the public sensitivities, fears and hopes?

66 D.E. Winickoff Genome and Nation: Iceland's Health Sector Database and its Legacy *Innovations* 2006, Vol. 1, No. 2, pp 80-105.

67 JH Barker Common-pool resources and population genomics in Iceland, Estonia, and Tonga. *Medicine, Health Care and Philosophy* 2003, 6: 133-144.

This section of the report reports on the findings of the Eurobarometer survey EB 73.1, 'Life Sciences and Biotechnology' that took place in 2010 and provides insights to these questions. This large-scale survey, conducted in 32 European countries, also contained 8 questions on biobanks.[68] The Eurobarometer is a series of surveys commissioned regularly by the European Commission. This section also draws on the findings of an international study on public opinion regarding biobanks that analysed qualitative data from focus groups.[69]

BOX 7 What is involved for participants

When people participate in a biobank study, they typically donate blood, tissue, and body fluid, including DNA data. Donating bio-specimens is unlike donating blood for blood transfusions. Once the blood is donated, it disappears into a large system of blood supply. However, in a biobank or cohort study, the samples attain their scientific value by being linked with personal information such as medical records and social and environmental data. Participants are often asked to allow the linkage of electronic medical records and admission records to samples. Donated tissue or DNA has the potential to become a scientific-technological resource for further research. This raises a range of ethical issues affecting donors and society including forms of consent, privacy and data protection, and benefit sharing.

5.1• A lack of public awareness

Currently, public thinking about biobanks in Europe is characterized by a striking heterogeneity that also exhibits a geographical orientation. However, public opinion is responsive to local as well as international events, so it is in constant state of flux. As such, attitudes towards biobanks still far from being settled in many countries. In general, there is a cluster of Northern European countries where the prospect of biobank research is greeted enthusiastically, whereas the publics of many Central and Southern European countries are generally more reserved about biobank research, donating tissue, and giving broad consent for research. This has implications for recruitment, as well as the operation and governance of biobanks. In gathering and maintaining public support, information and knowledge are key factors in the further development of biobank research perception in Europe.

One of the most remarkable findings of current public opinion research on biobanks is the limited awareness of Europeans concerning biobanks (Figure 1). More than two thirds of all Europeans said they have never heard of biobanks, and only 17 % answered that they had actively talked about or searched for information about biobanks in the past. Those who are better informed are concentrated in Northern Europe – in Sweden, Finland, and Iceland.

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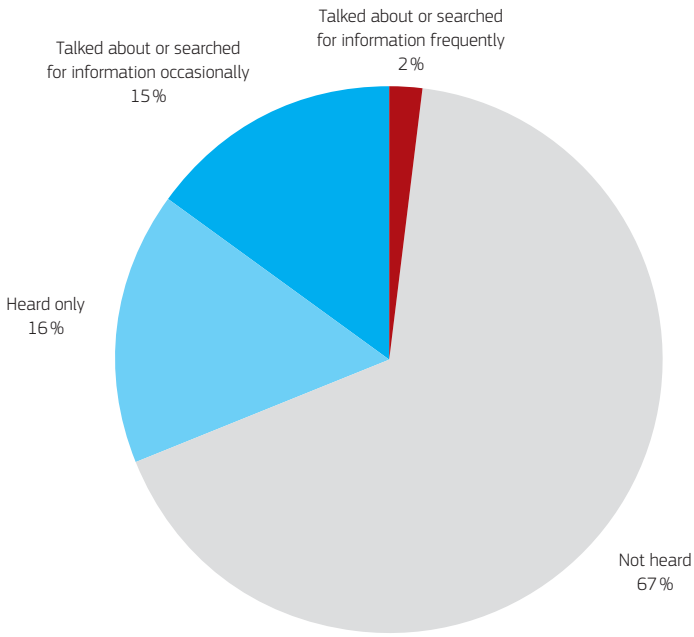
68 G. Gaskell et al., Europeans and Biotechnology in 2010: Winds of change? (2010), at http://ec.europa.eu/public_opinion/archives/ebs/ebs_341_winds_en.pdf

69 G. Gaskell H. Gottweis, J, Starkbaum, M. Gerber M. et.al. Publics and Biobanks: Pan-European Diversity and the Challenge of Responsible Innovation *Eur. J. Hum. Genet.* (in press).

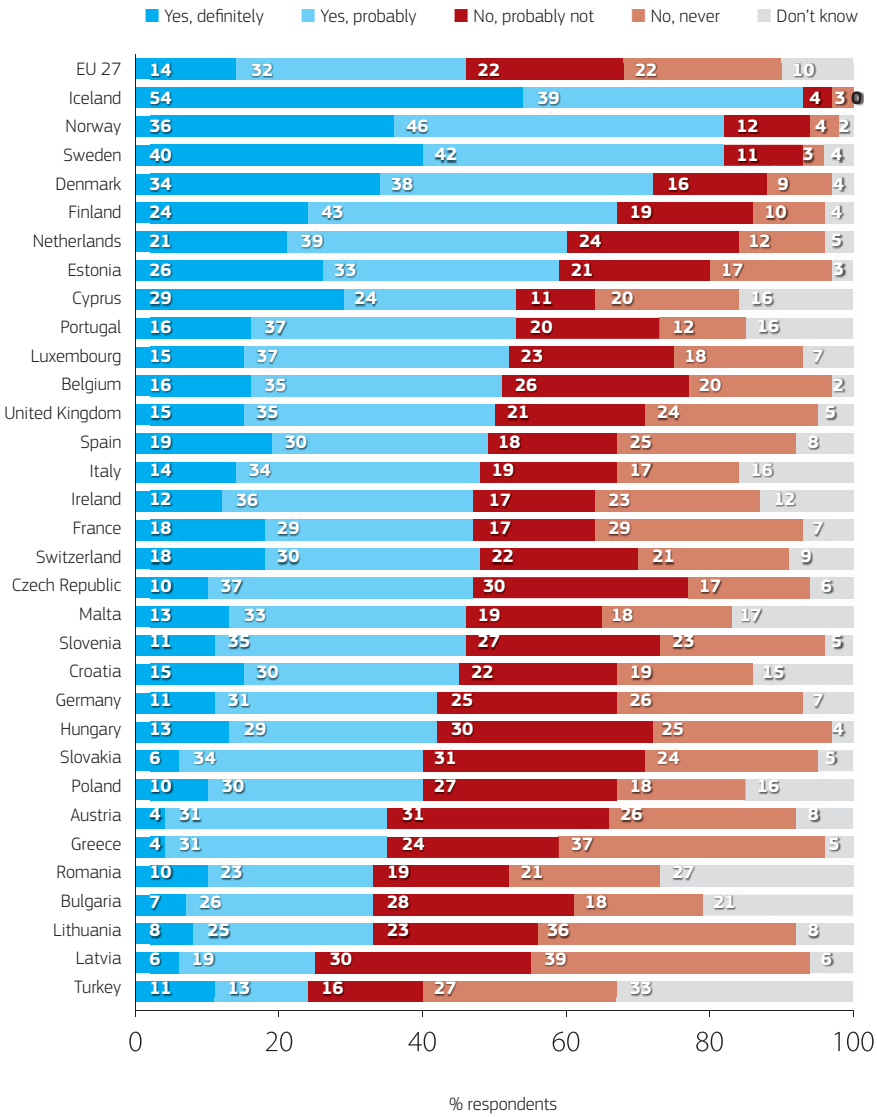
Figure 1: Awareness of biobanks, EU27 average



Source: G. Gaskell et al., Europeans and Biotechnology in 2010: Winds of change? (2010), p 60

This situation points to a critical knowledge deficit in Europe when it comes to biobank research. In terms of participation, we can observe wide variation in attitudes across Europe. There is a strong concentration of people in Northern European countries who say that they will 'definitely' or 'probably' participate in biobank research, whereas the publics in other countries in Europe are much more reluctant. Figure 2 shows the differences in people's willingness to provide data about themselves in the context of participating in biobank research across Europe.

Figure 2: Would you be willing to provide information about yourself to a biobank?



Source: G. Gaskell et al., Europeans and Biotechnology in 2010: Winds of change? (2010), p 61

In summary, the European landscape of public perceptions of biobanks is a picture of substantial heterogeneity and of potential concern to those planning and operating biobanks. While there is a willingness to participate in biobanks in Northern European countries, where there is a long history of sample and data collection, it is a minority opinion in many other countries.

5.2• Attitudes towards broad consent

One of the controversial aspects of biobanking has been the use of broad consent, rather than seeking the more conventional informed consent for participants enrolling in a biobank. While this has been seen as a practical solution to the fact that all research uses of the biobank cannot be determined when participants are enrolled, this approach appears not to be supported by the general public (Figure 3). Interestingly, attitudes in Europe towards broad consent are also shaped by levels of information: the more people know about biobanks, the more they are ready to give broad forms of consent, whereas the less they know the less likely are they to participate.[70] A broad consent has been seen as essential to facilitating biobank research.

Given the lack of awareness about biobanks and the concerns about privacy and data protection, the European stake-holders in biobank research need to work hard to develop efficient mechanisms for informing European citizens about biobank research, why it is there, and what it is doing. Creative and interactive solutions using a 'dynamic consent' model developed by the EnCoRe project[71] and the CHRIS project[72] use Web 2.0 information architectures to enable participants to give consent on an ongoing basis over time. Better information about biobanks will increase recruitment which is necessary for the long-term sustainability of biobanking, but also may be a key strategy for reducing the gap in support for biobanks between Northern European and Central and Southern European countries.

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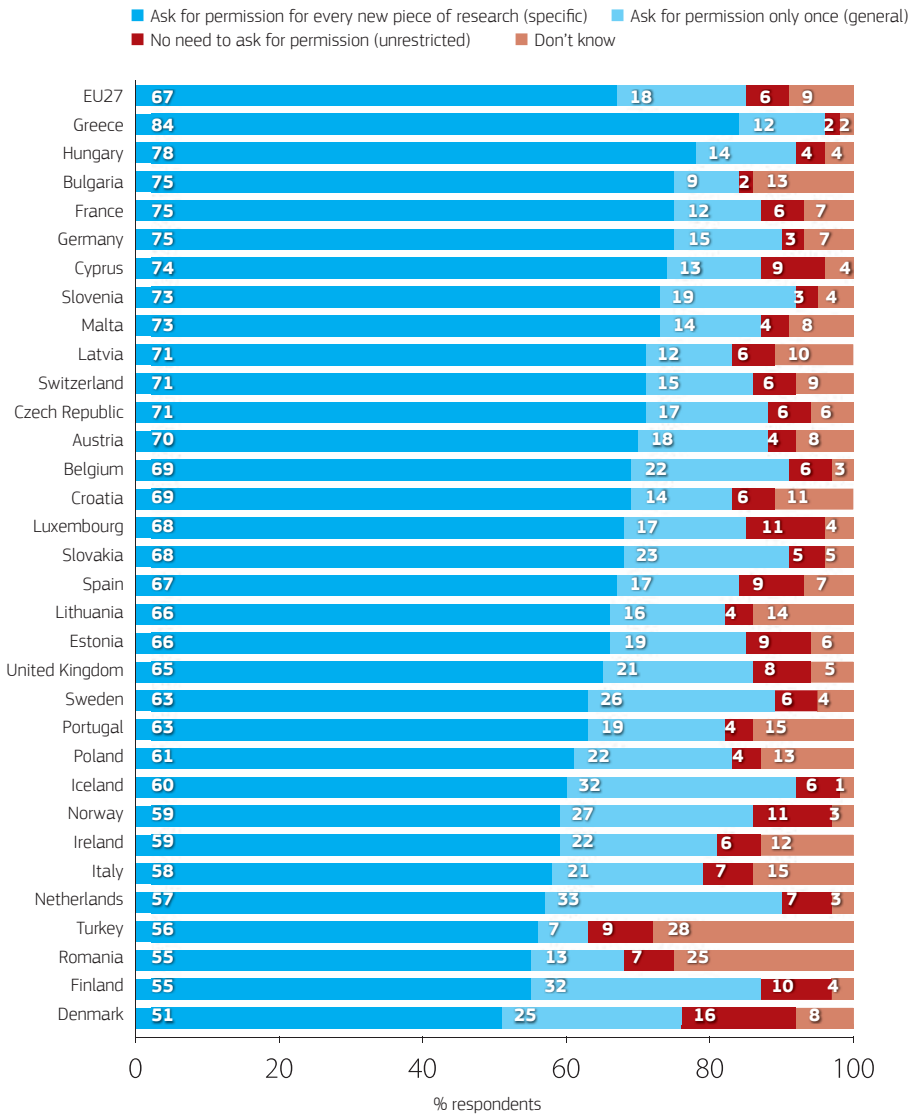
70 G. Gaskell H. Gottweis, J, Starkbaum, M. Gerber M. et.al., *ibid*.

71 EnCoRe / Oxford Radcliffe Biobank (UK) http://cyber.hwcomms.com/cyber/DynamicConsent

72 CHRIS – Cooperative Health Research in South Tyrol (Italy)
http://www.eurac.edu/en/research/institutes/geneticmedicine/chrisstudy/default.html

Figure 3: Form of consent for biobank research



Source: G. Gaskell et al., Europeans and Biotechnology in 2010: Winds of change? (2010), p 65

The striking feature of the findings presented in this graph is that across Europe, the majority of respondents agree that permission must be asked for every new kind of research done on a biobank. It was a minority of people who thought it appropriate not be asked for permission to have their details and samples entered into a biobank.

5.2.1• Protecting privacy as a key concern

When people participate in biobank research, questions of privacy and data protection are some of the first concerns to materialise. For people who have little or no engagement with biobanks, unwillingness to participate may be not so much a rejection of biobanks per se, but rather a reasonable hesitation to divulge personal information to a little-understood endeavour and purpose.

The international study involving focus groups showed that people in all countries of Europe seem to have serious concerns about data abuse by insurance companies or employers.[73] They expect biobanks to have the best possible security protections and oversight mechanism to prevent misuse of their personal information. Data security is an issue even in countries where people expressed broad support for biobanking.

Privacy issues were also considered by respondents in regard to wider societal developments, rather than being a consideration that just related to biobank research. Many people are accustomed to providing data in their daily lives and are resigned to privacy violations. However, all medical data, be it specimens or health records, is perceived as being sensitive compared to other personal data. While in the Netherlands, France, the UK, and Finland people seem more concerned about medical records, in Germany, Austria, and Greece people are most concerned about biological data and genetic profiles (Figure 4).

The boundary between personal and biological data is often blurred in people's perceptions; they dwell on the long-term nature of biobanks and the inevitable uncertainty of the future. It is often not what biobanks are, but what they might become, that frightens people.[74]

Next to the broad absence of information about biobanks, the issue complex of privacy and data protection might be the second important factor in interfering with biobank development in Europe. People demand the best possible solutions for this challenge and biobank organizers should respond accordingly. Privacy and data protection in biobanking will be essential for securing acceptance of biobank research across Europe.

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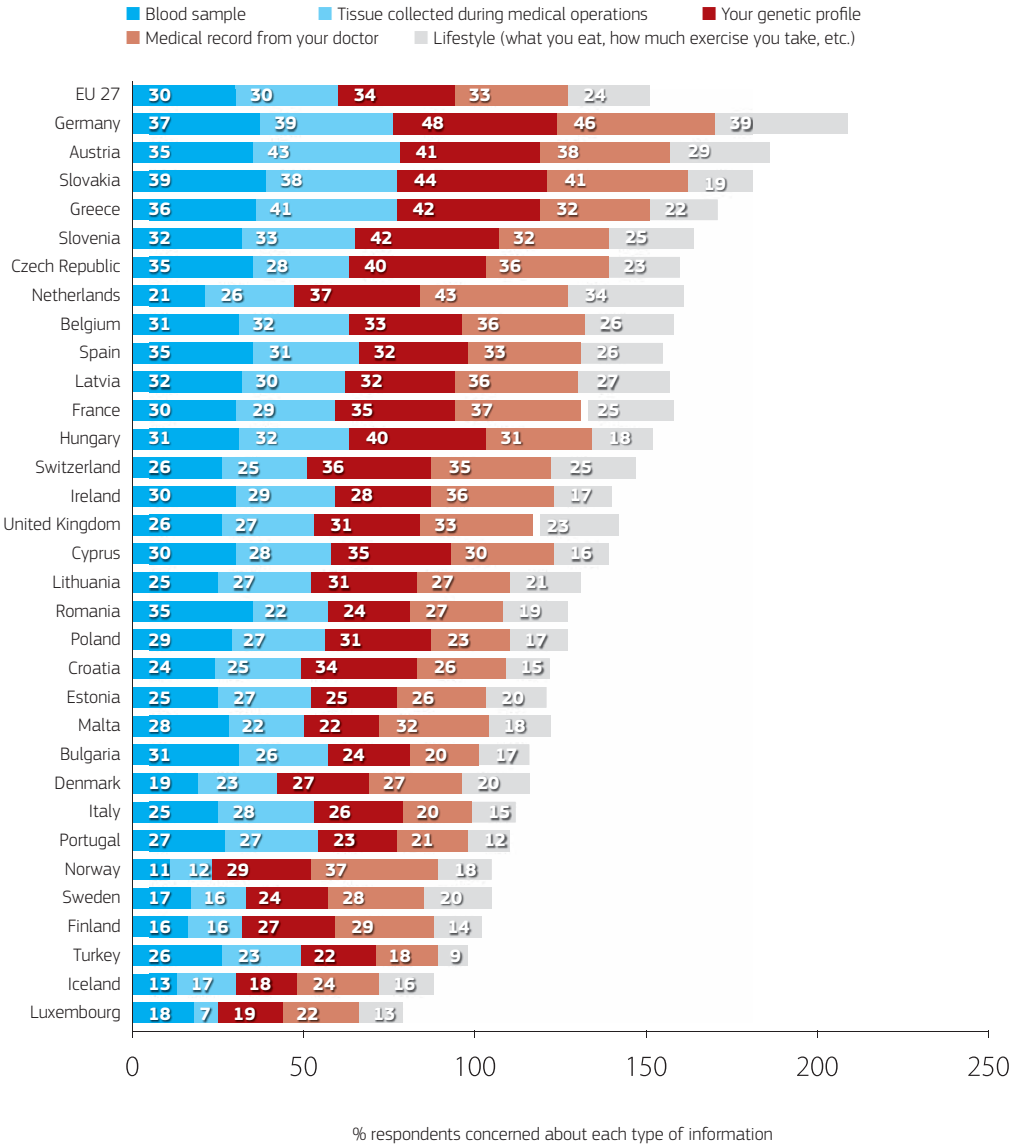
73 G. Gaskell H. Gottweis, J, Starkbaum, M. Gerber M. et.al, *ibid*.

74 G. Gaskell H. Gottweis, J, Starkbaum, M. Gerber M. et.al, *ibid*.

Figure 4: Levels of concern about giving different types of information to a biobank



Source: G. Gaskell et al., Europeans and Biotechnology in 2010: Winds of change? (2010), p 63.

5.3• Trust

When people donate to a biobank, many think that this is not a free gift; they participate with the expectation of getting something in return. Supporting science and medicine is a strong incentive across Europe. At the same time, many people assume that they will receive insights into their health status, and they look forward to the possibility of regular health checks with the opportunity of meetings with medical experts.

All human interactions are dependent upon mutual exchange where people constantly give and receive as part of daily life. When people give their blood or DNA to a biobank, as in other fields they expect something in return.[75] The Eurobarometer findings suggest that what can be returned to people and society in the context of biobank research needs to go beyond the general gesture of pointing at the potential benefits coming from biobank research one day in the future.

Trust is an essential societal precondition of biobank research. This raises the question of the organizational set-up of biobanks. Embedding biobanks in well-known and long-trusted structures will increase people's trust because of such institutions' commitment to advancing scientific knowledge and serving the public interest. Publicly funded research in universities, national research institutes, and hospitals are widely regarded as trustworthy.

People are certainly not ignorant of what might happen with their data, but they trust these institutions to handle data with care. Transparent structures and the feedback of findings are likely to improve public support. Confronted by the novelty of biobanks, and in the absence of a culture of trust, people may well opt for a precautionary approach. Those hesitating to sign up for and participate in biobanks have lower trust in key actors and have greater concerns about data privacy and security. Such concerns will only be allayed by building trust and transparency and by engaging the public as partners in the biobank project.

Additionally, trust creates a sense of reciprocity and is perceived as a mark of recognition for personal contribution and participation. In this regard, the uneven wiliness across Europe to participate in biobank research and the weak support for broad consent may be seen as a combination of lack of information, and also a lack of trust in those involved in operating biobanks. In this regard, biobanks will need to be very clear about their cooperation with other actors, especially from the private sector, as this involvement is widely perceived with suspicion.

5.4• Transparent Governance

People in Europe demand transparency about research aims, boundaries, and actors involved in biobank. Feedback on the research outcomes is also desired and seen as a step towards an open policy that involves and informs about progress and modes of operation. Decision makers will have

75 Gottweis, H.Gaskell, G. Starkbaum, J. Connecting the public with biobank research: reciprocity matters, *Nat Rev Gen* 2010, Vol.12, pp 738-739

to consider modes of inquiry and reflexive models of "lay participation" with diverse groups, a sort of "empirical," communicative ethics, possibly also Web 2.0 based, in order to develop sensibility of what the public interest might be on issues such as privacy or benefit sharing. Given that the individual and social meanings of terms like privacy and genetic information are by no means fixed, it is relevant to take into account the perceptions of the lay public. Trust can be generated neither by technical solutions nor by increased transparency alone. To increase the level of data security doesn't necessarily enhance the quality of a trust relationship. Likewise, benefit sharing is not easily implemented if it is to constitute more than a rhetorical strategy. The way these procedural questions will be negotiated and dealt with in the future will be crucial for the success or failure of biobanks and the building of infrastructure.

5.5• Patient Involvement

A clear recommendation was first published at the European level by the European platform for patients' organisations, science and industry (EPPOSI)[76]. In the EPPOSI conference of May 2006 (Amsterdam) all stakeholders discussed for the first time the future of biobanks intended as collections of human biological samples and associated data for research and therapy development. In particular, representatives of several patient organisations demonstrated: i) how their self-developed biobanks and databanks contribute to progress to effective therapies for their diseases, ii) what key role patient groups play in promoting the need for tissue and sample banks, iii) how they contribute to raise awareness about the usefulness of bio-banks and to accelerate the collection of precious biomaterial.

In order to promote and amplify the pivotal role of patient organizations, the members of EPPOSI highlighted the need to educate patient groups on how to start and structure a bio-bank[77] Furthermore, the example of the EuroBioBank (European network of DNA, cell and tissue biobanks for rare diseases) network,[78] also presented during the EPPOSI conference, demonstrated how patient involvement in biobanking is a powerful tool to actively influence therapy development and to optimize the use of rare collections. Since its establishment in 2001, this networking experience of small biobanks had also highlighted the urgent need for harmonization of the regulatory systems for biobanks. This harmonisation is expected to facilitate the exchange of samples across the borders particularly in the case of rare diseases where the "rare" specialists on a disease often have difficulties to access the specific rare samples needed to progress research.

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76 Smit, C. In: *EPPOSI conference, data-and bio-banking for research, towards joint ventures of patient organisations, science and industry on the road to validated expertise and new therapies*. May 6-9 2006 & October 25-27 2006.

77 http://www.epposi.org

78 http://www.eurobiobank.eu

The BBMRI (Biological and Biomolecular Resource Infrastructure)[79] Stakeholder's Forum provides an additional example of what patients' expectations are regarding biobanks and what patients think they can contribute to them. The "Consultation Document" drafted by the BBMRI Stakeholder's Forum patient representatives,[80] highlights the more relevant principles laid down in the European and international instruments that cover patient participation in networked biobanking activities. It also indicates existing examples of good practices to facilitate their implementation.

The patient representatives of the Stakeholder's Forum recommended 3 key principles that should govern the active participation of patients and patient organisations in biobanking activities. These are: *Inclusion, Engagement* and *Communication*.

Translating these key principles into practice involves;

1. Inclusion of patients and patient organisations as partners in the research effort, especially in the areas of communication, advocacy and recruitment (e.g. information to potential donors, preparation of informed consent forms)

2. When establishing sample, tissue and databanks the experience, knowledge and expertise of patients, families and carers should be considered.

3. Listening to patients' voices/expectations on research needs from their experience from participating in biobanking as donors.

4. Regular, general and reasonable feedback to patients regarding use, sharing and transfer of samples.

In particular, the patient involvement and inclusion should be extended to ethical aspects such as: informing Research Ethics Committees (RECs) of patients' interests; patient rights over their donation; access to samples from research groups out of the country; possible new use of existing samples after discontinuation of the biobank.

In summary, in the light of the handful of successful experiences of patient groups involved in the creation and management of biobanks, there is now a growing recognition of the importance of such early engagement of patient representatives in biobanks. Nevertheless, to facilitate the active participation of patients and patient organisations in research and biobanking activities, appropriate training is necessary and more information should be disseminated as to what patients can concretely contribute to research and biobanks in particular.

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79 http://www.bbmri.eu/index.php?option=com_content&view=article&id=52&Itemid=59

80 http://www.bbmri.eu/index.php?option=com_content&view=article&id=77&Itemid=66

6• The regulation of biobanks within Europe

Biobanking is governed under the general regulatory framework for biomedical research. This is a mosaic of formal legal instruments and regulatory bodies put in place at national and European levels, as well as more informal types of governance tools and instruments such as professional guidelines and best practice. Regulation of biomedical research consists of binding and non-binding legal instruments at both national and European levels. This is in the form of specific law for medical research – for example the Council of Europe Oviedo Convention 1997 – and more general legal instruments – such as human rights and data protection law – some of which have relevance for biobanking. Responsibility for the oversight of research and ensuring compliance with the legal requirements has largely been delegated to national bodies, such as research ethics committees.

This has resulted in a diversity of legal requirements for biobanking activities across Europe but also at national levels, as there is no one binding instrument that applies specifically to biobanks. This complexity places researchers, who collaborate across Europe, at risk of operating unlawfully if they share research data and samples across borders where different laws are in force[81] without operating due diligence. Biobank managers have expressed concern that the current regulatory framework for human biobanks within Europe creates uncertainty and inhibits the building of biobank infrastructure.[82] In addition to diversity in the legal requirements, national research ethics committees may have different requirements for collaborative research. This may have implications for research consortia that wish to share samples and data derived from different biobanks.

As well as uncertainty about the legal requirements that might apply for cross- border transfers, there are also areas, such as the use of tissue for research purposes, which are central to biobanking, that are not covered by binding European legal instruments. This has lead to differences in the formal legal requirements for the research use of tissue and data. However, there have been a number of advisory opinions by groups such as the Art. 29 Working Group that have developed opinions to help ameliorate these differences.

Therefore, identifying the legal instruments that apply to biobanking within Europe results in a complex picture of requirements and enforcement measures. The aim of this section is to give an overview of this complexity by discussing the legal requirements for biobanks at the European level and to provide a broad outline of the regulatory bodies that are responsible for ensuring best practice for biobanking activities.

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81 Kaye J. 2006 Do we need a uniform regulatory system for biobanks across Europe? *European Journal of Human Genetics* **14,** 245–248.

82 Budin-Ljøsne, I. et. al. 2012 ELSI challenges and strategies of national biobank infrastructures *Norsk Epidemiologi* 2012 21 (2): 155-160.

6.1• Legal Instruments and Guidance

Within Europe, the legal instruments that apply to medical research are a complex mix of specific as well as general legal instruments of different authorities. The Council of Europe and the European Union have formulated the general legal instruments that provide the foundation for the regulation of medical research and therefore biobanking practice. In Europe the laws that have been applied to biobanks have largely been drawn from the legal traditions and jurisprudence that have been developing around the protection of human rights and the advancement of public health.

6.1.1• The Council of Europe

The Council of Europe *Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine* (Oviedo, April 4 1997)[83] is the basis for safeguarding the rights of human subjects regarding scientific progress within Europe. This Convention stipulates general principles that are supplemented by additional protocols.[84] One of the issues for the wide spread adoption of the Convention is that its provisions are only mandatory for members which have ratified it.[85] This limits the scope of its effect. However, in some specific cases, also pertaining to biomedical research, Conventions of the Council of Europe can affect EU Member States via EU legislation in which reference is made to Council of Europe Conventions.[86]

The Council of Europe has been also the first intergovernmental organization in Europe to propose a general Recommendation on research on biological materials of human origin (2006)[87] which refers explicitly to biobanks. Although the text is only a recommendation, it is linked to the Convention and the accompanying Protocol on biomedical research. This Recommendation protects the rights of persons in particular for the 'secondary use' or re-use of stored biological material, which is the primary purpose of biobanks. It also outlines the requirements that apply to population biobanks, but does not exclude the fact that this protocol could also apply to other biobanks if they meet most of the definitional requirements (See BOX 2).

These specific provisions for biobanks require that there should be independent oversight, regular audits, reports on activities, measures to facilitate access as well as procedures for transfer and closure of the biobank. However, recent issues that have emerged out of biobanking are not covered by this recommendation such as the controversial issue regarding the "ownership" of samples, the responsibilities to report incidental findings arising out of whole genome sequencing or the specific questions surrounding the use of samples obtained from minors.

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83 Oviedo Convention, STE 164 available at http://conventions.coe.int/Treaty/fr/Treaties/Html/164.htm

84 Additional protocols adopted to date are: Protocol on cloning (1998), Protocol on transplantation (2002), Protocol on Biomedical Research (2005), Protocol on Genetic Testing for Health Purposes (2008).

85 To date the Convention has been signed by 35 Members of the Council of Europe and has been ratified by 29 http://conventions.coe.int/Treaty/Commun/ChercheSig.asp?NT=164&CM=&DF=&CL=ENG

86 Paula, L. The Oviedo Convention from the Perspective of DG Research, *Medical Ethics & Bioethics*, Vol. 16 (Suppl. 1) 2009, pp 7-9

87 https://wcd.coe.int/ViewDoc.jsp?id=977859. This Recommendation is currently under re-examination.

6.1.2• The European Union

Since the Treaty of Maastricht, the European Union (EU) has taken more of a role in the field of health. Currently the EU is active in the field of public health and research, with a shared competence with Member States in compliance with the principle of 'subsidiarity'. The policies adopted by EU can provide the Union with common tools in the protection of public health or the implementation of a policy for an internationally competitive scientific research.

The European Union's existing regulatory framework in biomedical research, does not have a specific regulation for biobanks-based research. More specifically, the rules found in the Directive 2001/20/EC on clinical trials do not apply to biobank-based research and, furthermore, the existing rules applicable to (the use of) biological samples do not deal with their use for research purposes. Likewise, the Directive 2004/23/EC (on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells) does not cover research using human tissues and cells (see Recital 11 and Article 1). However, biomedical research carried out by using personal data is regulated, albeit in very general terms (as discussed below), in the EU Data Protection Directive (95/46/EC).[88] Despite this lack of a specific legal instrument, the principles contained in the clinical trials and data protection laws provide the main basis for the "regulatory building blocks" for the protection of research participants. These lay down the relevant procedural rules to ensure the protection of individuals participating in biobank-based research.

6.1.2.1• *The Clinical Trials Directive*

The Clinical Trials Directive (2001/20/EC) enshrines the major principles of medical research practice – that consent must be obtained from participants before the research commences and that they have the right of withdrawal; and that all research must be reviewed by a research ethics committee prior to commencement. The principles have also been applied to biobanking and so any research using personal information and/or biological samples require the participants' "informed consent" and an assessment exercise by ethics committees. The requirement for informed consent comes traditionally from the patient-doctor relationship, has moved to the clinical trials area, and is now extending its scope to the biomedical and biological research at large, as highlighted by the Article 3(2) of the Charter of Fundamental Rights of the European Union.

Despite this, there are significant differences between biobank-based research and clinical trials. Once collection of a sample is made, biobanking research does not entail any further direct physical intervention with individuals. Unlike some clinical trials, the risks inherent in the use of the biobank have nothing to do with the physical dimension of the individual but rather have implications for individual privacy and further decision making by the individual. With biobanks there is the risk of abuse of unauthorized (or unexpected) access to the data collected by third parties as well as concerns about the potential impact of incidental findings. This issue is becoming more controversial especially with the introduction of exome/whole genome sequencing.

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88 This approach seems not to be changed in the new regulations that will amend the Data Protection Directive 95/46/EC. This is the Proposal for a Regulation of the European Parliament and of the Council on the protection of individuals with regard to the processing of personal data and on the free movement of such data General Data Protection Regulation, COM (2012) 11, 25.1.2012.

6.1.2.2• *The Data Protection Directive*

The other regulatory model that has been relied upon in the European legal system is the Data Protection Directive (95/46/EC). This stipulates the principles that must apply to the protection of personal data within the Europe. Given the processing of personal data in biobanks-based research, which can involve sensitive data, such as health and genetic information, socio-demographic data, life style and behavioural data, the requirements found in the Directive have been important for biobanks. As well as providing the principles for fair processing, the Directive also stipulates that data protection supervisory authorities should provide oversight and supervisory roles. This model is now mirrored, at the highest level, in the EU sources, within Art. 8 of the Charter of Fundamental Rights of the European Union and Art. 16 Treaty on the Functioning of the European Union (TFEU), provision applicable to all the matters falling under EU competence.

Following the solution adopted by the Council of Europe Convention of 28 January 1981, No. 108 (Article 6), the Directive 95/46/EC also allows the use of personal data (sensitive data included) for research purposes, providing Member States adopt "*suitable safeguards*". This is a wide discretion. In particular, some provisions contained in the Directive (see BOX 8) allow enough flexibility to allow the processing of personal data for secondary historical, statistical or scientific research purposes, as long as there are appropriate safeguards in place. This means that in the case of research, there are exemptions from two of the fair processing principles. Under this exemption, data can be kept for a longer than the original purpose and if the provision of information about secondary research purposes proves impossible, or would involve a disproportionate effort ,or if recording or disclosure is expressly laid down by law, then information about the processing does not need to be given to research participants.

BOX 8 The Data Protection Directive with regard to scientific research

Recital (29) "Whereas the further processing of personal data for historical, statistical or scientific purposes is not generally to be considered incompatible with the purposes for which the data have previously been collected provided that Member States furnish ***suitable safeguards****; whereas these safeguards must in particular rule out the use of the data in support of measures or decisions regarding any particular individual".*

Article 6(1)(b) "Further processing of data for (...) scientific purposes shall not be considered as incompatible provided that Member States provide ***appropriate safeguards****".*

Article 6(1)(e) "Member States shall provide that personal data must be [...] kept in a form which permits identification of data subjects for no longer than is necessary for the purposes for which the data were collected or for which they are further processed. Member States shall lay down **appropriate safeguards** *for personal data stored for longer periods for (...) scientific use".*

Article 11(2) and Recital 40: Derogations from the obligation to inform data subjects are allowed for, "where, in particular for (...) scientific research, the provision of such information proves impossible or would involve a disproportionate effort or if recording or disclosure is expressly laid down by law. In these cases Member States shall provide ***appropriate safeguards****".*

(emphasis added)

Accordingly, the above provisions – whose purpose was to ensure sufficient flexibility and to reconcile data protection principles and research needs – have left a considerable margin of maneuver to Member States. This discretion allows them to determine (via domestic legislation) if, and how, to strike a satisfactory balance between protecting basic values of individuals and safeguarding medical and scientific research along with public health goals.

In the case of biobank-based research, it should be highlighted that the data protection regulatory model with its major principles (e.g. fairness, lawfulness, transparency, finality, necessity, security, etc.) must be applied not only to the processing of personal data, but also – albeit with some ambiguities – to the biological samples used for research purposes (so far they can be referred directly or indirectly to the participant). In biobank research it is not the tangible features of biological samples that are at issue but the informational content. It is therefore the information derived from biological samples rather than the biological sample as such that really matters in a biobank-based research.It might be argued that the biological sample (in its physical dimension) plays basically an ancillary role – being the container or vehicle of the information at issue. This is the stance taken by the Article 29 Working Party[89] in its "Working Document on Genetic Data" adopted on 17 March 2004 (WP91)[90] as well as by some European data protection authorities.[91]

This is in line with the European Court of Human Rights' decisions and the Council of Europe's Recommendations R (92) 1 on the use of analysis of deoxyribonucleic acid (DNA) within the framework of the criminal justice system (Principles 7 and 8); and R (92) 3 on Genetic Testing and Screening for Health Care Purposes (Principle 8a). The same views would appear to underlie the decisions by the European Court of Human Rights in *S. and Marper v. UK*[92] and in *Van Der Velden v. The Netherlands*.[93] In the Marper case the Court said that "namely fingerprints, DNA profiles and cellular samples, constitute personal data within the meaning of the Data Protection Convention as they relate to identified or identifiable individuals".[94]

This means that the principles applying to the retention and circulation of biological samples should not differ significantly from personal data protection principles even if the legal framework devised for personal data were not found to be directly applicable.

If this is the case appropriate privacy and data protection impact assessments must be carried out on sample collections. This would apply in the case of biobanking infrastructure where there is the establishment of a common application or processing platform where several data controllers interact. These assessments are designed to identify the degree of specific risks to the rights of the

89 This Working Party has been established by Article 29 of Directive 95/46/EC. It is the independent EU Advisory Body on Data Protection and Privacy, composed of representatives of EU Member States authorities.

90 In determining the safeguards applying to genetic data, the Working Party found it necessary to consider and regulate the legal status of biological samples as well to the extent such samples can be a source of personal data.

91 This is the case in Denmark (in the Data Protection Act) and Italy (by way of a general authorization 24th June 2011).

92 8 December 2008, case nos. 30562/04 and 30566/04, para 68.

93 7 December 2006, case No. 29514/05

94 *S. and Marper v. UK* 8 December 2008, case nos. 30562/04 and 30566/04,

participants and may require consultation with a competent authority, such as the data protection authority for prior checking.[95]

6.1.3• National Law

Despite the wide discretion given to Member States and probably due to the lack of a legislative specific framework at European level, some European governments have implemented national legislation. The way in which governments have responded to the regulation of biobanking activities has varied across Europe. Two main positions emerge within Europe: either specific legislative acts are adopted focusing on biobanks activities (Iceland, Estonia[96], Hungary[97], Sweden[98], Spain[99] and Belgium[100]), or provisions about biobanks or bio-collections are integrated into broader administrative[101] and legislative instruments (France[102] and the United Kingdom[103]). The use of biological samples for research purposes has been addressed by some countries alongside other applications such as health care and diagnosis.[104] In many cases, however, the rules on the use of biological samples for research purposes have to be pieced together taking into account a number of different regulatory instruments.

These different approaches point to different national styles in addressing regulatory challenges, and that not one approach is appropriate for all. It can be assumed that there are good reasons why some countries have opted for legislative approaches towards biobank research, while others have chosen more integrative strategies. What matters, however, is that there are responsible regulatory bodies that can deal with the challenges of biobank governance.

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95 This is in line with the Proposal for a Regulation of the European Parliament and of the Council on the protection of individuals with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation), COM (2012) 11, 25.1.2012, in part. Section 3 (articles 33 and 34).

96 Icelandic Act on Biobanks no. 110/2000, 13 May 2000, Estonian Human Genes Research Act RT I 2000, 104, 685

97 Hungarian Parliamentary, Act No XXI of 2008 on the protection of human genetic data and the regulation of human genetic studies, research and biobanks

98 The Swedish Biobank Act, 2002:297

99 Biomedical Research Act 2007

100 Law on Biomedical Research 14/2007 July 3rd, on Biomedical Research

101 See, regarding Italy, the mentioned general authorisation concerning genetic data has been issued on the 24th June 2011 adopted by the Italian Data protection Authority pursuant to Section 90 of the data protection law (legislative decree No. 196/2003).

102 Law n° 2011-814, 7 July 2011 on Bioethics, JORF n°0157 of 8 July 2011 page 11826

103 UK Human Tissue Act, 2004

104 See in Lithuania the Law on ethics of biomedical research, 11 May 2000 No VIII-1679; in Spain the law 14/2007 on biomedical research; in Belgium see the loi 19 decembre 2008, Loi relative à l'obtention et à l'utilisation de matériel corporel humain destiné à des applications médicales humaines ou à des fins de recherche scientifique (and the following regulations); in Portugal, see the Law No. 12/2005, January 26, Act on personal genetic information and information regarding health). Relevant rules are provided, in France, through the (amendments introduced in the) *Code de la santé publique*.

The inconsistencies between domestic laws are a direct result of that fact that Directive 95/46/EC allows for a margin of appreciation in implementation by member states, but also because its provisions are highly general in their scope. While this flexibility can be beneficial allowing member states to determine the way that the Directive is implemented in a national internal system, this is highly problematic for ongoing (and future) biomedical research on biobanks. To facilitate cross-border research will require more than the present piecemeal approach. Instead, there needs to be the development of a common approach to regulation and the standardisation of data processing and the use of samples.

The degree of national regulation makes it difficult to provide an updated, detailed and complete overview of the (sometimes complex) legal framework in force in all jurisdictions across Europe. This can have a significant effect on the ability of scientists to collaborate and plan international initiatives. Therefore, it is advantageous to have a coherent legal framework[105] and to ensure that national governance structures are in harmony with other jurisdictions and not in conflict. Harmonisation of this kind could have the effect of enhancing collaboration and the sharing of data and samples. To combat these concerns the European Union has agreed to create a new legal structure for biobanking in the form of a European Research Infrastructure Consortium (ERIC[58]) (see section 8.1).

6.1.3.1• *Common features of national regulatory instruments*

Despite the fact that there is significant heterogeneity in the legal instruments described above, there are some common traits that are starting to emerge. In particular, most of the national regulatory instruments (including those on population biobanks) provide that:

- biobanks' accreditation should be sought with the competent national authorities (usually the Ministry for Health, the Ministry of Research or local pharmacology agencies)[106];
- the creation of a biobank should be notified, and the competent national authorities (including the data protection authorities)[107] should accordingly set up registries of biobanks[108];
- supervision should be carried out by the competent national authorities alongside the supervision by the national data protection authority[109];

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105 R. Lattanzi, Ricerca genetica e protezione dei dati personali, in P. Zatti – S. Rodotà, Trattato di biodiritto, Milano, 2011.

106 See the Belgian law 19 December 2008, Loi relative à l'obtention et à l'utilisation de matériel corporel humain destiné à des applications médicales humaines ou à des fins de recherche scientifique (art. 7); art. 64, Spanish law n. 14/2007, de 3 de julio, de Investigación biomedical; see also § 25 Norvegian Act 2008-06-20 No. 44, Act on medical and health research (the Health Research Act).

107 See e.g. in Portugal, art. 19, Lei n. 12/2005, *Informação genética pessoal e informação de saúde*; Ch. 2, Sect. 5 seq. Swedish Biobanks in Medical Care Act (2002:297). In some cases the data protection laws provide a duty to notify the processing of genetic data: see, for instance, art. 37, Italian data protection law (legislative decree n. 196/2003).

108 See, for instance, § 4 Norvegian Act relating to Biobanks (2003); Ch. 2, Sect. 5 and 6, Swedish Biobanks in Medical Care Act (2002);

109 See, for instance, § 17 Norwegian Act relating to Biobanks (2003); Sect. 9 and 21 seq. Latvian Human Genome Research Law (2002); Ch. 6, Sect. 3, Swedish Biobanks in Medical Care Act (2002);

- management of biobanks should be committed to a specific individual/entity, usually from the medical (or biological) profession[110];
- suitable security measures should be taken to protect biological samples (on top of those already set forth at domestic level to ensure the protection of personal data), often provided through by-laws[111];
- where it proves impossible to use anonymous or anonymised data or biological samples because of the specific features of a research, such data and samples may be used after being "coded" (pseudonymised); ad-hoc safeguards are envisaged in some cases to ensure that data and samples are pseudonymised under stringent confidentiality rules (e.g. double code) and the cases are specified in which it may prove necessary to de-code (de-crypt) the information in question;
- research ethics committees should assess the purposes to be achieved by setting up the given biobank[112]; in some cases, ethics committees are required to assess each research project that is expected to rely on biological samples[113]. However, it is rarely the case that the specific issues to be considered by ethics committees are spelled out and different approval procedures based on different arrangements are usually envisaged in the individual legal systems[114];
- limitations and/or specific safeguards should be applied in case biological samples are transferred abroad[115];
- as a rule, it is provided by law that a proxy consent may be given in case children or other vulnerable individuals are involved in a research[116];
- in some cases, the use of biological samples from deceased individuals is regulated expressly;

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110 § 7 Norwegian Act relating to Biobanks (2003)

111 § 9 Norwegian Act relating to Biobanks (2003); Art. 4, Portugese Act on personal genetic information and information regarding health No. 12/2008

112 § 4 Norwegian Act relating to Biobanks (2003); art. 22, Belgian Loi relative à l'obtention et à l'utilisation de matériel corporel humain destiné à des applications médicales humaines ou à des fins de recherche scientifique (2008)

113 Art. 12(2) (and 3), Lithuanian Law on Ethics of Biomedical Research (2000); Ch. 2, Sect. 3, Swedish Biobanks in Medical Care Act (2002); art. 2, Spanish Law on Biomedical Research, No. 14/2007; art. 22, Belgian Loi relative à l'obtention et à l'utilisation de matériel corporel humain destiné à des applications médicales humaines ou à des fins de recherche scientifique (2008)

114 Regarding the secondary uses of rest material, the art. 21, Belgian Loi relative à l'obtention et à l'utilisation de matériel corporel humain destiné à des applications médicales humaines ou à des fins de recherche scientifique (2008) provides that "Le comité d'éthique se prononce au moins sur les matières suivantes: 1° la pertinence de l'utilisation secondaire et son but; 2° le respect de la présente loi et de ses arrêtés d'exécution; 3° l'adéquation des informations communiquées et la spécificité et la portée suffisantes du consentement; 4° dans les cas visés à l'article 20, § 1er, alinéa 3, l'impossibilité de demander son consentement au donneur ou le caractère exceptionnellement inapproprié de cette demande".

115 Ch. 4, Sect. 8, Swedish Biobanks in Medical Care Act (2002); Sect. 15, Latvian Human Genome Research Law (2002);in Portugal, art. 17, Lei n. 12/2005, *Informação genética pessoal e informação de saúde*; Sect. 12 Norwegian Health Research Act 2008

116 Ch. 3, Sect. 1, Swedish Biobanks in Medical Care Act (2002); Sect. 20, Finnish Act on Medical Use of Human Organs and Tissues No. 101/2001

- consent by the participant may be withdrawn freely, which often entails destruction of the relevant biological sample(s) along with any personal information relating thereto[117], where possible and, in some cases, upon a specific request by the participant/data subject[118].

Thus, in principle, there are quite a few features that are shared by the regulatory instruments enacted so far. They could therefore represent a (common) starting point at a European (and general, supra-national level) of common and coherent principles for biobanks. Indeed, shared and adequate guarantees in force in different countries could facilitate the sharing of samples (as has happened for data protection laws).

6.1.4• Guidance

While at the EU level, for the time being, there does not seem to be a clear plan of engaging directly on the regulation of biobanks, this does not mean that European institutions have ignored this issue. The European Group on Ethics in Science and New Technologies adopted an opinion touching on this topic[119] that has been considered by a number of ad-hoc study groups.[120] In addition various societal studies have been conducted at the European level. The EU has moved a step forward in recognizing the importance of building biobank infrastructure at the European level, as part of the regulation of infrastructures in the life sciences.[121]

Among the intergovernmental framework, the main texts on biobanks have been adopted in part by the Organization of the United Nations Educational, Scientific and Cultural Organization (UNESCO) and partly by the Organization Co-operation and Development (OECD). Even though these texts are not legally binding, they are very important in the affirmation of common principles (UNESCO) and to standardize practices (OECD). They serve as a reference for researchers and public authorities. Although their violation cannot in any way cause a direct sanction, they can influence the adoption of more stringent texts. Finally they offer flexibility as they can be revised periodically.

UNESCO has adopted Declarations emphasizing on the need to protect genetic data derived from the human genome. The organization has primarily emphasized the common heritage of mankind. The protection of the genome is necessary to safeguard the human species (The Universal Declaration on the Human Genome and Human Rights adopted November 11, 1997). Secondly, UNESCO has made a recommendation in the field of the use of genomic knowledge (International

117 Ch. 3, Sect. 6, Swedish Biobanks in Medical Care Act (2002); Art. 11, Latvian Human Genome Research Law (2002)

118 § 14 Norwegian Act relating to Biobanks (2003)

119 Notably Opinion n°11, 21/07/1998 – Ethical aspects of human tissue banking available at http://ec.europa.eu/european_group_ethics/docs/avis11_en.pdf

120 McNally E. (Chair), Cambon-Thomsen A. (Rapporteur) et al. The 25 recommendations on the ethical, legal and social implications of genetic testing. European Commission. EUR 21120 – Luxembourg: Office for Official Publications of the European Communities 2004 – 25 pp. http://europa.eu.int/comm/research/conferences/2004/genetic/pdf/recommendations_en.pdf

121 For the European initiative on infrastructures see CORDIS website at http://cordis.europa.eu/esfri/roadmap.htm

Declaration on Human Genetic Data adopted October 16, 2003). These Declarations deal with the specificity of genetic information among other biological information and propose a particular mechanism to protect them.

The OECD has developed a proposal on the provision of common tools for Biological Resource Centres (BRC) (broadly defined as encompassing all types of resources: micro organisms, plant cells, animal or human). The guidelines adopted in 2007 devoted a chapter specifically to human biological resources and the scientific use of the BRC[50]. The use of resources and data for genetic research is considered more comprehensively in the Guidelines for Human Biobanks and Genetic Research Databases[51].

Among the texts adopted by professional organizations, the Declaration of Helsinki[122] can be considered as the leading instrument. This Declaration applies to biomedical research on human subjects and specifies provisions for the use of human samples. The aim of this statement of ethical principles is to provide guidance to those developing research protocols. Although not binding, it is recognized as the "gold standard" in the conduct of research involving human beings (this is particularly true in the context of international collaborative research). Biobanks are not expressly covered as such by the Declaration (the term is not used in the text) but the use of biological research is not ignored. The Declaration requires that informed consent must be sought by physicians prior the commencement of any biomedical research but in cases where it is impossible to obtain consent, the research can only be undertaken after consideration and the approval of a research ethics committee.[123]

6.2• Regulatory Bodies

The formal oversight and compliance assessments for medical research and biobanks are carried out at a national level. As described above the basic principles of medical research governance (following the model of the Clinical Trials Directive) requires that all research protocols should be reviewed by a research ethics committee (REC) or an equivalent independent body. The formal bodies that are common to all countries of Europe are the RECs which are active in reviewing biobank protocols and the Data Protection Authorities that are responsible for oversight of data processing. In some jurisdictions there are additional bodies sanctioned by the State, which are responsible for biobanking activities, such as the Human Tissue Authority in the UK. Another level of oversight is undertaken by the institutions where a biobank is based or by local health authorities who may host the biobank. Finally, while not responsible for oversight, National Bioethics Committees have been influential in developing guidance that applies to biobanking activity.

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122 World Medical Association (WMA). 2008. *World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects*. Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, amended in 1975, 1983, 1989, 1996, 2000, 2002, 2004, and 2008. http://www.wma.net/en/30publications/10policies/b3/

123 Art. 25 of the Declaration.

6.2.1• Research Ethics Committees

Research Ethics Committees (RECs) or institutional review boards (IRBs) are common to most jurisdictions. These bodies are the key decision-makers in reviewing and allowing a research protocol to proceed and therefore hold considerable power in the research governance system. Thus, RECs have emerged as an essential element in European biobank governance and also enjoy wide social acceptance.[124] Any research that is carried out using samples and information from a biobank will be required to seek REC approval. RECs have been responsible for approving the establishment of biobanks.

6.2.2• Data Protection Authorities

Due to provisions contained in Directive 95/46/EC (which is currently under revision), Data Protection Authorities also have an important role in overseeing data processing not only within biobanks, but also the use of data and samples by researchers. For example, Data Protection Authorities have been empowered to identify the rules that can be relevant for biobank research in Italy[125]; have given guidance to stakeholders in Germany[126]; were responsible for monitoring the creation and operation of the Health Sector Database in Iceland[127] and have issued an authorisation to the legislators in Portugal on biobanks[128]; been involved in public hearings in the national Parliament of Sweden[129]; and, in some cases, have used their enforcement powers[130].

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124 G. Gaskell et al., Europeans and Biotechnology in 2010: Winds of change? (2010),59.

125 Like in the above mentioned case of the authorisation provided by the Italian Data Protection Authority on the 24th June 2011.

126 See for example Unabhängiges Landeszentrum für Datenschutz Schleswig-Holstein, *Datentreuhänderschaft in der Biobank-Forschung bdcAudit (Biobank Data Custodianship/Audit Methodology and Criteria). Methoden, kriterien und Handlungsempfehlungen für die datenschutzrechtliche Auditierung der Datentreuhänderschaft in der Biobank-Forschung*, Schlussbericht, 30.April 2009.

127 See art. 12, Act on Health Sector Database, No. 139/1998 passed by the Alþingi, 17th of December 1998.;

128 See, e.g., the authorisation n. 7435/2011 given by the Portugese Data Protection Authority on the 11.7.2011.

129 For instance see the (appellate) decision taken on the 16 December 2011 by the Swedish Data Protection Authority (Datainspektionen), concerning the lawfulness in the collection of biological samples and health data to the biobank infrastructure LifeGene.

130 See, e.g., the statements regarding biobanking research of T. Weichert during the *öffentliche Anhörung am 25. Mai 2011 zur Thema "Humanbiobanken"* before the *Ausschuss für Bildung, Forschung und Technikfolgenabschätzung* at the *Bundestag*: kann man erkennen, dass die Transparenz für die Betroffenen und die demokratische Öffentlichkeit nachvollziehbar sind. Angesichts der Sensibilität dieser Daten wäre in diesem Bereich noch einiges zutun. Aus diesen Gründen sind wir als Datenschützer seit Langem für eine gesetzliche Grundlage, die für alle Beteiligten Rechtsichereit herstellt".

7• Challenges for Governance

As in other innovative fields, those establishing new biobanks have had to negotiate with regulatory bodies to gain acceptance and approvals for this new way of doing science. As a result, new norms and practices have been developed especially for biobanking. The key challenges for governance can be grouped around: the development of standards, oversight mechanisms and bodies; patient and research participant interests and; articulating the responsibilities and obligations of the custodians of the biobank.

As stated previously, biobanks have challenged traditional governance mechanisms for medical research because they are established as resources to be used by many researchers and research projects. While biobanks are based in a given jurisdiction, the researchers who use them might be located elsewhere. Increasingly, research is conducted at a global level, often involving large international research collaborations that pool and share samples and data. Biobanks can emerge out of these collaborations, or be used as a basis for research carried out by these consortia. This new way of carrying out scientific research has challenged the nationally based systems of governance.

Traditional governance systems for medical research have been developed with the main purpose of assessing individual, hypothesis-based projects where the research is undertaken in one jurisdiction. These systems were not designed to assess interdisciplinary, multi-jurisdictional research involving large numbers of collaborating researchers. The establishment of biobanks as infrastructure and resources built for many different types of research purposes has forced a review of the (traditional) ethical and legal framework that underpins research governance within Europe.[131] Over the past decade, considerable effort has been invested in developing best practices and new models of oversight for the collection, storage and management of samples and data to augment the existing governance system and to address key legal and ethical concerns.

One of the main challenges has been, and still is, to identify ways to protect the autonomy and dignity of patients and research participants and their fundamental rights (e.g. private life and data protection, especially in case of loss of control on personal data/data misuse, discrimination) with fostering the public interest in carrying out medical research to address the central public health challenges (such as cancer, cardiovascular and metabolic diseases). Much effort has been spent on how to design governance systems that protect privacy rights for cross-border research collaborations; how to develop a consent process for biobanks that meets ethical and societal expectations; how to deal with participants' concerns with commercialization and Intellectual Prop-

131 Rial-Sebbag E., Cambon-Thomsen A. Governing biobanks through an infrastructure: ELSI challenges. In Ethics, Law and Governance of Research Biobanks: National, European and International Profiles. Edited by Deborah Mascalzoni, Springer (in press)

erty benefits[132]; and how to maintain public trust and confidence by involving more members of the public. More recently, the use of whole genome sequencing has raised the issue of whether incidental findings to participants should be returned to individuals.[133]

Biobanks have also raised new kinds of ethical issues around the responsibilities and role of custodians of the biobank in relation to research participants and other stakeholders. Other issues are the kinds of ownership rights that exist over the samples in the biobank;[134] how to ensure fair acknowledgement for the establishment of the biobank; and the development of a fair and equitable system of access for researchers wishing to use the biobank. As these issues have not been encountered in this way before, new approaches have had to be developed to address the legal, ethical and social issues that they raise. In this section, we will not attempt to address all of these concerns, but will discuss key challenges that emerge around the existing regulatory framework and the protection of research participant and custodians' interests.

7.1• The lack of a clear legal framework

As stated above, a pan-European legal instrument that lays out clearly the requirements for biobanking that can be understood by all stakeholders does not currently exist. Within the European Union, the principles and legal requirements for biobanking have been drawn from more general documents for data protection and clinical trials – but neither of these directives explicitly covers human tissue. There is a need to review the requirements that apply to the use of human tissue in research within Europe to address this deficit. The margin of appreciation that is given to members states to decide how to implement these European directives has helped to develop diversity in how biobanks are governed across Europe. This has lead many states to develop specific legislation or regulations to cover biobanking, which in turn has lead to further variation in requirements. Despite this, it does appear as if consensus is developing as to common governance structures, norms and practice that are necessary for biobanks in national legal instruments (see 6.1.3.1).

However, diversity in the regulation of biobanking remains and it is difficult to ascertain what the legal requirements are in each country across Europe. A good example is the requirements for secondary use of non-sensitive personal data for research purposes without the consent of the data

132 Greely HT Informed consent and other ethical issues in human population genetics *Annual Review of Genetics* 2001 35 785; S Wilson Population biobanks and social justice: commercial or communitarian models? A comparative analysis of benefit sharing, ownership and access arrangements. *TRAMES* 2004 8(1/2) 80.

133 S Eriksson Should results from genetic research be returned to research subjects and their biological relatives? *TRAMES* 2004 8(1/2) 46.

134 AC da Rocha 'Ethical aspects of human genetic databases: distinctions on the nature, provision, and ownership of genetic information' (2004) 8(1/2) *TRAMES* 34

subjects across Europe. A recent report[135] demonstrated that some Member States fail to provide any safeguards (in manifest breach of the Directive); some lay down minimal (i.e., insufficient) safeguards (e.g. that the data may not be used to take decisions on the data subjects, or may only be used for the research in question); and some lay down rather abstract "balance" tests or only say that the research must be based on an "appropriate research plan". On the other hand, the laws in some countries provide for detailed rules which limit the data and the processing and stipulate that the research must be approved by an academic "ethics committee", or require researchers to apply for a special authorisation from the Data Protection Authority. The resolution of this issue is fundamental to the future of biobanking research.

Diversity in legal requirements will have an effect on the development of a common infrastructure for biobanks and the sharing of data and samples from biobanks across borders for scientific purposes. The importance of addressing this issue has been noted in a report of the European Commission that stated that "New specific laws regarding biobanks have been implemented or are under discussion at national level. The ability to optimise the use of biobanks across Europe is an important basis for ensuring progress in European biomedical science, including in the development of genetic testing and pharmacogenetics. However, effective collaboration is becoming increasingly difficult in a complex world where the principles governing public and private biobanks differ from one country to another".[136]

To address these concerns, the Council of Europe 2006 Recommendation[17] and the OECD Guidelines for Human Biobanks and Genetic Research Databases[51] could provide a basis for the development of a binding legal instrument within Europe. For example, the OECD Guidelines on the Protection of Privacy and Transborder Flows of Personal Data, adopted on 23 September 1980 provided useful elements for the Data Protection Directive 95/46/EC. We feel that the Council of Europe is in a strong position to develop an additional protocol to the Oviedo Convention, specifically on biobanking. Taking into account the major role played by personal data protection rules and principles in the context of biobank-based research, it would be of great benefit if the Article 29 Working Party could be asked to provide an opinion on the data protection implications regarding biobanks. In addition, the differences between the way that data and tissue is regulated for research should be addressed. It should be made explicit that the general principles applied to the use (collection, retention and distribution) of personal data in biobanks should also apply to biological samples to address the current differences in the express legal requirements between these two different entities.

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135 Directorate-General Justice, Freedom and Security, *Comparative study on different approaches to new privacy challenges, in particular in the light of technological developments*, Contract nr: JLS/2008/C4/011 – 30-CE-0219363/00-28, submitted by LRDP Kantor Ltd (Leader) Final Report association with Centre for Public Reform, 20 January 2010, final, 29 (at http://ec.europa.eu/justice/policies/privacy/docs/studies/new_privacy_challenges/final_report_en.pdf)http://ec.europa.eu/justice/policies/privacy/docs/studies/new_privacy_challenges/final_report_en.pdf))

136 Report from the European Commission to the European Parliament, the Council, the Committee of the Regions and the European Economic and Social Committee – Life sciences and biotechnology – A strategy for Europe – Third progress report and future orientations, COM/2005/0286 final

Recommendation 1

Member states and European institutions should develop a consistent and coherent legal framework for biobanking that should protect participants' fundamental rights, in particular in the areas of privacy, data protection and the use of human tissue in research.

7.2• Oversight Bodies

To establish a biobank requires approval and this has to be done by an appropriate oversight body. One of the oversight bodies that are common to most jurisdictions are research ethics committees and they have been responsible for approving biobanks and the research that is carried out on the biobank. However, as outlined previously, the decisions of such bodies can vary between committees, regions and countries and their powers of enforcement are limited to their own jurisdiction. This has the effect of slowing down the research process and potentially the attractiveness of using biobanks.

There is currently no mechanism for the mutual recognition of research ethic committee decisions, or a pan-European research ethics approval. This means that collaborators using the same protocol must apply to the research ethics committee in their own country for ethics approval. The other difficulty with RECs is that their authority is nationally based so there are jurisdictional issues if they wanted to investigate non-compliance with their requirements by secondary researchers not based in their country. This could happen in a situation where samples and information from a biobank was shared with collaborators who were unaware of the conditions of the original research permission.

Such issues are also relevant when (primary) researchers conduct research abroad. As Chalmers explains:

'Establishing procedures for single review of multicentre research, without compromising proper ethical safeguards, is a continuing governance challenge. While facilitating international multicentre research, it is important that researchers conform not only to their own national ethical standards but also to any local ethical standards in the country in which the research is conducted.'[137]

The legal requirements specified above make it clear that there is a legal obligation on member states to guarantee effective protection to participant's rights through the oversight of biobanking activity by independent bodies. Better coordination and collaboration between national oversight bodies (e.g. data protection authorities and ethics committees) would go some way to mitigate some of the concerns about differences in opinions between national bodies. Mutual recognition of decision-making would help to eliminate unnecessary duplication of oversight and compliance requirements, but training would be needed to support this.

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137 Chalmers D. 2011. Viewpoint: Are the research ethics committees working in the best interests of participants in an increasingly globalized research environment? *J. Intern. Med.* 269:392–95

Recommendation 2

There should be better coordination and collaboration between national oversight bodies (e.g. data protection authorities and ethics committees) as well as mutual recognition of decision-making to eliminate unnecessary duplication of oversight and compliance requirements, with training to support this.

7.3• Engaging publics

Biobanks involve many people and raise complex issues that concerns individual participants and their families but also the wider society. One of the challenges of biobanking has been how to engage potential recruits but also to canvas support from the wider public. The importance of engaging the public in all aspects of biobank planning and establishment has been learnt through some of the more high-profile biobanking projects.[138,139,140]

An example is Iceland, where a strong ethical and political body, Mannvernd – the Association of Icelanders for Ethics in Science and Medicine – was formed in direct response to the database project.[141] While the company deCODE genetics had developed a business plan and vision for its biobank project in Iceland, a gap had widened between some parts of the Icelandic society and deCODE that at a certain point could no longer be reconciled. This example demonstrates that it cannot be taken for granted that societies are always in favor of all types of scientific projects especially if they are large in scale. The common feature of biobanks is that they are dependent on taxpayers' money and therefore require strong political support. Different biobank projects have found unique ways to engage with their social environment and in bring together the most relevant 'publics'. To integrate different points of view and maintain support for a biobank is an important task in biobank governance for the future.[142] Public participation and involvement in biobank research and transparency in the operation of biobanks will be essential for linking up biobank research with the goal of responsible innovation.

Another challenge has been how to engage participants in the long-term operation of biobanks. Currently, the examples of a real patient involvement in the creation and governance of a biobank are still exceptional, but there are examples within the rare disease patient community. This is due in part to the limited knowledge that patients and patient groups have of the highly technical

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138 Haddow G, Cunningham-Burley S, Bruce A, Parry S: Generation Scotland: consulting publicsconsultingpublics and specialists at an early stage in a genetic database's development. Crit Public Health 2008; 18: 139–149.

139 Godard B, Marshall J, Laberge C, Knoppers BM: Strategies for consulting with the community: the cases of four large-scale genetic databases. Sci Eng Ethics 2004; 10: 457–477.

140 Burgess M, Tansey J: Technology, democracy, and ethics: democratic deficit and the ethics of public engagement; in Einseidel E (ed): Emerging Technologies: From Hindsight to Foresight. Calgary, University of Calgary Press, 2008, pp 275–288.

141 Palsson G. The rise and fall of a biobank: the case of Iceland. In: Gottweis H, Petersen A, editors. Biobanks Governance in comparative perspective. London: Routledge; 2008. pp. 41–55.

142 Gottweis, H. & Lauss, G. (2011), Biobank governance: heterogeneous modes of ordering and democratization, Journal of Community Genetics, 12/2011, doi 10.1007/s12687-011-0070-0.

field of biobanking, and in part to the limited understanding by researchers of how patients could contribute to biobanks and more widely to research. The success of any biobanking project is certainly directly related to the quality of the biological material, of the scientists involved and of their scientific hypothesis, but more importantly it depends on the trust of participants who accept to donate their samples to be linked to very sensitive information on themselves and their relatives.

However, a cultural revolution is slowly happening as over the last two decades some patient groups not only have advocated for the constitution of disease specific biobanks, but have also invested their budget in the establishment of new sample collections or even in the creation of brand-new biobank infrastructures. Examples are the Généthon DNA biobank for genetic diseases in France,[143] the US-based Angioma Alliance[144], Bank On A Cure (a myeloma-specific DNA bank) in the USA[145], and the Genetic Alliance PXE Biobank[146]. The need to secure the trust of participants has been taken into account also by several recent population biobank projects such as UK Biobank[147] and the Canadian CARTaGENE project.[148]

In addition, new forms of governance incorporating deliberative democracy techniques[149] have been applied in biobanks such as the Mayo Clinic Biobank.[150] These mechanisms involve patients and research participants in the policy and decision-making of the biobank. Others have proposed that in order to overcome the inadequacies of the informed consent process, which focuses on individuals and is at the beginning of the research process, that research participants and members of the public are involved as active members on the key committees within the governance framework of the biobank itself.[151]

Recommendation 3

For European biobanks to operate successfully there need to be sustainable governance mechanisms to involve and engage the public, and in doing so ensure their continual participation, trust and support.

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143 The Genethon DNA and Cell Bank is driven by the French Association against Neuromuscular Diseases (AFM).

144 http://www.angiomaalliance.org/

145 http://myeloma.org/PortalPage.action?tabId=4&menuId=129&portalPageId=9

146 The American Genetic Alliance Biobank that was set up in 2003 by the Genetic Alliance. The biobank is based on the organisational strategies of the PseudoXantoma Elasticum (PXE) International, an advocacy group set up by two parents whose children were diagnosed with the incurable condition PXE.

147 www.ukbiobank.ac.uk/ see BOX 3 above

148 www.cartagene.qc.ca/

149 K O'Doherty,K. Ibrahim T., Hawkins A., Burgess M., Watson P. Managing the Introduction of Biobanks to Potential Participants: Lessons from a Deliberative Public Forum Biopreservation and Biobanking. February 2012, 10(1): 12-21. doi:10.1089/bio.2011.0029.

150 http://mayoresearch.mayo.edu/biobank/index.cfm

151 O'Doherty K., 2011 From Consent to Institutions: Designing Adaptive Governance for Genomic Biobanks *Soc. Sci. & Med.* 73 : 367-374

7.4• Protecting the Interests of Participants

Medical research governance is concerned with protecting the interests of research participants, but biobanking activities have led to the development of new approaches and ways of dealing with these concerns. In this section, we focus on the most significant changes that have occurred in research governance to accommodate biobanking and enable the protection of research participants.

7.4.1• From informed consent to broad consent

The fundamental principle that underpins the governance framework for medical research is that individual research participants must be respected. One way that this is demonstrated is through the requirement that consent must be obtained from research participants before the research commences and this should be informed and voluntary. This is a fundamental requirement for medical research and is enshrined in guidelines such as the Declaration of Helsinki[152]. In practice, there are a number of different kinds of consent, from explicit through to broad consent that are used in different types of research, which must be justified in the public interest or according to law.

The requirement that there must be consent is reinforced by a number of procedures, practices, policy and legal requirements that have developed over time. Within most countries medical research proposals must be reviewed by Research Ethics Committees (RECs) or Institutional Review Boards (IRBs) before the research commences. Biobanks raise particular concerns and have challenged this orthodoxy as it is not possible to stipulate all of the research uses of samples and data contained in the biobank at the time that participants are recruited into a biobank. This is contrary to traditional requirements of informed consent as outlined in the Declaration of Helsinki and the Clinical Trials Directive. However, the law also allows a deviation from the requirement of informed consent if this is authorised by an ethics committee or some other supervisory body.

Broad consent has become a practical solution to this problem and now is the norm for biobank recruitment. Participants are asked to consent to the use of samples and data within a biobank, at the time of collection rather than to a specific project or types of research as specified in traditional formulations of informed consent. The use of broad consent has lead to a heated debate within the bioethics community as to whether this is ethically appropriate. It is also something that the general public are uncertain about as demonstrated in the Eurobarometer report (see 5.2.1).

7.4.2• Protecting privacy and data protection

Biobanks collect large amounts of different kinds of information on many individuals over long periods of time. The aim is to build up detailed datasets on individuals to identify the etiology of disease and the complex interactions between genes, environment and lifestyle. There is a growing

152 World Medical Association (WMA). 2008. *World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects*. Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, amended in 1975, 1983, 1989, 1996, 2000, 2002, 2004, and 2008. http://www.wma.net/en/30publications/10policies/b3/

awareness of the scientific need for well-characterised case studies of disease as well as large datasets that can be used for population studies. The detailed nature of the data held in a biobank, particularly as exome / whole genome sequencing becomes more common, raises issues about how best to protect individual privacy and the confidentiality of the data.

Finding ways to maximize the research use of data while protecting the interests of research participants is a constant tension in the oversight of biobank research. To facilitate this, best practice has been to remove identifiers and to give each research participant a code. The code is then encrypted for use by outside researchers. Although patient information and biospecimens are not provided to researchers in an identifiable form, they must remain potentially re-identifiable by the custodians of the biobank to allow the on-going linkage of different sources of data to the one individual. Therefore, it is necessary to be able to have a means to go back to individuals and link information on a continual basis. The difficulty with such rich and detailed datasets is that the indirect disclosure risks increase over time. With the addition of whole genome sequencing information, that is unique to individuals, the potential to 'distinguish' an individual in a dataset increase.[153,154]

The Eurobarometer research shows that privacy is a key issue for the general public (5.2.1). This issue should be carefully considered as part of the governance mechanisms put in place for a biobank, but also these safeguards should be communicated as part of an ongoing public engagement exercise.

7.4.3• Returning benefits

There is a growing need to optimise the use and value of the biological sample by constantly updating the clinical status of the donor/patient. This challenge is slowly changing the nature of the relationships between the biobankers and the patients and will inevitably impact any future revisions of sensitive data management policies. A recent pilot study conducted by Salvaterra et al.,[155] among a group of researchers working in biobanks handling samples and data derived from children in some European countries is indicative of how the relationships between biobankers/researchers and patients is changing. The survey reported that researchers expressed a preference to keep a link with patients from whom biospecimens and data were stored to provide them and/or their relatives with relevant information on ongoing studies. This would mean that there would have to be reversible anonymisation of the biological samples so that results could be returned to the participants and their families. However this challenges the existing regulatory framework that makes a distinction between the responsibilities of clinicians and researchers. In research

153 Homer N, Szelinger S, Redman M, Duggan D, Tembe W, et al. 2008. Resolving individuals contributing trace amounts of DNA to highly complex mixtures using high-density SNP genotyping microarrays. *PLoS Genet.* 4:e1000167

154 Malin B, Karp D, Scheuermann RH. 2010. Technical and policy approaches to balancing patient privacy and data sharing in clinical and translational research. *J. Investig. Med.* 58:11--18

155 Salvaterra, E. et al. Pediatric Biobanking: A Pilot Qualitative Survey of Practices, Rules, and Researcher Opinions in 10 European Countries *Biopreservation and Biobanking* Vol 10, No 1, 2011.

projects there is no responsibility to return results to individuals whereas this is the main concern of a clinician.

In the case of chronic and genetic diseases such long-term interaction and exchange of information is paramount not only to establish and increase the trust of families in the researchers responsible for the storage and use of their biological samples, but also to ensure the establishments of a two-direction exchange of information on the results of the research and on the progression of the disease. The update of the clinical data associated to each sample is in fact, key to increase the value of the sample and to allow a meaningful correlation between the results of the research and the disease specific features. The challenge is how to develop the biobanking policy and management pathways to enable this to happen.

Recommendation 4

Sustainable governance mechanisms for creating a relationship of reciprocity between biobanks and European society need to be encouraged so that Europeans can understand and obtain the benefits from biobank research.

7.5• Custodian's interests

Biobanking has developed a new way of working and has raised a number of issues for the custodians of the biobank – the people who are responsible for its establishment, curation and long-term management. Custodians have had to understand their responsibilities and obligations to research participants, funders, institutions and researchers who may want to access the resource. Articulating these different responsibilities has been essential for custodians and to help maintain public trust.

One of the challenges has been how to reward and recognise the effort and expertise involved in establishing a biobank. In the past, there was a direct link with the researcher who set up a data set, who would use it for their own research and the basis for many publications. In biobanking the relationship between the custodian and the biobank is very different, as it is established as a resource that is open to others. The custodian of the biobank may, or may not, carry out research on the biobank. Therefore the traditional ways of recognising researchers through publications which then leads on to career advancement is difficult for the custodians of biobanks. 'Many journals require that data production should be acknowledged, but how this is done is largely left up to individuals, who follow the norms that exist in their particular discipline.'[156]

156 Kaye J, Heeney C, Hawkins N, de Vries J, Boddington P. ´Data sharing in genomics – re-shaping scientific practice´. *Nat Rev Genet* 2009*;* Vol. 10, pp. 331-335

8• Innovations in Biobanking Governance

In response to the challenges mentioned in the previous chapter, new governance mechanisms have been proposed and adopted to enable biobanking to proceed. The purpose of this section is to document some of the important innovations that have been developed to date. Some of them use information technology to offer best privacy protection or to enable greater patient participation. Increasingly information technology is being used to enable research but also potentially as a form of governance – or e-governance.[157]

8.1• European Research Infrastructure Consortium (ERIC)

In 2009, in response to concerns about the legal differences that existed across Europe and the effect that this was having upon biobanking, the European Union agreed to create a new Community legal framework for biobanking. This has taken the form of a European Research Infrastructure Consortium (ERIC).[58, 158] This allows activities to be undertaken under a common legal structure.

The preparatory phase for networking biobanks has taken place through the BBMRI (BOX 6)[54] which is the body that has applied to become a BBMRI-ERIC. The BBMRI has submitted an application to the Commission which should assess, with the help of independent experts whether the proposed research infrastructure is in conformity with regulation. In particular, the evaluation will take into account the need for a declaration of the host Member State recognising the ERIC as an international body. This must be done by member states rather than individual research teams.

The application must emphasise the added value of implementing such an infrastructure at the European level and must provide statutes defining the role of each partner, the financial contribution, the voting rules and the internal governance of the infrastructure. The ERIC can propose various "common services".

To date, in life sciences research, the ECRIN (European Clinical Research Infrastructures Network) is the only consortium that has applied for such a statute in July 2011. BBMRI will probably do the same during 2012. Until then, BBMRI will rely on the various national hubs set up since the end of

157 Kaye J. From single biobanks to international networks: developing e-governance. *Hum Genet.*. 2011; Vol. 130, No. 3, pp. 377-382.

158 Council Regulation n° 723/2009, 25 June 2009

the preparatory phase in the following countries: Sweden[159], Italy[160], The Netherlands[161], Norway[162], Finland[163], France[164] and Denmark[165]. All research fields are potentially concerned, including the life sciences, in order to facilitate scientific cooperation at the European level and to avoid national legal disparities.

8.2• New Advisory Bodies

At the same time, new oversight bodies have emerged which operate within the existing regulatory/ethical structures but are designed especially for biobanks. As part of the governance structure, biobanks will typically have a scientific advisory board and data access committee. These bodies have been seen as essential for transparency and accountability and ensuring confidence in the governance of the biobank.

The Ethics and Governance Council (EGC) of UK Biobank is an example of an advisory body attached to a biobank. It is an independent guardian of the UK Biobank's Ethics and Governance Framework and is tasked to advise on the best ethical practice to provide a sound basis for fostering public trust and confidence in the project. These bodies have been seen as a flexible way to make policy beyond the limits of the law.[166]

Biobanks also will have access committees to protect research participants' interests but also to ensure that the resource is not depleted or misused. These bodies have the ability to make case by case decisions that are sensitive to the local biobank and how it has been established. In doing so the chain of trust between participants and custodians is maintained.[167] A possible future difficulty with these bodies is that they may have the effect of slowing down research if a new application is needed for every new research project when samples and data are drawn form a number of biobanks for composite research projects. It is important that these bodies work together with

159 http://www.bbmri.se/en/

160 http://www.bbmri-eric.it/

161 http://www.bbmri.nl/

162 http://www.forskningsradet.no/servlet/Satellite?c=Informasjonstekst&cid=1253961994504&pagename=infrastruktur%2FHovedsidemal

163 http://www.bbmri.fi/fi/

164 http://www.crbfrance.fr/

165 http://www.ssi.dk/Service/OmSSI/Organisation/Organisationsdiagram/Afdeling.aspx?id=e4091b0d-0269-4445-9fe5-9db500a0483e

166 Laurie G. Reflexive governance in biobanking: on the value of policy led approaches and the need to recognise the limits of law. *Hum Genet*. 2011 Sep;130(3):347-56.

167 Anderson NR and Edwards KA Building a chain of trust: using policy and practice to enhance trustworthy clinical data discovery and sharing. ACM Annual Meeting December 2010. Accessible at: http://www.acsac.org/2010/workshop/p15-anderson.pdf.

more formal oversight bodies to develop an efficient meta-level system of governance within Europe that will allow research to proceed efficiently but also will protect stakeholder interests.

The various international bodies that have been influential in shaping and developing policy in this new field should be approached to help develop this governance strategy, as they represent practitioners working in the field. Examples of these bodies are: Biomedical Informatics Grid[168] and European Prospective Investigation into Cancer and Nutrition[169] (cancer); Public Population Project in Genomics; and PHOEBE[170] (population biobanks); EuroBioBank (rare diseases)[171]; GenomeEUtwin[172] (sib and twin cohorts); TuBaFrost[173] (frozen human tissue bank); and NUGENOB[174] (nutrition and obesity) and the International Society of Biological and Environmental Repositories (ISBER)[175].

Recommendation 5

The new governance bodies that have emerged specifically for biobanks should be integrated into the existing governance system to help to develop a meta-governance system for biobanking within Europe.

8.3• Embedding Biobanks in Clinical Care

One solution to the financial insecurity that biobanks face is to embed them within the healthcare structure. A model that embeds a biobank within clinical care is the CuraRata model[176], which has been recently developed at Leiden University in the Netherlands. It provides an example of how a biobank can be embedded within the healthcare structure and used for the dual purpose of diagnosis and research. It is designed to promote personalised medicine and ensures the financial sustainability and attractiveness of biobanks for clinicians, researchers and/or the industry.

The CuraRata strategy consists of four major steps: a) ascertainment – where an individual strategy is customized for each patient who consents to storage and resampling of their biological materials together with associated medical data; b) collection – whereby a given patient continu-

168 http://cabig.nci.nih.gov

169 http://epic.iarc.fr/ centers/iarc.php

170 http://www.phoebe-eu.org

171 http://www.eurobiobank.org/

172 http://www.genomeutwin.org/

173 http://www.tubafrost.org

174 http://www.nugenob.org

175 International Society for Biological and Environmental Repositories (ISBER). 'Best practices for repositories: collection, storage, retrieval and distribution of biological materials for research'. *Cell Preserv. Technol.*, 2008, Vol. 6, pp. 3–58; http://www.isber.org/Pubs/BestPractices2008.pdf.

176 http://www.curarata.nl/uk/25/patients/about-us/curarata-the-basics.html

ously supplies data, samples and receives relevant feedback from ongoing medical research; c) data consolidation and comparison – where data from patients suffering from similar conditions are integrated and analyzed by cutting-edge methodologies; and d) adjustment – which involves customization of patient´s individual medical care based on the outcomes from steps a) to c). However, developing this model so that it can be applied more broadly in other healthcare systems in different countries will require resources and shared learning.

Recommendation 6

To ensure their sustainability, biobanks need to become embedded in the public healthcare structure as valuable resources that can be used for clinical care, personalized medicine and translational research.

8.4• e-governance Solutions

The use of Information technology to enable good practice and to address some of the ethical, legal and social challenges that are created by biobanking has enormous potential. There is the possibility to develop a system of e-governance that will integrate existing systems of expert review with technologically based forms of governance. This approach is just starting to be developed but it offers great potential to help address the ethical, legal and social issues (ELSI) raised by biobanks but also to enable new forms of governance to emerge. By designing these solutions with these considerations in mind we start to move to a situation where these concerns are embedded deeply within the governance structures as 'ELSI by design'. This is equivalent to the concept of 'privacy by design' but also has the potential to be far broader. 'Privacy by design' is where privacy and data protection are embedded throughout the entire life cycle of technologies, from the early design stage to their deployment, use and ultimate disposal.[177]

Recommendation 7

Greater investment should be made in the development of e-governance tools to embed "ELSI by design" solutions, which can be used to augment existing governance structures and facilitate the sharing of samples and information between biobanks and researchers at a meta-level.

8.4.1• Dynamic Consent

The potential to use information technology and web 2.0 technologies to involve participants in research and to obtain consent has been developed for biobanking in the EnCoRe[178] and the

177 European Commission, *A Digital Agenda for Europe*, EUC, 26/8/2010, COM(2010) 245 final/2.

178 EnCoRe / Oxford Radcliffe Biobank (UK) http://cyber.hwcomms.com/cyber/DynamicConsent

CHRIS[179] projects for biobanks. The dynamic consent model developed through the EnCoRe project provides a tool to enable participants in a biobank to give consent to the use of their samples over a long period of time. Individual consent can be obtained from research participants – not just at the beginning of the consent process but on a continuous basis. This allows a more continuous and interactive relationship with participants – or a dynamic consent – rather than the one off broad consent that is currently the only practical solution for many projects or biobanks. These systems allow patient samples and data to be tracked across research studies to remove bias and erroneous identification and provide a mechanism for re-contacting individuals for recruitment into new studies, as well as being used as a basis for cutting down on research ethics oversight for secondary research.[180] These initiatives are part of broader movement to use Web 2.0 technologies to engage people in medical research in general.[181]

Recommendation 8

The potential to use web 2.0 technologies to involve patients, research participants and the wider public, in the governance of biobanks should be supported to ensure that Europeans can have trust in biobank research and those organizations that establish and maintain biobanks.

8.4.2• Protecting privacy

There are a number of initiatives that are already underway that could form the basis of a digital global governance system. For example, DataSHIELD enables simultaneous parallelized analysis of the individual-level, harmonised data of each study without data having to leave its location. 'Only anonymous summary-statistics, results or aggregate information can be shared with other researchers in other institutions. This means that individual-level data never leaves the collecting organisation and there is no breach of European data protection law or research governance requirements.[182] This has the benefits of protecting privacy but also restricting the amount of data that is transferred. These mechanisms could be used for biobanks but also research projects.

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179 CHRIS – Cooperative Health Research in South Tyrol (Italy) http://www.eurac.edu/en/research/institutes/geneticmedicine/chrisstudy/default.html

180 Kaye J. From single biobanks to international networks: developing e-governance. *Human Genetics*. 2011; Vol. 130, No. 3, pp. 377-382.

181 Kaye J, Curren L, Anderson N, Edwards K, Fullerton SM, Kanellopoulou N, Lund D, Macarthur DG, Mascalzoni D, Shepherd J, Taylor PL, Terry SF, Winter SF. From patients to partners: participantcentric initiatives in biomedical research. Nat Rev Genet. 2012 Apr 3. Epub ahead of print.

182 Wolfson M, Wallace SE, Masca N, Rowe G, Sheehan NA, Ferretti V, LaFlamme P, Tobin MD, Macleod J, Little J, Fortier I, Knoppers BM, Burton PR (2010) DataSHIELD: resolving a conflict in contemporary bioscience—performing a pooled analysis of individual-level data without sharing the data. *Int J Epidemiol* 39:1372–1382.

8.4.3• Rewarding custodians

One of the new ethical concerns is how to recognise the efforts of those who have established the biobank and maintain it. There is the potential to use digital identifiers as governance tools. The concept behind a biobank research impact factor is to provide a global register that could be used for biobanks or other repositories.[183] By giving a unique identifier to to a biobank, it could be used to record the use of biobanks in publications and funding grants. The ORCID ID[184] is currently being developed to track individual researchers' publications. There is the possibility that an ORCID ID could be used to verify a researcher's *bonafides* for carrying out research on a biobank.[185] . Another innovative initiative to create incentives for the sharing of bio-resources is the concept of a bio-resource research impact factor[186] (BRIF). The BRIF initiative is developing a framework for creating a tool for calculating the research impact of bioresources (based on a metric (algorithm) and a unique digital resource identifier) and for assessing requirements for citation/acknowledgement of bioresources, in order to trace their use in research.

Recommendation 9

New accreditation systems need to be developed to reward and acknowledge the effort of scientists who establish and build biobanks.

183 Cambon-Thomsen A, Thorisson GA, Mabile L, BRIF workshop group (2011) The role of a bioresource research impact factor as an incentive to share human bioresources. Nat Genet 43:503–504.

184 http://www.orcid.org

185 Thorisson GA (2011) ORCID and data publication—identifying knowledge contributors to motivate sharing. Data Citation Principles Harvard (via slideshare)

186 Cambon-Thomsen A and al., The role of a Bioresource Research Impact Factor as an incentive to share human bioresources, Nat Genet. 2011 Jun;43(6):pp. 503-504.

9• Conclusion and Recommendations

The challenge for the future of biobanking within Europe is how to develop meta-level governance that supports a pan-European biobanking infrastructure. Currently regulatory systems are not aligned to enable the easy sharing of samples and data in ethical and legally compliant ways across borders. This does not facilitate cutting-edge research across borders in the most efficient and economical manner. The governance structure for medical research needs to move from being designed around 'one-researcher, one-project, one-jurisdiction' model to enable the flow of samples and data between biobanks as part of regional/global networks for research. One way to achieve this is to use information technology to develop e-governance systems that can increase the transparency of the research done and augment existing expert committee review and national systems of oversight. This will enable biobanks to become component parts of the healthcare structure and a tool to enhance a personalised medicine approach to healthcare, respecting the participants' fundamental rights and researchers' needs. Any future developments should be undertaken in consideration of efforts elsewhere in the world.

Recommendations:

1. Member states and European institutions should develop a consistent and coherent legal framework for biobanking that should protect participants' fundamental rights, in particular in the areas of privacy, data protection and the use of human tissue in research.

2. There should be better coordination and collaboration between national oversight bodies (e.g. data protection authorities and ethics committees) as well as mutual recognition of decision-making to eliminate unnecessary duplication of oversight and compliance requirements, with training to support this.

3. For European biobanks to operate successfully there need to be sustainable governance mechanisms to involve and engage the public, and in doing so ensure their continual participation, trust and support.

4. Sustainable governance mechanisms for creating a relationship of reciprocity between biobanks and European society need to be encouraged so that Europeans can understand and obtain the benefits from biobank research.

5. The new governance bodies that have emerged specifically for biobanks should be integrated into the existing governance system to help to develop a meta-governance system for biobanking within Europe.

6. To ensure their sustainability, biobanks need to become embedded in the public healthcare structure as valuable resources that can be used for clinical care, personalized medicine and translational research.

7. Greater investment should be made in the development of e-governance tools to embed "ELSI by design" solutions, which can be used to augment existing governance structures and facilitate the sharing of samples and information between biobanks and researchers at a meta-level.

8. The potential to use web 2.0 technologies to involve patients, research participants and the wider public, in the governance of biobanks should be supported to ensure that Europeans can have trust in biobank research and those organizations that establish and maintain biobanks.

9. New accreditation systems need to be developed to reward and acknowledge the effort of scientists who establish and build biobanks.

Annex 1: Survey of Biobanking activities in Europe

As part of the 2010 IPTS/ESTO study "Biobanks in Europe: Prospects for Harmonisation and Networking", a structured questionnaire was sent to 176 European biobanks, identified through various sources, with 126 subjects returning their partial or full answers[41]. Response behavior was mainly influenced by a) reluctance of survey participants to provide commercially sensitive information, b) in some instances there was general caution to disclose information (e.g. in Eastern Europe), c) there was a lack of consistent terminology and variable interpretation of European regulation which led to confusion, including d) language issues.

It must be noted that despite their size and strategic importance it was impossible to gather information on biobanks collected by private pharmaceutical companies, which mostly operate at a transnational basis. Another important consideration is the fact that consent practices for biobank donors are not standardized, and in some instances (e.g. in Eastern Europe) even absent, which may present a "moral hazard" for the entire field of biobanking.

The majority of biobanks were found in Scandinavia (Denmark, Sweden), followed by the United Kingdom, Hungary and Romania. Approximately 80% of European collections are public with majority of them located at universities or national/ regional research institutions. However, most of them are small to medium size, consisting mainly of DNA, serum and whole blood and, to a lesser extent, tissue samples stored under diverse conditions. The quality of sample annotation is also very heterogeneous. Furthermore, almost 70% were single collections, functioning within isolated and heterogeneous informatics systems.

Given the predominantly public and generally academia-based character of surveyed biobanks, a) access was free in two thirds of all instances, b) scientific peer-to-peer collaborations were strong, and c) in approximately 86% of all cases, ethics boards are responsible for biobank operations. Another positive feature is related to the fact that about 74% of surveyed biobanks do not plan to discontinue their sampling in the near future[41].

The strong research potential of biobanks is generally understood and has been supported by university hospitals or research institutions in which these biobanks are predominantly located. Interestingly, given the academic hospital-based ascertainment, the majority of biobanks protect the privacy of their donors only by coding (similar to routine clinical data operations within hospital databases and/or laboratory information systems) and 57% of biobanks reported data back to the patient. In this context reidentification of donors is possible and reporting of actionable results back to the patients was generally viewed as positive and supportive of sustainable recruitment of donors. Terminology and related concepts of sample anonymization were commonly misunderstood and led to confusion, thereby hindering proper review of current practices. Biobank links to disease registries were generally considered as being useful[13,14,15]. Typical examples of such

mutually beneficial collaborations include Umea and Malmö biobanks, which operate within the Swegene research framework[187].

There are also successful models of public–private collaborations in the area of biobanking, with several projects identified e.g. in Scandinavia[41]. The European survey provided evidence that intersectoral research was carried out primarily by academic scientists who had worked in close collaboration with their industrial partners. There were no accounts of intersectoral transfers of "academia-based" biological materials. The general notion coming out of the survey was that industry is mainly interested in collaboration, rather than in the biological materials themselves. This may reflect a pragmatic approach on the part of industry given a) the continuous recruitment of donors, and that b) the potential of updating sample data annotation could only be efficiently carried out, at low costs, within an academic hospital setting. Contemporary industrial research mostly utilizes HGRDs due to their easier standardization and relatively lower sample quality requirements for DNA–based studies. However, further surveys are needed since the reluctance of commercial biobank operators to disclose proprietary information may present a reporting bias with regards to above presented conclusions.

In summary, this survey objectively substantiated the wealth of biobanking activities in Europe. Furthermore, strong evidence was presented for the creation of an international umbrella or network organisation that would foster harmonisation and standardisation of biobank practices[93]. As in other areas of biomedicine, European national activities have the potential to act in concert and thus in aggregate set the stage at the world-wide perspective. A later survey confirmed these outcomes and provided important updates[188]. Continuously updated information on the current status and developments of biobanking in Europe is provided at the BBMRI Portal website[189].

187 http://swegene.omv.lu.se/biobanker/index.php

188 Wichmann HE, Kuhn KA, Waldenberger M, Schmelcher D, et.al. Comprehensive catalog of European biobanks. *Nature Biotechnology 2011,* Vol. 29, No.9, pp. 795-797

189 https://www.bbmriportal.eu

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This expert group report on the ethical and regulatory challenges of international biobank research has been authored by an interdisciplinary group with experts from science, law, governance and ethics.

Biobank research is rapidly evolving, and in close interaction with developments in informatics and genomics. The size and breath of the collections of biological samples and associated data that can be assembled has increased exponentially. This opens up a vast range of new options for research and diagnosis, but at the same time also holds an important challenge for the governance of these activities. In this report, the expert group makes specific recommendations for good governance of Biobanks

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