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OPEN BIOBANKS
Reframing intellectual property rights in biobanking

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ABSTRACT

This thesis faced the challenge of answering the question if intellectual property rights that are created by the biobanks can be managed more openly to ensure the equitable distribution of knowledge and improvements of the genetic research. The proposal is made to encourage the biobanks to use more broadly open licenses in their copyrighted works, databases and patented inventions. To ease the transfer of knowledge between biobanks and ensure that the genetic research is improving, the reflection to apply open licenses is made. The thesis describes the open sharing model and supports the possibilities to use IP rights in a non-restricting way.

The thesis also proposes to use broad informed consent in the biobanks' activities. Broad informed consent would ensure the right balance between individual rights and biobanks' need to share collected information, especially, because there are incentives to treat human genetics as a common good. Open consent can be used in the biobank's activities to ensure that the tissues are not left unutilised. Such form of consent can assure the maximum value of the collected biological tissues. If collected samples are not restricted to the one-time or one-research use, we can expect that other studies perform research on the same samples and the broader scientific information is presented.

Keywords: open biobanks; intellectual property rights; open licenses; broad informed consent.

RESUMEN

Esta tesis se enfrentó al reto de resolver la cuestión sobre si los derechos de propiedad intelectual creados por los biobancos pueden gestionarse más abiertamente para garantizar la distribución equitativa del conocimiento y las mejoras de la investigación genética. Se propone fomentar que los biobancos usen licencias más abiertas en sus obras protegidas por derechos de autor, bases de datos e inventos patentados. Para facilitar la transferencia de conocimiento entre biobancos y garantizar que la investigación genética mejore, se realiza una reflexión sobre la aplicación de licencias abiertas. La tesis describe

el modelo de intercambio colectivo y apoya la posibilidad de usar derechos de propiedad intelectual de forma no restrictiva.

La tesis también propone el uso del consentimiento informado amplio en las actividades de los biobancos. Un consentimiento informado amplio garantizaría el equilibrio adecuado entre los derechos individuales y el derecho de los biobancos de compartir la información recogida, especialmente, porque existen incentivos para tratar la genética humana como patrimonio común. El consentimiento abierto puede usarse en las actividades del biobanco para garantizar que los tejidos no permanecen sin uso. Este tipo de consentimiento puede asegurar el máximo valor de los tejidos biológicos recogidos. Si las muestras recogidas no están restringidas a un solo uso o a una sola investigación, podemos esperar que otros estudios lleven a cabo investigaciones sobre las mismas muestras y se presente información científica más amplia y relevante.

Palabras clave: biobancos abiertos, derechos de propiedad intelectual, licencias abiertas, consentimiento informado “amplio”.

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ABBREVIATIONS AND ACRONYMS

BBMRI	Biobanking and Biomolecular Resources Research Infrastructure
Bermuda Principles	The principles of accelerated data release, developed from 1996-1998 during the international Human Genome Project
Biotechnology directive	Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions
CC	Creative Commons organization/license
cDNA	DNA synthesized from a single stranded RNA template in a reaction catalyzed by the enzyme reverse transcriptase.
CIOMS	Council for International Organizations of Medical Science
CJEU	Court of Justice of the European Union
CNIO	Spanish national cancel research center
Common Rule	US Federal Policy for the Protection of Human Subjects
Convention on Human Rights and Biomedicine	Convention for the protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (adopted 04 April 1997, entered into force 01 December 1999) ETS No.164

Database directive	Directive 96/9/EC of the European Parliament and of the Council of 11 March 1996 on the legal protection of databases OJ L 77, 27.3.1996, p. 20–28.
DDBJ	DNA Database of Japan
ENA	European Nucleotide Archive
EPC	The European Patent Convention (16th edition)
EPIC	The European Prospective Investigation into Cancer and Nutrition
EPO	European Patent Office
ESHG	European Society of Human Genetics
EU	European Union
EC	European Commission
FDA	US Food and Drug Administration
GA4GH	Global Alliance for Genomics and Health
GDPR (General Data Protection Regulation)	Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive

	95/46/EC.
HeLa cells	Cells taken from female Henrietta Lacks, that can divide in the laboratory.
HGP	Human Genome Project
HIPAA	Health Insurance Portability and Accountability Act of 1996
HUGO	Human Genome Organization
ICMJE	International Committee of Medical Journal Editors
INSDC	The International Nucleotide Sequence Database Collaboration
IPR	Intellectual property rights
IRB	Institutional Review Board of the Biobank
ISBER	International Society for Biological and Environment Repositories
NCBI	National Center for Biotechnology Information
NIH	U.S. National Institutes of Health
OECD	Organization for Economic Cooperation and Development

PCT	Patent Cooperation Treaty
R&D	Research and Development
REC	Research Ethics Committee
PSI Directive	Directive 2003/98/EC on the re-use of public sector information
SME	Small and Medium-sized Enterprises
TRIPS	Agreement on Trade-related Aspects of Intellectual Property
UN	United Nations
UNESCO	United Nations Educational, Scientific and Cultural Organization
WCT	World Intellectual Property Organization Copyright Treaty
WIPO	World Intellectual Property Organization
WMA	World Medical Association
WTO	World Trade Organisation

INTRODUCTION

I. Intangible assets in biobanking (or where is the problem?)

In 1950, Henrietta Lacks, a young mother of five children, entered the colored ward of the Johns Hopkins Hospital to begin treatment for an extremely aggressive strain of cervical cancer[1]. During the treatment, the cells of the cancerous cervical tissue was taken without her knowledge or consent and given to the hospital personnel performing tissue research. Researchers at that time were attempting to create an immortal line of human cells that could be used in medical research. Unexpectedly, Henrietta's cells (later named HeLa) started to proliferate. Days and weeks later the cells were still dividing in the lab. Astonishingly, HeLa cells were still "alive" long after Henrietta Lack has passed away.

Many types of research and doctors used immortal HeLa cells. A search of the U.S. Patent and Trademark Office database turns up more than seventeen thousand patents involving HeLa cells. Moreover, there's no way to quantify the professional gain many scientists have achieved with the help of HeLa.[2]

At that time when the cells were taken from the woman's body, no issues of the protection of personal data, informed consent was raised. Not to mention that nobody has considered the possibility of intellectual property rights that the HeLa cell can generate. Henrietta and her family have profited little if anything from the use of HeLa. Henrietta have never known that her cell has been taken, the family members have been informed a long time after the cells have already been multiplied and used for various purposes (no one told her family that the cells existed until the '70s, when scientists wanted to do research on her children to learn more about the cells[3]).

Today, after more than 60 years have passed, collecting biosamples becomes a norm. With recent advances in molecular biology, human tissue samples have become enormously valuable for medical use. Biospecimens such as blood, surgical tissue, saliva, and urine contain genetic material that researchers analyze to identify gene variations associated with human diseases[4].

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1 Rebecca Skloot, *The Immortal Life Of Henrietta Lacks* (Broadway Paperbacks 2010).
2 Ibid.
3 Ibid.
4 Karen J Maschke, 'Biobanks: DNA and Research' in Mary Crowley (ed), *From Birth to Death and Bench to Clinic: The Hastings Center Bioethics Briefing Book for Journalists, Policymakers, and Campaigns* (The Hastings Center 2008) 11.

Human or animal samples are collected and stored in different biorepositories. A type of biorepository called biobank stores biological samples (usually human) for use in research. A biobank is defined as a generally extensive collection of human biological materials (biospecimens) linked to relevant personal and health information and held explicitly for use in health and medical research[5]. Biobanks have become of the relevant importance. Today, mostly all developed countries have public biobanks. Only in European countries, there are around 150 functioning biobanks[6]. Furthermore, to maximize the utilization of biobanking resources, regional and transnational biobank networks, such as the BBMRI-ERIC (Biobanking and Biomolecular Resources Research Infrastructure), the International HapMap Project and the International Cancer Genome Consortium, have been established[7].

Biobanks currently exist on every continent, including Antarctica, with most located in North America and Europe[8]. Even the developing countries like China, Gambia, Jordan, Mexico and South Africa, have placed significant effort into building their biobanks and biobanking networks[9]. Biobanks are growing not only in quantity but also in scope, the amount of data stored in biorepositories. For example, UK Biobank now contains tissue specimens gathered from more than 500,000 middle-aged Britons[10]. This evolution in biologic data research only shows that genetic studies are a powerful tool to investigate genetic, social, environmental and behavioral determinants of human diseases.

Of cause, the spread of biobanks not only resulted in an avalanche of genome-wide association studies but also caused a wide variety of legal and ethical questions, which have not been foreseen when cells samples were started to be collected. Several issues can be flagged with the expansion of biobanks, such as questions about policies governing data sharing and security, privacy and the identifiability of genomic information, how and when to return research results and incidental findings, how governance structures function at genomic repositories, and informed consent issues caused by the multiple uses for samples by genome researchers.

As with Henrietta Lacks case, no consent has been given from the patient when biosamples were taken. The doctrine of informed consent – the requirement to inform participants in a research study of all planned experiments – has been a central component in

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5 Australian Government National Health and Medical Research Council, 'Biobanks Information Paper' (2010) 8.

6 Eleni Zika and others, *Biobanks in Europe: Prospects for Harmonisation and Networking* (2010) 12.

7 Haidan Chen and Tikki Pang, 'A Call for Global Governance of Biobanks' (2015) 93 Bulletin of the World Health Organization 113.

8 Eric M Meslin and K Goodman, 'Biobanks and Electronic Health Records: Ethical and Policy Challenges in the Genomic Age' (2009) Indiana University Center for Applied Cybersecurity Research Workshop: A Research Agenda for Privacy and Security of Healthcare Technologies 5.

9 Projects like H3Africa, China Kadoorie biobank, King Hussein Cancer Center Biobanks can be named as en examples.

10 UK Biobank <http://www.ukbiobank.ac.uk/> accessed 8 May 2018.

research ethics since human-rights abuses (such as experiments on concentration camp inmates in Nazi Germany, and the Tuskegee Syphilis Experiment in which US physicians left victims untreated to study the course of the disease) and resulted in worldwide abhorrence and regulation[11]. Till today a lot has been done in this field, and the obligation to seek permission to obtain and use parts of an individual, whether for research or treatment purposes is among the most settled issues in bioethics and law[12]. The issue in biobanking is not whether to obtain consent, but when, under what conditions and with what degree of specificity.

It has become standard for the consent process to alert potential participants of the potential for research findings to one day become commercialized in the form of tests or products offered in the marketplace[13]. Therefore, donors not willing to take part in research that is going to be commercialised can withdraw. It has also become common to accept that patents or other forms of intellectual property rights may be acquired during the commercialisation process. Moreover, even if the issue of 'gene' patents remains controversial, about 3,000 to 5,000 patents on human genes have been granted in the United States[14]. The patent on a recombinant DNA method was granted in December 1980, six months after the US Supreme Court ruled in Diamond v. Chakrabarty that a life form could be patented[15].

In Europe, a human gene, which existed before but was "hidden" from the public in the sense of having no recognised existence, can be patented when it is isolated from its environment or when it is produced by means of a technical process and as long as its industrial application is disclosed in the patent application[16]. According to Article 53 of the European Patent Convention "methods for treatment of the human <…> body by surgery or therapy and diagnostic methods practiced on human <…> body" shall not be patented. However, gene sequences can be patented as long as the industrial application of the sequence

11 Bernice S Elger and Arthur L Caplan, 'Consent and Anonymization in Research Involving Biobanks: Differing Terms and Norms Present Serious Barriers to an International Framework' (2006) 7 EMBO Reports 662.

12 An equally exhaustive literature exists on consent. See for example, Sass, H. M. 'Genotyping in clinical trials: towards a principle of informed request' (1998) J Med Philos 23(3): 288-96; Shickle, D. 'The consent problem within DNA biobanks' (2006) Stud Hist Philos Biol Biomed Sci 37(3): 503-19; Skolbekken, J.-A., L. Ã. y. Ursin, et al. 'Not worth the paper it's written on? Informed consent and biobank research in a Norwegian context'(2005) Critical Public Health 15(4): 335-347; Stegmayr, B. and K. Asplund 'Informed consent for genetic research on blood stored for more than a decade: a population based study' (2002) BMJ 325(7365): 634-5; Wendler, D. 'One-time general consent for research on biological samples' (2006) BMJ 332(7540): 544-7. Williams, G. and D. Schroeder 'Human genetic banking: altruism, benefit and consent' (2004) New Genet Soc 23(1): 89-103.

13 BM Knoppers and MH Zawati, 'Biobanks' (2012) in Ruth Chadwick (ed), Encyclopedia of Applied Ethics (San Diego: Academic Press, 2012), 246-250.

14 Robert Cook-Deegan, 'Gene Patents' in Mary Crowley (ed), From Birth to Death and Bench to Clinic: The Hastings Center Bioethics Briefing Book for Journalists, Policymakers, and Campaigns (Garrison, NY: The Hastings Center 2008) 69.

15 Ibid. 70.

16 'Biotechnology Patents at the EPO' <https://www.epo.org/news-issues/issues/biotechnology-patents.html> accessed 8 May 2018.

is disclosed in the patent application and all other patentability criteria are fulfilled[17]. In the US the future of gene patenting should distinctly change after the US Supreme Court decision where court unanimously ruled in the case *Association for Molecular Pathology (AMP) et al. v. Myriad Genetics, Inc., et al.*[18] that genes are not patent eligible.

Juridical possibility to patent biotechnological invention, including genes or their sequences, has a great influence in biobank's intellectual policy. Increasing commerciality of biotechnology research could lead researchers to delay the communication of important findings over substantial periods of time to protect commercial interests. Gene patents can become a burden to future researches and restriction to innovation in bio sector. The wish of the researchers and companies to gain a monopoly towards their discoveries, puts at stake here the very understanding of the role of science. The ethics of solidarity and the 'public good' that underpin participation in population biobanks that serve as research infrastructures is weakened by commercialisation that ultimately does not serve these purposes as well[19].

Professor James Boyle maintains that there are many arguments against gene patents (e.g. religion, "common heritage of humanity", creeping commodification of nature, ownership of DNA by people whose bodies contain them, etc.), but most are dismissed by intellectual property scholars as not comprising legitimate discourse[20]. What does the debate over gene patents teach us about the structure of our legal discipline, about our pattern of inquiry? Acquiring intellectual property protection over research outcomes hinders the very *raison d'être* of population biobanks – to further biomedical research through the ideal of the common good. Therefore, I question if gene patenting is the right path to follow for the biobanks, or more widely in the biotechnology sector.

Another question related to patented inventions is arising from the data stored in biobanks. The data, bio samples, shall belong to a patient. However, if a patented invention is based on such samples, has a patient any rights to this intellectual property? To whom the intellectual property rights shall belong? Do the fields "Applicant" and "Inventor" in the patent application are sufficient to dedicate all intangible rights?

No fewer challenges in biobanks are caused by copyrights or databases protection. Could information in biobanks be treated as an object of copyright law? According to the Article 2(5) of the Berne convention of the for the Protection of Literary and Artistic Works *"Collections of literary or artistic works such as encyclopedias and anthologies which, by*

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17 The European Patent Convention Implementing Regulations to the Convention on the Grant of European Patents (with amendments) (1973), Rule 29(3).

18 *Association for Molecular Pathology et al Petitioners v Myriad Genetics, Inc, et al,569 US 576 (2013).*

19 BM Knoppers and MH Zawati, 'Biobanks' (2012) in Ruth Chadwick (ed), Encyclopedia of Applied Ethics (San Diego: Academic Press, 2012), 246-250.

20 James Boyle, 'Enclosing the Genome: What the Squabbles over Genetic Patents Could Teach Us' (2003a) 50 Advances in Genetics 97-122.

reason of the selection and arrangement of their contents, constitute intellectual creations shall be protected as such, without prejudice to the copyright in each of the works forming part of such collections". Does this definition cover databases of genetic sequences? Especially when in the European Union additional legislation[21] protecting *"collections of works or collections of <...> material such as <...> numbers, facts, and data; <...> collections of independent works, data or other materials which are systematically or methodically arranged and can be individually accessed[22]"* has been in effect since already 1996. Not only the databases of the biobanks can fall under the protection of copyright. More typical examples would be software for interviews with participants, health questionnaires, security set-up, bioinformatic-related software, publication materials arising from biobank research.[23]

So far, there is no consensus on intellectual property issues in biobanking. This is an area in much need of ethical guidance. Indeed, in the absence of a clear policy, protracted discussions with those seeking to access the data or samples and protect eventual intellectual property may defeat the very purpose of population biobanks. Despite efforts to simplify the process of securing intellectual property rights (IPR) (e.g. international treaties, centralised patent offices), such rights are still created by national laws and apply only in the countries that grant them. Therefore, the regulations applied in biobanks are either national or even established in internal biobank rules.[24]

In the last three decades, it has been more challenging to balance between the goal of making scientific data highly accessible and encouraging scientists to pursue practical applications of the research by filing patents. The reason of that is increasing commercialisation of academic research that has undermined the traditional Mertonian notion[25] of collaborative science[26]. Efforts to create a practice of data-sharing are indistinguishably linked to the topic of the right way of creating and using intellectual property and publication policies to support data- sharing efforts[27].

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21 Directive 96/9/EC of the European Parliament and of the Council of 11 March 1996 on the legal protection of databases OJ L 77, 27.3.1996, p. 20–28.

22 Preamble of the Directive, para. 17.

23 Edward S Dove and Yann Joly, 'The Contested Futures of Biobanks and Intellectual Property' (2012) 11 Teoría y derecho 135.

24 For example, UK Biobank Ethics and Governance Framework 2007.

25 The term Mertonian norms has been introduced by American sociologist Rober K. Merton in his work 'The Normative Structure of Science' (1942) *The Sociology of Science Theoretical and Empirical Investigations*. Norms are described as four sets of institutional imperatives comprising the ethos of modern science: universalism, communalism, disinterestedness, and organised scepticism. It presents the basic principles on which is based the ethos of science, that is the ethical values shared by all scientists. Because of the practice of this ethos, the activity of the scientists is so productive and so different from the babbling and agitating of the ideologues and of the politicians.

26 Donna M Gitter, 'The Challenges of Achieving Open Source Sharing of Biobank Data' [2010] International Conference on Comparative Issues in the Governance of Research Biobanks: Property, Privacy, Intellectual Property, and the Role of Technology, Department of Legal Sciences of the University of Trento, Italy 3.

27 Gitter (2010) 13.

The sharing between biobanks can also be aggravated by informed consent doctrine; research investigators must provide potential subjects with an evident appreciation and understanding of the facts, implications, and future consequences of submitting biological samples to a biobank[28]. Donors require more accountability, transparency, and information about the research studies they participate in. Even if researchers can overcome their reluctance to share data with one another, open access models of data release are nonetheless difficult to achieve in light of researchers' legal and ethical obligations toward their research subjects[29]. Research participants may decline to participate in scientific research if they are afraid that they will lose control over the use of their tissues. When data and samples are transferred from one researcher to another quickly, it is hardly possible to control such flow of information and detect where the particular sample is.

The question that I aim to address in this thesis is an *empirical* one, that is whether or not the actual use of intellectual property rights and protection of personal rights in biobanks, as they stand today, pose a barrier to research in biotechnology or pharmaceutical fields? Another question, closely related to the first one, is whether the use of open source or open access means can better advance genetic research and benefit social welfare? In other words, who would win if research findings would be freely available to use for all interested parties?

In the research, I will analyse the possibility of creating "open" biobanks, otherwise called open source, open science biobanks or even marked under the Creative Commons licenses. When data is acquired through biomedical research, the terms "open biotechnology" or "open science" means that data from the project is released rapidly into the public domain, including a requirement that data users do not exercise their intellectual property rights in a way that would preclude other users' access to the basic data[30]. Ensuring private data protection in open biobanks would also lead to a better accessibility of bio samples and so better research results.

Thus, for the purposes of this thesis, the key question concerning intellectual property rights and data protection of individuals is whether, different intellectual assets in biobanks can bar, or unduly limit, the genetic research or innovation, creation and entering into the market of a new technology or drug? If so, can and should the intellectual property rights be limited in biobanking field and transformed to open science biobanks?

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28 'Coriell Institute for Medical Research Official Page' <https://www.coriell.org/> accessed 8 May 2018.

29 Gitter (2010) 19.

30 Robin Feldman and Kris Nelson, 'Open Source, Open Access, and Open Transfer: Market Approaches to Research Bottlenecks Market Approaches to Research Bottlenecks' (2008) 7 Northwestern Journal of Technology and Intellectual Property 17-20.

I hypothesize that if we adequately take into account several factors:

- the impact of intellectual property rights to innovation,
- the problem of rare disease research and social welfare,
- the scope and vast of biosamples collected,
- also, the scale of money and investment required:

we will conclude that the goals of biobanks can be better reached using open innovation, open science and open technologies. Indeed, in the absence of a clear policy, protracted discussions with those seeking to access the data or samples and protect eventual intellectual property may defeat the very purpose of population biobanks. Today biobanks do not have sufficient legislative regulations and judicial precedents to address the intellectual property challenges. Thus, as one of a set of building structural protections of the public interest in the biotechnological field, countries will have to address intellectual property questions in structuring their biotechnological markets to ensure maximum social benefit.

II. Defining relevance and framework

The role of genomics in medicine is rapidly and pervasively increasing. Medicine is no longer one size fits all. Collections of human biospecimens promise many ambitious developments, including personalised and precision medicine, and tailored drugs. Genomics knowledge is full of promise for the development of targeted therapies in rare diseases[31]. Genes (or at least their coding regions) comprise only a tiny fraction of human DNA, but they represent the major biological function of the genome and the main focus of interest by biologists[32]. The ultimate goal is to compile a complete list of all human genes and their encoded proteins, to serve as a 'periodic table' for biomedical research[33]. From the very early history of clinical pathology, studies of archived human biological materials including specimens of blood, DNA, but also bone, organs and other tissues have played a prominent role in the diagnosis and treatment of diseases as diverse as cancer, heart disease, diabetes, and stroke, as well as other diseases of significant public health impact[34]. Despite such positive predictions about the research benefits to be achieved through the use of biobank specimens and related information, there is continuing concern that this aim may not be realised any time soon. The reason is a lack of international consensus on appropriate

31 Deborah Mascalzoni, Angelo Paradiso and Matts Hansson, 'Rare Disease Research: Breaking the Privacy Barrier' (2014) 3 Applied and Translational Genomics 23.
32 ES Lander and others, 'Initial Sequencing and Analysis of the Human Genome' (2001) 409 Nature 892.
33 E Lander, 'The New Genomics: Global Views of Biology' (1996) 274 Science (New York, NY) 536.
34 Meslin and Goodman, 4.

regulatory standards, restrictions to use the stored data, limitations of sharing biobank's resources freely.

The aim of this thesis is to construct a proper basis for analysis, with clear operational definitions for what constitutes biobank, what is (or must be) the extent of intellectual property rights in biobanks, what constitutes open source technologies in biotechnology, what is the role of gene patenting in the use of biobanks' data. In this way the research aims to go beyond the simplistic framing that focuses on the static question of specific examples of IP protected information not being available to researchers and society and focuses instead on targets for action: for tools; for scope; and for geography. The significance of the thesis will be in suggesting the possible tools, that would ensure a balanced IP rights protection with the social benefits.

State-of-the-art about IP regulation in biorepositories is inconsiderable. So far there is little research about intellectual property rights in biobanking. The relevant studies about operating biobanks target different questions from my research. A study performed by Laura M. Beskow[35] and others were related to the informed consent doctrine. The group's goal was to create simplified consent form for biobanking that comprises the minimum information necessary to meet ethical and regulatory requirements. The research study by Uppsala University member[36] targets individual rights in biobanking. Another study initiated by the European Commission,[37] addresses issue of biobanks' governance, touches upon ethical problems and donors' data protection. This secondary data, together with the analysis of case studies, legislation and judicial decisions, will form a significant part of a research. However, the main aim of this research is not only to analyse the relevant literature and deal with important historical examples (such as Henrietta's Lack case, Havasupai people's case, etc.) but also to reflect on the empirical study performed. The data acquired from the representatives and researchers from the biobanks are the primary sources of information. Data is gained by performing semi-structured interviews and questionnaires. The qualitative and quantitative forms of analysis from the collected data discloses information about current status of IPR in biobanking. Such methodology ensures a comprehensive and reliable data and a complete and detailed research.

35 Laura M Beskow and others, 'Developing a Simplified Consent Form for Biobanking' (2010) 5 PLoS ONE.

36 Joanna Stjernschantz Forsberg, 'Biobank Research: Individual Rights and Public Benefit' [2012] Doctoral thesis, Uppsala University, Disciplinary Domain of Medicine and Pharmacy, Faculty of Medicine, Department of Public Health and Caring Sciences, Centre for Research Ethics and Bioethics.

37 European Commission Directorate-General for Research and Innovation, 'Biobanks for Europe - a Challenge for Governance' (2012). Available at <http://www.coe.int/> accessed 8 May 2018.

CHAPTER I

FROM BIOBANKING TO BIG DATA

I. Definition of a biobank

The medicine today is developing from reactive approaches – acting when the patient is sick, to proactive – centered on disease therapy for a personalized, predictive, preventive and participatory medicine ("P4 medicine")[38]. The medical treatment, therefore, is being centered towards an individual medicine, having a goal to establish the wellness of the patient not just to cure a disease. It analyses OMICs data (neologism omics informally refers to a field of study in biology ending in *-omics*, such as transcriptomics, proteomics, metabolomics, lipidomics, etc.) and its relations with the general body functions.

Biobanks in this context are playing an important role by providing high-quality biological samples for genomics and functional genomics research.[39] The crucial input of a biobank for genomics/functional genomics research is the availability of high quality-well annotated biological samples. High throughput technologies such as transcriptomics or proteomics employ systems for parallel processing of samples[40]. One could imagine building a collection (library or bank) of genetically different human stem cell lines, which as a whole could more or less be representative for the entire human population and use this as an "in vitro laboratory-based clinical trial"[41]. Cell cultures in such a library with similar specific genetic predispositions can be used to test toxic side effects of a drug, help to identify particular patients at risk, prior to administering the drug. Utilizing an individual genetic profile in prescribing medications for various diseases will prevent unwanted side-effects and allow drugs to work more efficiently.

Since over the last decades, several different types of data were generated, and huge efforts were dedicated to create database repositories for above mentioned purposes. Genetic biobanks are a new organization in the genetics and are largely linked to the rise of cancer

38 José A Bengoechea, 'Infection Systems Biology: From Reactive to Proactive (P4) Medicine' (2012) 15 International Microbiology 55.

39 Ayşe Yüzbaşıoğlu and Meral Özgüç, 'Biobanking: Sample Acquisition and Quality Assurance for "omics" Research' (2013) 30 New Biotechnology 339.

40 Babett Bartling and others, 'Comparative Application of Antibody and Gene Array for Expression Profiling in Human Squamous Cell Lung Carcinoma' (2005) 49 Lung Cancer 145.

41 Christine Mummery and others, *Stem Cells. Scientific Facts and Fiction* (Elsevier 2011) 291.

research and, more recently, the advent of genomics. Whatever their specific background, biobanks are organisations that collect, store, distribute, and analyse biological materials as well as medical and biomedical data associated with these materials. The benefits for the personalized medicine from the data stored in biobanks are double: first, it enables or supports researchers in reproducing and validating the analysis of other labs, and second it allows researchers to analyze data in novel ways and with different methodologies that were not originally considered by the team who generated the data firstly.[42] That is, the samples and data stored or generated by the biobank members or researchers usually can be used more than once and as well, it may be useful for different medical purposes and research. Historically, biobanks have often been linked to a specific issue or question, such as the verification of a diagnostics test, or a specific research question.[43] However, recently the data in biobanks is not necessarily linked with a specific research question. Nowadays it is essential to have data that can be used for different purposes and reused. That is one of the reasons why biobanks are becoming more and more important in the medical sector.

From the day biobanks arose, they have been defined in many different ways. The term "biobank", with its synonyms such as biorepositories, biospecimen resources, biological resource centers, can have more than one meaning. In the beginning, it was assumed that biobanks were merely collections of materials maintained by a cryogenic facility. However more recently they are defined as the collections of samples of human bodily substances, that can be associated with personal data and information on their donors.[44] Any inventory or archive of biological material can be named as a biobank, also because biobank is a very broad term crossing many fields of study e.g. from storage of seeds for agriculture to human samples for medical research[45]. Some other authors define biobank as an entity that receives, stores, processes, disseminates specimens (blood, tissue, urine, saliva etc.) and encompasses the physical location and the full range of operational activities[46].

Biobanks can be described as referring to a hybrid infrastructure that links collections of biological materials obtained from healthy or diseased individuals to diverse collections of medical or biomedical data and including patient records[47]. The common notion, coined by the international scientific and medical literature, defines a biobank as an organized set of

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42 David Gomez-Cabrero and others, 'Data Integration in the Era of Omics: Current and Future Challenges' (2014) 8 BMC systems biology 2.

43 BBMRI Project, 'Biobanks and the Public. Governing Biomedical Research Resources in Europe' (2013) 23.

44 Mark Perry, 'Accessing Accessions: Biobanks and Benefit-Sharing', Comparative Issues in the Governance of Research Biobanks: Property, Privacy, Intellectual Property, and the Role of Technology (2013) 267.

45 Peter Riegman, Maria Grazia Daidone and Jacqueline Hall, 'Biobanking: FAQs' 7. Available at <http://www.ecpc.org/pressroom/news/projects/biobank-faq-eurocanplatform-wp10> accessed 8 May 2018.

46 Jim Vaught, 'International Biobanking: Overview of Key Practices and Policies' (2016)., in The Biomedical & Life Sciences Collection, Henry Stewart Talks Ltd, London (available at <https://hstalks.com/bs/3218/> accessed 8 May 2018).

47 BBMRI Project, 'Biobanks and the Public. Governing Biomedical Research Resources in Europe' (2013) 13.

human biological samples for diagnostic, therapeutic, and research ends[48]. Other authors tend to signify the governance and structure of a biobank, where biobanks are identified as a biomedical scientific/infrastructural development that warrants a political/legal/ethical reaction with the goal to integrate biobanks into the preexisting fabric of regulation, medicine, law and society[49]. The Swiss Academy of Medical Sciences provides the following definition: "Biobanks are systematic collections of samples of human body substances (e.g. organs, tissue, blood, cells etc.) and DNA as a carrier of genetic information. Data that contain information on the donor (demographic data, type of disease etc., but also genetic data) are stored, either together with the samples or separately".[50]

A very detailed description of a biobank has been given by the European Commission: (a) to collect and store biological materials that are annotated not only with medical, but 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 reidentifiable in order to provide clinically relevant information back to the donor; 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[51].

There are few legal instruments regulating the establishment and functioning of the biobanks. I will describe broader those instruments in the later chapters. Some of these instruments define what a biobank is, or describes similar establishments. For example, 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[52] defines the 'tissue establishment' as a tissue bank or a unit of a hospital or another body where activities of processing, preservation, storage or distribution of human tissues and cells are undertaken. It may also be responsible for procurement or testing of tissues and cells (Article 3(o)). The OECD Recommendation on Human Biobanks and Genetic Research Databases aims to provide guidance for the establishment, governance, management, operation, access, use and discontinuation of human biobanks and genetic research database,

48 Antonella de Robbio, 'Biobanks Patents or Open Science' (2013) 13 Woodhead publishing series in biomedicine 6.

49 H Gottweis and K Zatloukal, 'Biobank Governance: Trends and Perspectives' [2007] Pathobiology 206–211.

50 Swiss Academy of Medical Sciences, 'Biobanks: Obtainment, Preservation and Utilisation of Human Biological Material', Basel (2006) 4.

51 European Commission Directorate-General for Research and Innovation, 'Biobanks for Europe - a Challenge for Governance' (2012).

52 Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.

and describes such structured resources as being used for the purpose of genetic research and providing human biological materials and/or information generated from the analysis of the same; and extensive associated information[53].

More commonly, the definition of a biobank is given in the national legislation. The Norwegian Biobanks Act defines biobank as a collection of human biological material contributed for medical examination, diagnosis and treatment. The term research biobank as used in the act means a collection of human biological material and data obtained directly by the analysis of this material, and that is used or is to be used for research purposes[54]. Iceland law defines biobank as a collection of biological samples which are permanently preserved[55]. Finish biobank law says that a biobank means a unit maintained by an operator engaging in biobanking activities for the purposes of collecting and storing samples and information associated with the samples for future biobank research[56]. Spanish biobank act defines a biobank for biomedical research purposes as a public or private, non-profit establishment which stores one or more collections of biological samples of human origin for biomedical research, organized in as systematic order, regardless of whether it stores samples for other purposes[57]. Estonian Human Genes Research Act, regulating the establishment and maintenance of a Gene Bank, describes "Gene Bank" as a database established and maintained by the chief processor consisting of tissue samples, descriptions of DNA, descriptions of state of health, genealogies, genetic data and data enabling the identification of gene donors[58].

Biobanks can have different origins and can be set-up for differing purposes. While some biobanks were started simply with the intention to facilitate the storage and distribution of human cells or tissues for biomedical investigations ("research biobanks"), others were set-up with the purpose of storing tissues for therapeutic applications ("therapeutic biobanks"), while yet others have emerged as by-product of medical "cohort studies" of a given population over extensive period of time ("population-based biobanks")[59]. Gottweis and Zatloukal distinguish four large types of biobanks (1) Clinical case/control biobanks that are based on biological

53 Organisation for Economic Cooperation and Development 1.

54 Norwegian Act Relating to Biobanks 2003(available at: <https://www.regjeringen.no/no/tema/helse-og-omsorg/innsikt/bioteknologi/Act-relating-to-biobanks/id229516/> accessed 8 May 2018); Act on medical and health research (the Health Research Act) 2008 20 para 4(c) (available at: <http://app.uio.no/ub/ujur/oversatte-lover/data/lov-20080620-044-eng.pdf> accessed 8 May 2018).

55 Iceland Biobanks and Health Databanks Act No. 110/2000, as amended by Act No. 27/2008, No. 48/2009 and No. 45/2014. Article 3(5).

56 Finnish Biobank Law 688/2012 of October 2, 2012. Section 3(1).

57 Real Decreto 1716/2011, de 18 de noviembre, por el que se establecen los requisitos básicos de autorización y funcionamiento de los biobancos con fines de investigación biomédica y del tratamiento de las muestras biológicas de origen humano, y se regula el funcionamiento y organización del Registro Nacional de Biobancos para investigación biomédica, Artículo 2(b).

58 Estonian Human Genes Research Act of 2000 December 13, published RT I 2000, 104, 685 2000, Article 2(10).

59 Australian Government National Health and Medical Research Council 57.

specimens from patients with specific diseases and from non-diseased controls. (2) Longitudinal population-based biobanks that contain biological samples from (parts of) the general population with or without disease. The UK and Estonian Biobanks are examples for this type of biobank. (3) Population isolate biobanks, which are characterized by the homogeneous genetic and environmental setup of the population represented (e.g., the Icelandic Biobank). (4) Twin registries, such as GenomEUtwin, which contains samples from monozygotic and dizygotic twins, and, therefore, is particularly suited to distinguish between the genetic and non-genetic basis of diseases.[60]

Today, there is no single and internationally accepted definition of a biobank. Nevertheless, the central point of a clear definition of a biobank is to ensure that regulatory actions or standards would be applied equally for the same operators. The "polymorphism" of terminology, as we see today, creates ambiguity as regards the application of certain norms and rules[61]. The sample definitions given above make it clear that there is widespread disagreement about what a biobank is. This may have important implications for regulation of the use of biological samples, as well as sharing of the data, cooperation issues. If a researcher does not think he is dealing with a biobank, he will most likely not follow the relevant biobank standards or regulations that apply[62]. This means that the use of samples might not be proper, ethical or it can be in contradiction with the other laws. As well, a researcher will not respond to any local, national or international communications if he will not be sure he is dealing with a properly established biobank or biobank network. Researchers also are less likely to share the data they generate or return the samples to an entity that doubtfully can be called a biobank[63]. Ignorance or denial that a collection is a biobank can act as a barrier to share samples and biological data even if the quality and governance of the entity are rather high.

A relevant and very important for this subject research has been performed in Switzerland by Shaw D.M., Elger B.S., Colledge F.[64] The research was directed towards defining the most relevant aspects of a biobank. A study concluded that the best definition of a biobank would be one that does not refer to the size of sample collections or the richness of data but does state that the purpose of the biobank is performing different research.

In the study the size of the collection was found to be unimportant, and regardless of the number of samples stored in the database, it still could be called a biobank, ensuring it

60 H Gottweis and K Zatloukal, 'Biobank Governance: Trends and Perspectives' [2007] Pathobiology 206, 206–211.

61 Antonella de Robbio, 'Biobanks Patents or Open Science' (2013) 13 Woodhead publishing series in biomedicine 5.

62 DM Shaw and others, 'What Is a Biobank ? Differing Definitions among Biobank Stakeholders' (2014) 85 Clin Genet 223–227.

63 Shaw and others 223.

64 Ibid.

confirms the research purpose requirement. The study concluded, that adding the research criterion to the definition has the dual benefits of reflecting current biobank practices and regulating what needs to be regulated without accidentally catching collections that do not put scientific research requirement for their intended purpose. So, the samples used for research would be regulated, and the ones used for quality control, diagnostics or forensics (none of which require donor's consent) would not. The proposed study's definition goes the following: "***A biobank is any collection of human biological samples and linked data that is to be used for research"***[65].

Even if it can vary, the most common purpose, understood by the scientific community and general population, is that of the biobank not just storing genetic information but also performing genetic research. No matter how different the definition of the biobank can be, the clear is that they all share one common goal: the material in biobanks is collected for the purpose of research, from basic science to drug development, rather than for a medical use or forensic identification. I strongly agree with such a definition. And in this thesis, a biobank will be regarded as a biorepository that collects and stores biological samples and genetic data for the research purposes. In the research, I focus on biobanks that store and collect human samples such as blood, saliva, urine, cells, skin biopsies or other tissue samples. However, it is not an obligatory requirement for the biorepository to be called a biobank – as other biological materials generated from animals or plants, can also form part of biobank's collection.

II. Types of biobanks

1. Public v. private

Biobanks can be divided according to their funding sources, scope, availability of collected data. 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[66]. The functionality and organisational structure of a biobank can also influence how the intellectual property rights are created or dealt with within an institution.

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65 Shaw and others 227.

66 BBMRI Project, 'Biobanks and the Public. Governing Biomedical Research Resources in Europe' (2013) 52–55.

When the first large biobank projects were announced, there was a certain perception—both in research and the general public—that the output concerning new medical and therapeutic advanced would follow straight. In some countries, like before-mentioned Estonia, early biobanks projects were marketed as a new way to benefit on the "patrimony", and to boost backward economies into the new world of the technology[67].

With the time such naïve views have changed, given way to a more realistic assessment. For example, in 2009 the Reykjavik-based deCode biobank filed for bankruptcy protection in 2009, after nine years of establishment[68]. In fact, some of the largest biobanks projects, like the UK Biobank, are only now becoming available for scientific uses. It may take years, or even decades, for the scientific output from the biobank infrastructure investments undertaken today to fully actualize.

But the governments, research agencies, and private corporations continue to spend significant amounts of funding on biobanks. As an example, the world's biggest health imaging study, performed by UK Biobank, costs £43m[69]. The initiative was financed by public and private funds - Medical Research Council[70] (governmental funds), Wellcome Trust[71] (charitable foundation) and the British Heart Foundation[72] (charity organisation). The half of the amount has been funded by the UK Government[73].

The survey performed by the European Commission shows that most of the biobanks active today are public establishments, funded by the government or its bodies. From approximately 107 biobanks, which participated in the survey, 78% were owned by universities or national/regional agencies, 19% were owned by the non-profit organisations and only a few (3%) were private[74]. However, the survey has been held from mid-March until mid-May 2006, and the numbers might have changed over the years, but the fact is that public funds are the most common financial resources of the biobanks.

Numerous countries in Europe and abroad have national biobanks. To mention some of them:

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67 ibid 22.

68 Hirschler. Available at: <https://www.reuters.com/article/us-amgen-decode-idUSBRE8B90IU20121210> accessed 8 May 2018.

69 University of Oxford, 'UK Biobank Launches World's Biggest Body Scanning Project' [2016] *Medical Xpress*. Available at <http://medicalxpress.com/news/2016-04-uk-biobank-world-biggest-body.html> accessed 8 May 2018.

70 Medical Research Council, 'Web Page' <https://mrc.ukri.org/> accessed 8 May 2018.

71 Wellcome Trust, 'Web Page' <https://wellcome.ac.uk/> accessed 8 May 2018.

72 British Heart Foundation, 'Web Page' <https://www.bhf.org.uk/> accessed 8 May 2018.

73 University of Oxford.,'UK Biobank Launches World's Biggest Body Scanning Project' [2016] Medical Xpress. Available at <http://medicalxpress.com/news/2016-04-uk-biobank-world-biggest-body.html> accessed 8 May 2018.

74 Zika E and others, *Biobanks in Europe: Prospects for Harmonisation and Networking* (Publications Office of the European Union 2010), 16-19.

1. Estonian Biobank at the EGCUT is funded by the Estonian Government through the budgets of the Ministry of Social Affairs and the Ministry of Education and Research[75].
2. Biobank Norway is funded by The Research Council of Norway. Funding of 80 million NOK for the year 2011-2013[76].
3. Belgian Biobank Consensus Platform – research infrastructure involving three Belgian network biobank initiatives i.e. Belgian Virtual Tumourbank project assigned to the Belgian Cancer Registry (BVT-BCR; Federal Initiative), Bibliothèque de la Fédération Wallonie-Bruxelles (BWB; Walloon Initiative) and the Flemish Biobank Network (Flemish Initiative)[77].
4. Spanish National Cancer Research Center – a public, non-profit organisation that hosts several collections of human biological samples for biomedical research[78].
5. China Kadoorie biobank – funded by different UK and Chinese government institutions, such as Medical Research Council, National Natural Science Foundation of China, Ministry of Science and Technology of China, National Health and Family Planning Commisison of China[79].

European Commission is also strongly involved in the biobanking initiatives. European Commission's FP6 project (2002-2006) funded EuroBioBank[80], the first operating network of biobanks in Europe providing human DNA, cell and tissue samples as a service to the scientific community conducting research on rare diseases. It is the only network dedicated to rare disease research in Europe. Commission's FP7 (2007-2013) project funded BBMRI[81], a Biobanking and Biomolecular Resources Research Infrastructure, and has granted five mln. EUR funding (2008-2011) to the Preparatory Phase of BBMRI. Horizon 2020 (2014-2020) continued financing this initiative, approving 4,9 mln. funding for the year 2015-2018[82]. The description of the project is a BBMRI-ERIC (the Biobanking and BioMolecular resources Research Infrastructure - European Research Infrastructure Consortium) and it aims to establish, operate and develop a Pan-European distributed research infrastructure in order to facilitate the access to biological resources and its facilities and to support high-quality

75 The Estonian Biobank, 'Estonian Genome Center, University of Tartu' <https://www.geenivaramu.ee/en/about-us> accessed 8 May 2018.

76 Biobank Norway, 'Financing and Project Period' <https://www.ntnu.edu/biobanknorway/finansing> accessed 8 May 2018.

77 The Biobanking and Biomolecular Resources Research Infrastructure, 'Welcome' <https://www.bbmri.be/welcome/> accessed 8 May 2018.

78 CNIO Biobank, 'About' <https://www.cnio.es/ES/grupos/plantillas/presentacion.asp?grupo=50004308> accessed 8 May 2018.

79 Kadoorie Charitable Foundation, 'Funding Agencies' <http://www.ckbiobank.org/site/About+the+Study/Funding+Agencies> accessed 8 May 2018.

80 EuroBioBank network, 'About' <http://www.eurobiobank.org/about/> accessed 8 May 2018.

81 CORDIS European Commission, 'BBMRI Report Summary' <https://cordis.europa.eu/result/rcn/162431_en.html> accessed 8 May 2018.

82 'EU Open Data Portal' <https://data.europa.eu/euodp/en/home> accessed 8 May 2018.

biomedical research. The continuing BBMRI-ERIC initiative aims to increase and accelerate implementation of BBMRI-ERIC and its services. BBMRI-ERIC is a specific European asset that became a fundamental component in addressing the ongoing and future requirements particularly of Europe's health service frameworks, including competitiveness and innovativeness of health-related industries. BBMRI-ERIC provides a gateway access to the collections of the European research community, expertise and services.[83]

Apart from this continental initiative, Horizon2020 Framework Programme gives funding to several other biobank projects. For example, the PhenoMeNal,[84] the New therapies for uveal melanoma project,[85] the Biobanking and the Cyprus Human Genome Project,[86] Regulating Umbilical Cord Blood Biobanking in Europe project,[87] Bridging Biobanking and Biomedical Research across Europe and Africa (B3Africa) project[88]. Some Horizon 2020 funded projects are going to use or are using the data stored in biobanks (as an example: Rise of scientific excellence and collaboration for implementing personalised medicine in Estonia, Risk Stratification for Sudden Cardiac Death, Exploring selected long non-coding RNAs as diagnostics and therapeutic targets for heart failure).

It is also common for the universities to have their biobanks. For example, University of Liverpool has a Bio-Innovation Hub[89] biobank, Institute of Human Genetics (IHG) of the Technical University Munich (TUM) established the biobank in 2001[90], University of Tartu as

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83 CORDIS European Commission, 'ADOPT BBMRI-ERIC' <https://cordis.europa.eu/project/rcn/199793_en.html> accessed 8 May 2018.

84 Projects goal is to develop and deploy an integrated, secure, permanent, on-demand service-driven, privacy-compliant and sustainable e-infrastructure for the processing, analysis and information-mining of the massive amount of medical molecular phenotyping and genotyping data, that is information collected and stored in a biobanks, generated by metabolomics applications now entering research and clinic.

85 It is a virtual biobank registry, linking existing biobanks into a harmonised network, which will prospectively collect primary and metastatic UM samples.

86 An initiative to create a contemporary Biobank and a research facility for developing the Cyprus Human Genome Project.

87 The research proposed for this fellowship is a study of the establishment of national and European regulation on Umbilical Cord Blood (UCB) biobanking in a comparative perspective (the UK, Germany, France, Italy and Spain) and with an in-depth analysis of the implementation of regulation in the everyday practice of UCB practitioners, through a bi-national comparison in the UK and Italy. Given the importance assigned by the European Union to the development of stem cell research and the coordination of biobanks, the research also aims to offer useful policy suggestions to improve the harmonization and optimization of the EU circuit of supply of UCB units for biological research and medical applications.

88 B3Africa aims to implement a cooperation platform and technical informatics framework for biobank integration between Africa and Europe. The collaboration harmonises the ethical and legal framework, biobank data representation and bioinformatics pipelines for sharing data and knowledge among biobanks and allowing access for researchers from both continents.

89 University of Liverpool, 'Liverpool Bio-Innovation Hub Biobank' <https://www.liverpool.ac.uk/translational-medicine/research/lbih/> accessed 8 June 2018.

90 The Institute of Human Genetics (IHG) of the Technical University Munich (TUM), 'Biobank Network Munich' <http://www.bbmri-mbi.de/en/info_TUMIHG_E.html> accessed 8 May 2018.

well has its own biorepository[91]. The US has quite a lot universities with established biobanks: New York University, Washington University, University of Minnesota, and other[92].

And on the other side, there are the biobanks that are funded by the private investments and revenues it generates from the services provided. With the progress in biotechnology, biobanks are getting more and more useful and important. Therefore, private biobanks are becoming more common.

Commercial, business-driven biobanks will play critical roles in biospecimen availability. In the early 2000s, a number of commercial biobanks, such as Ardais, Asterand, Genomics Collaborative, were set up to fill the increasing needs for specimen and data of researchers both in academia and the pharmaceutical industry. Typically, the commercial banks sign an agreement with hospitals from where the specimen is collected, and the specimen is either banked or supplied directly to the end user. Because such banks are commercially driven, they are more business oriented, are not limited by institutional or national boundaries so are better able to acquire the number and type of samples required by a researcher faster[93].

Biobank activities in the private sector have increased considerably over the past two decades and the cell and tissue collections managed by pharmaceutical firms and biotechnology companies will continue to grow[94]. For example, in 2012 the U.S. biotechnology group Amgen Inc. bought Decode Genetics for $415 million in cash and established as a public biobank of Iceland[95]. Later, in 2015, as a spinout from deCODE genetics - NextCODE Health, was purchased by the Chinese company WuXi PharmaTech for $65 million[96]. Now the company is called WuXiNextCode and is providing a data analysis services, research- or clinical-grade sequencing[97]. DeCode, on its part, still a subsidiary of Amgen, is functioning in Iceland[98]. Another example of a private biobank is Cell&Co Bioservices, a commercial company based in France and having a branch in the USA. The company collects and stores different types of biological samples, also offers transport

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91 The Estonian Biobank, 'Estonian Genome Center, University of Tartu' <https://www.geenivaramu.ee/en/about-us> accessed 8 May 2018.The Estonian Biobank, 'Estonian Genome Center, University of Tartu' <https://www.geenivaramu.ee/en/about-us> accessed 8 May 2018.

92 More biobanks can be found at SpecimenCentral.com, 'Global Biobank Directory, Tissue Banks and Biorepositories' <http://specimencentral.com/biobank-directory/> .

93 Somiari B. Stella and Somiari I. Richard "The Future of Biobanking: A Conceptual Look at How Biobanks Can Respond to the Growing Human Biospecimen Needs of Researchers" in Feridoun Karimi-Busheri (ed), *Biobanking in the 21st Century* (Springer International Publishing Switzerland 2015).

94 BBMRI Project, 'Biobanks and the Public. Governing Biomedical Research Resources in Europe' (2013).

95 Ben Hirschler, 'Amgen Buys Icelandic Gene Hunter Decode for $415 Million' *The Thomson Reuters* (2012).

96 WuXi PharmaTech (Cayman) Inc., 'WuXi PharmaTech Acquires NextCODE Health to Create Global Leader in Genomic Medicine'(2015). Available at: <http://www.prnewswire.com/news-releases/wuxi-pharmatech-acquires-nextcode-health-to-create-global-leader-in-genomic-medicine-300018311.html> accessed 8 May 2018.

97 WuXi NextCODE, 'Home Page' <https://www.wuxinextcode.com/> accessed 8 May 2018.

98 deCODE genetics, 'Company' <https://www.decode.com/company/> accessed 8 May 2018.

services and consultancy services in this field, as it states - a complete one-stop-shop solution for managing biological and clinical samples[99].

The PrecisionMed biorepository declares to be the largest private global source of longitudinally collected Human Cerebrospinal Fluid from living normal and diseased populations. Its biorepository consists of human tissue, cerebrospinal fluids **(**CSF), CSF Pellets, DNA/EDTA blood, PAXGene, serum, plasma, PBMCs and urine samples[100]. The company provides sample collection services from collection concept to banked samples, for single-centre or multi-centre collections. These services apply to all disease areas including cancer biomarkers. For example, the company offers for purchase completed collections of particular CSF samples, of elderly (>60 years old) or normal donors (<60 years old), with or without a diagnosed specific disease[101]. The company is based in US, California.

Biotechnology corporations and large pharmaceutical firms also are storing the samples their possess and assembles their own internal repositories of human cells and tissues for a variety of research purposes, from genetics to the toxicological evaluation of new drugs. Pharmaceutical companies keep human cell, and tissue samples from patients enrolled in drug trials and clinical studies and are thus building up increasingly large collections[102]. Asterand Bioscience, a biorepository with locations in the US, Europe (United Kingdom) and Japan, has been formed in 2006 through the merger of Asterand, a human tissue biorepository and Pharmagene a drug discovery company. The company provides human tissue and associated clinical information and delivers molecular pathology and genomics data to support the selection and validation of drug targets and biomarkers in human tissues[103]. Its repository has around 200,000 human tissues and biofluids.

It is not always easy to separate if the biobank is public or private, especially, because it is quite common that a biobank receives fundings from the public and also the private bodies. For example, Spanish national cancer research centre (CNIO) informs that during the year 2015 the centre was involved in 143 projects[104]. Most of these projects have been funded either by the European bodies (mostly, the European Commission) or national government (by different ministries or municipal bodies). However, the data also shows that several projects have been funded by commercial enterprises: Volkswagen Foundation, Hward Hughes medical institute, AstraZeneca, BBVA foundation, Fundación Fero, and similar. The question is, how much the biobank is still public if it receives funding from commercial sources?

99 Cell & Co Bioservices, 'Services' <http://www.cell-and-co.com/en/services/> accessed 8 May 2018.
100 PrecisionMed, 'Company' <http://www.precisionmed.com/> accessed 8 May 2018.
101 PrecisionMed, 'Biorepository' <http://www.precisionmed.com/inventory/> accessed 8 May 2018.
102 BBMRI Project, 'Biobanks and the Public. Governing Biomedical Research Resources in Europe' (2013) 23.
103 BioIVT, 'ANTIBODY VALIDATION FOR RESEARCH' <https://www.bioivt.com/antibody-validation-ihc/ > accessed 8 May 2018. Human Tissue Specimens BioIVT's clinical specimens now include the ASTERAND Human Tissue Specimens
104 Spanish National Cancer Research Centre, 'Annual Report 2015' 200–211.

Biobanks, that get funding from a state, or an European Union body, as well as the biobanks established on the premises of the public universities (that receives financial support from the government), I consider as a public biobanks, regardless if any additional income is received from the private funds (like tuition fees, private donations). Already mentioned UK biobank receives allocations from the national government and the Wellcome Trust, Britain's largest charity, having shares of GlaxoSmithKline and also Diamond Light Source Ltd[105]. Regardless these double income, it is still considered as a public biobank and least in the current research.

The funding is quite crucial for the intellectual property rights protection in a biobank. Federal funding agencies or projects supported by the European Union, in most cases, do not claim ownership. IPR resulting from the project belongs to the participant who generated it[106]. The findings and outcomes of such projects are also usually freely available and can be accessed by any interested party free of charge (Horizon 2020 guidelines mandates beneficiaries of the programme to publish scientific research articles under the open access models).

Most universities, on the other hand, consider all data and specimens collected by an investigator with a formal affiliation with that university to be owned by the university[107]. Such ownership rights are often spelt out in institutional technology transfer offices and patent policies. From the university perspective, funding awards are made to institution and not to individual investigator, giving the university with both the responsibility for ethical and compliant research as well as the ownership of the research product, be it information or specimens[108].

Naturally, a commercial entity is much more willing to protect the IP generated, to which it has invested significant amounts. Privately funded researchers claim ownership of their investigations and any other rights that arise from it. Such conditions are generally foreseen in the funding agreement. A research that is done under a private contract, for example between an oncology cooperative group and pharmaceutical company, usually establishes that the specimens collected on behalf of the research sponsor (ex. pharma company) will be maintained in their biobank and also that any other rights (including IPR) arising from the research will belong to the sponsor[109].

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105 Quite a controversial article about UK Biobank GeneWatch UK, 'Bioscience for Life? The History of UK Biobank, Electronic Medical Records in the NHS, and the Proposal for Data-Sharing without Consent'. published by GeneWatch UK in 2009.

106 European Commission, 'Guide to Intellectual Property Rules for FP7 Projects'.;The European IPR Helpdesk, 'Your Guide to IP in Horizon 2020'.

107 *Washington University v Catalona, 490 F 3d 667.* For a description of the arguments used by one educational institution in favour of university's ownership of biospecimens.

108 Grigorenko and Bouregy 43.

109 Grigorenko and Bouregy 43.

Howard Hughes Medical Institute is one of the institutions that funds biomedical researches. Institute clearly states that the IPR created belongs to the Institute. When the institute finances a foreign project, the investigator legally becomes an employee at the Institute (even if he/she remains in the host institution, for example, his home university). All investigators generally are required to assign to the Institute any intellectual property rights that arise from their research. The Howard Hughes Medical Institute can assign its IP rights to the host institution, subject to a research use license retained by the investor. The host institution typically then takes the lead in patenting or licensing intellectual property rights following the terms of the collaboration agreement. The Institute can cooperate in the IP costs, but also expect the host institution to share the licensing or other income arising from it.[110]

The AstraZeneca project "Open Innovation" started in 2014, also established similar rules for IPR.[111] In general, the goal of the project is collaboration sharing knowledge and resources between AstraZeneca and other scientists, organisations. It is an umbrella project that covers several different initiatives in different medical fields (like cardiovascular and metabolic diseases, oncology, etc.). As every project performed under this initiative includes different actors (European Commission, UK Medical Research Council, the Lead Discovery Center GmbH, and more other commercial or public establishments[112]), the contractual conditions regarding the IP policy might also differ radically according to from one project to another. As far as it is disclosed in the general and available information, new IP rights arising from the projects follow ownership framework taking into account the contribution of each party and where possible using the well-established academic-industry templates. Publications are encouraged after allowing AstraZeneca to comment, patent to be filed, and if AstraZeneca's confidential information is protected. If the collaboration generates positive findings (for example income from patents), AstraZeneca has an option to negotiate a license to advance further towards commercialisation. For compounds 'live' in development, AstraZeneca minimally receives non-exclusive, royalty-free, fully paid license, with the right to sublicense without limitation, for all purposes for project IP.[113]

2. Large-scale biobanks v. small-scale biobanks

The sample size is a characteristic that can be used to distinguish different kinds of biobanking activities. The advent of genomics, proteomics and various other technologies that

[110] Howard Hughes Medical Institute, 'Intellectual Property Guide for Host Institutions' (2017).Available at https://www.hhmi.org/sites/default/files/About/Policies/host-guide.pdf accessed 8 May 2018.

[111] AstraZeneca, 'Open Innovation' <https://openinnovation.astrazeneca.com/> accessed 8 May 2018.

[112] Full list of projects can be found at http://openinnovation.astrazeneca.com/partner-with-us/open-innovation-partnerships/ accessed 8 May 2018.

[113] 'Collaboration Opportunities', <http://openinnovation.astrazeneca.com/partner-with-us/frequently-asked-questions/> accessed 8 May 2018.

make it possible to analyse increasingly large quantities of samples at a reasonable cost has had a significant impact on the reality of biobanking[114]. The number of tissue samples in US banks alone was estimated at more than 300 million at the turn of the century and is increasing by 20 million a year[115]. The need for ever larger numbers of samples has increased over the past year. Projects throughout the world are now aiming at sequencing the entire genome of various individuals.

The definition given by the Council of Europe points out the most relevant aspects of the population – large-scale – biobanks. Such biorepositories were described as the "collections of biological materials having 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 associate personal data, which may include or be linked to genealogical, medical and lifestyle data and which may be regularly updated; (and) iv. it receives and supplies materials in an organised manner**[116]**." Within the European context, large-scale biobanks include the UK Biobank, deCode-associated Icelandic Biobank, the Estonian Biobank and the Genome Austria Tissue Bank (GATiB) projects. To further the understanding of common disease risk and human health, population genomics draws on basic data on genomic variation and on lifestyle behaviours and environmental factors[117].

As already mentioned, for a biorepository to be regarded as a biobank, the database must not necessarily be wide in scope. While large-scale biobanks are relatively recent, small collections established for specific research projects have been more the norm. A "small science" biobanks, performed by individual investigators or small and autonomous research groups operating outside large, organized research programs often function with non-federal sources of funding. Most small biobanks pertain to particular well-characterized collections from groups of a limited size, such as collections of specific ethnic groups or particular families; of a particular sub-condition, like particular subtype of a particular disorder; or a important environmental exposure, like specimens from children of individuals exposed to a particular environmental condition (for example, famine).[118] Small biobanks usually are disease-oriented – they collect biological samples from patients, aiming at discovery and

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114 BBMRI Project, 'Biobanks and the Public. Governing Biomedical Research Resources in Europe' (2013) 20.

115 Elisa Eiseman and Susanne B Haga, *Handbook of Human Tissue Sources: A National Resource of Human Tissue Samples* (RAND Corporation 1999) 141.

116 Council of Europe Committee of Ministers, 'Recommendation Rec(2006)4 of the Committee of Ministers to Member States on Research on Biological Materials of Human Origin and Its Explanatory Memorandum' (2006).

117 Paul R Burton and others, 'Size Matters: Just How Big Is BIG ? Quantifying Realistic Sample Size Requirements for Human Genome Epidemiology' (2009) 38 International Journal of Epidemiology 263.

118 Elena L Grigorenko and Susan Bouregy, 'Biobanking on a Small Scale: Practical Considerations of Establishing a Single-Researcher Biobank' [2009] Stanford Journal of Law, Science & Policy 35.

validation of genetic and non-genetic risk factors of diseases[119]. A single-lab, single-investigator bank typically contains a relatively small number of specimens, but these specimens are most commonly donated by well-characterized donors from distinct samples or populations[120]. Therefore, small biobanks are particularly important as they contain unique collections of specimens that cannot be easily replaced or newly collected[121].

Despite their different research focus and their often-limited statistical power, these smaller scale projects represent an indispensable scientific resource complementary to large-scale biobanks.[122] The attendants of the Wellcome Trust meeting[123] noticed that apart from large-scale 'community resource projects' many valuable small-scale data sets could come from other sources. Unlike large-scale projects, those resources emerge from research efforts the primary goal of which does not resource generation but concentration on the quality of the samples. Therefore, the data collection stored in such repositories can be more valuable for particular research or study.

Big-scale biobanks and small-scale biobanks address different questions one from another. 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[124]. A population-based biobank that collects dried blood and health data may be used for example to determine the genetic risk factors for breast cancer, whereas a disease biobank that collects tumor samples might be used to reveal different molecular forms of breast cancer[125].

The size of the biobank can also influence the protection of IPR. Like the small size, disease-oriented biobanks have the exact research targets and goals; then they also foresee beforehand the hypothesis of the research and possible IPR that can arise (the publication of primary findings or patenting a drug at a later stage). Big biobanks, on the other hand, has as a primary target to collect, store and provide samples and data of the population and collect information about the general wellbeing of the humans, their habits, and environmental conditions that can influence different diseases. Therefore, population biobanks are not looking forward to protecting their information, but oppositely – to ensure the dissemination of knowledge and stimulate research. Also, what is related with public/private biobanks

119 Deborah Mascalzoni and others (eds), *Ethics, Law and Governance of Biobanking. National, European and International Approaches* (Springer Science 2015) 17.
120 Grigorenko and Bouregy 36.
121 Ibid.
122 European Commission Directorate-General for Research and Innovation, 'Biobanks for Europe - a Challenge for Governance' (2012) 14.
123 The Bermuda Principles developed from 1996-1998 during the international Human Genome Project (HGP).
124 European Commission Directorate-General for Research and Innovation, 14.
125 Monya Baker, 'Building Better Biobanks' (2012) 486 Nature 141. Available at http://www.nature.com/nature/journal/v486/n7401/full/486141a.html accessed 2018 May 8.

separation, small biobanks most often does not have public support, that is why they are also more keen to keep the research results in secret and try to protect them with IPR for commercialisation purposes.

3. "Closed" biobanks v. "open" biobanks

Sharing data and biospecimens is essential for the discovery, new knowledge creation and translation of various biomedical research findings into improved diagnostics, biomarkers, treatment development, patient care, health service planning and general population health[126]. Physicians and researchers would unequivocally require access to the biological database to perform their studies or analysis. Physicians must access the database to aid in determining which drugs will cause the fewest side-effects and most effectively treat their patients' conditions and researchers must also have the ability to access the database in order to make comparisons of genetic profiles to determine which genes affect drug-metabolizing enzymes[127]. Biobanks have been established to provide information to the general public for free, or access to such information can be restricted either by payment of an equivalent fee or by other specific obligations (the purpose of the research, the status of the applicant).

Private biobanks, funded by commercial enterprises, usually have financial goals and provide bio data only for a particular fee. Like already mentioned French company Cell&Co Bioservices, allows to order the needed biospecimens online. Different human cell lines can be purchases starting from $6,000.00[128]. Other private biobanks, such as WuXiNextCode or PrecisionMed biorepository, does not have fixed prices and it depends on case to case analysis. UK Biobank is claiming that the data is accessible for *bona fide* researchers for health-related research that is in the public interest[129]. Commercial companies can also use the UK Biobank resources, with the condition they act on the bona fide requirements.

UK Biobank claims to be an open-access resource. However, the registration of the potential user is obligatory, and also researchers must submit a statement of the research, indicating its purpose and aims, so that UK Biobank could evaluate the grounds of the research and decide to approve or disapprove the request. Furthermore, any application is evaluated only when a particular fee is made: an initial fee of £250 must be paid at preliminary application submission. Also, if the application requests data extraction, the fee increases up to £1,500. An additional cost of £500 is applied for access to any bulk data files

126 Deborah Mascalzoni and others, 'International Charter of Principles for Sharing Bio-Specimens and Data' [2015] European Journal of Human Genetics 721.

127 Berrie Rebecca Goldman and Berrie Rebecca Goldman, 'Pharmacogenomics : Privacy in the Era of Personalized Medicine Privacy in the Era of Personalized Medicine' (2005) 83 Nw. J. Tech. & Intell. Prop. 83.

128 Cell & Co Bioservices, 'Services' <http://www.cell-and-co.com/en/services/> accessed 8 May 2018.

129 UK Biobank, 'Scientists' <http://www.ukbiobank.ac.uk/scientists-3/> accessed 8 May 2018.

(includes MRI/ DXA/ carotid ultrasound, OCT and fundus images, ECG raw data, HES data, genetic data, built environment data and accelerometer data).[130] UK Biobank gives a discount to students for the purpose of producing their thesis and the institutions resident in a low or low-middle income countries. However, even with the reduction (ranging from £250-£500), for developing countries or students without any additional funding, the fee to access the data is still quite high.

The EuroBioBank network, dedicated to rare disease research in Europe, is the first operating network of biobanks in Europe providing human DNA, cell and tissue samples as a service to the scientific community researching rare diseases. Originally funded by the EC between 2003-2006, the EuroBioBank received further EC support between 2007-2011 within the European Network of Excellence TREAT-NMD (FP6), which covered the cost sustained by Eurordis for the network coordination and website hosting. Each biobank of the network is financed by its Institution or charitable organization. As of January 2012, the Fondazione Telethon provides the administrative support for coordinating the EuroBioBank network and hosting the website. Moreover, BBMRI is an active collaborator of EuroBioBank.[131]

The EuroBioBank network was established by patients and researchers to facilitate research on rare diseases by guaranteeing quick and easy access to samples via an online catalogue. The catalogue lists the samples available throughout the EuroBioBank network by type of biomaterial. A search engine enables a search by disease or by bank contact. A sample, located in the catalogue, can be requested by email. In such way, the biological material is exchanged faster. The EuroBioBank network adheres to international ethical guidelines that are in force, in particular, rules concerning the non-commercialisation of human biological material. Processing and shipping fees may apply.[132]

European Prospective Investigation into Cancer and Nutrition (EPIC) founded at the International Agency for Research on Cancer (IARC, part of the World Health Organization), financially supported by Europe Against Cancer Program of the European Commission, provides it's biological resources (samples and data) to investigators affiliated with *bona fide* research organisations, seeking to answer important health and disease research questions. EPIC Steering Committee and the IARC Ethics Committee approval is needed.[133] For studies where data *and* biospecimens are requested, related sample access charges are applicable[134].

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[130] Ibid.

[131] Euro Biobank, 'Collaborations' <http://www.eurobiobank.org/collaborations/> accessed 8 May 2018.

[132] Euro Biobank, 'Access Samples' <http://www.eurobiobank.org/sample-catalogue/access/> accessed 8 May 2018.

[133] World Health Organization International Agency for Research on Cancer, 'The European Prospective Investigation into Cancer and Nutrition (EPIC) Study', vol 33 (2014).

[134] World Health Organization, 'EPIC Study' <http://epic.iarc.fr/access/gain_access.php> accessed 8 May 2018.

Another well known international initiative – the Public Population Project in Genomics and Society (P³G), provides much information about the access of P³G and partners' genetic databases. 42 projects are provided by P³G and more that one hundred project from different partners (such as Biobanking and Biomolecular Resources Research Infrastructure (BBMRI), Canadian Partnership for Tomorrow (CPT), the Diabetes Biobank, European Network for Genetic and Genomic Epidemiology (ENGAGE), Network on Genetic Isolates (INGI), the Renal Biobank, etc.)[135].

Every project under the P³G umbrella has different access requirements. It depends on the partner's policy and national regulations applicable to the exact biobank. For example, the data from the Genome Database of Latvian Population study is available for researchers outside the study. Data and samples can also leave the country and be transporter to any geographical location. However, data and samples can be used only to particular studies, that has been agreed by the participants (in the inform consent form). Formal approval from the national institution is needed before data and samples can be given. Data of this study can be access free of charge and scalable fees to access samples vary according to the investigator (e.g. national investigators, students, public/private institutions, etc.)[136]. Another study, the Health 2000 Study, performed by National Institute for Health and Welfare of Finland does not set any restriction related to the categories of investigators requesting access or limitation towards the scope of the projects using the data/samples. However, fees are payable, and approval from a committee is needed. Furthermore, study obliges to negotiate with a study representative any intellectual property rights resulting from the research using data/samples. Results/data need to be given back to the study (e.g. GWAS, biochemical tests, etc.)[137].

A large-scale population-based cohort study in Australia – the 45 and Up Study – provides data for a fixed fee ranging from $4,185 to $8,370. Furthermore, before the publication of a paper reporting analyses of the 45 and Up Study data, including an abstract for a conference presentation, it should be submitted to the study coordinating centre for prior review and approval.[138]

Canadian Health Measures Survey (funded by Canada government) collects information on Canadians' health and health habits. As part of the Survey, blood, urine and DNA samples (biospecimens) are collected from consenting participants. With respondents' consent, these samples (from 22,000 Canadians) are stored at the National Microbiology Laboratory in Winnipeg for use in future health studies. Only *bona fide* researchers who conduct research in

135 'P3G Observatory catalog' <http://www.p3gobservatory.org/network/partnerCatalogs.htm> accessed 8 May 2018.
136 Ibid.
137 Ibid.
138 Sax Institute, 'Researcher Toolkit' <https://www.saxinstitute.org.au/our-work/45-up-study/for-researchers/> accessed 8 May 2018.

Canada and work under the direction or supervision of a recognized public or private organization can access this data.[139]

A release of the biological material and data from the Estonian Genome Center, University of Tartu (EGCUT) are available for research projects. The biobank's information may be used only for scientific research, treatment of illnesses of gene donors, public health research and statistical purposes. Use of the biobank for other purposes, primarily to collect evidence in civil or criminal proceedings or for surveillance, is prohibited.[140] The applicant needs to reimburse the costs of material release, regardless of whether the data are issued for scientific or commercial purposes. The research project has to obtain approval from the Ethics Review Committee. Approval for DNA and plasma sample release takes 4 to 6 months.[141] The biobank is funded from the state budget[142].

There is now a growing international movement for "open science", by which is meant making publication of scientific concepts and the data on which they are based readily accessible to all, together with procedures for sharing important data sets[143]. The Budapest Open Access Initiative has a goal to accelerate progress to make research in all academic fields freely available. It defines "open access" to peer-reviewed research literature, as freely available on the public internet, permitting any users to read, download, copy, distribute, print, search, or link to the full texts of these articles, crawl them for indexing, pass them as data to software, or use them for any other lawful purpose, without financial, legal, or technical barriers other than those inseparable from gaining access to the internet itself[144]. A piece of data or content is open if anyone is free to use, reuse and redistribute it. A requirement to attribute and share-alike the new information is also crucial to open content data[145].

However, it seems that hardly any biobank can be regarded as an open science biobank. Yann Joly proposes that, at a minimum, an open biotechnology project should meet the following criteria[146]:

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139 Statistics Canada, 'Canadian Health Measures Survey' <http://www.statcan.gc.ca/eng/survey/household/5071#a2> accessed 8 May 2018.

140 Estonian Human Genes Research Act of 2000 December 13, published RT I 2000, 104, 685. § 16 (1) "Permission to use Gene Bank"

141 The Estonian Biobank, 'Estonian Genome Center, University of Tartu' <https://www.geenivaramu.ee/en/about-us> accessed 8 May 2018..

142 Estonian Human Genes Research Act of 2000 December 13, published RT I 2000, 104, 685 2000. § 1271 "Financing of chief processor of Gene Bank"

143 Giovanni Destro Bisol and others, 'Perspectives on Open Science and Scientific Data Sharing: An Interdisciplinary Workshop' (2014) 92 Journal of Anthropological Sciences 1–22.

144 Budapest Open Access Initiative, 'Ten Years on from the Budapest Open Access Initiative: Setting the Default to Open' <http://www.budapestopenaccessinitiative.org/boai-10-recommendations> accessed 8 May 2018.

145 Giovanni Destro Bisol and others, 'Perspectives on Open Science and Scientific Data Sharing: An Interdisciplinary Workshop' (2014) 92 Journal of Anthropological Sciences 6.

146 Yann Joly, 'Open Biotechnology: Licenses Needed' (2010) 28 Nature Publishing Group 417.

1. Make use at one stage or another of the internet and other information technologies (e.g. to promote quicker dissemination of results, promote collaboration and to improve project coordination).

2. Be designed in a way that will permit other members of the scientific community to collaborate on the project.

3. Include a strategy to ensure rapid public dissemination of the information and research results it generates.

4. Permit members of the scientific community **to use its results** without having to conclude restrictive agreements that would limit research freedom and integrity.

5. **Not use intellectual property (IP) to limit access to the project**, its results or to discriminate between different uses or different users. (*emphases added*)

Maybe not all of these criteria must be accomplished by a biobank to be considered as an open. However, the recent empirical study showed, that despite the consensus of the scientific community concerning the importance of open access of scientific resources, there are still sample and data sharing barriers among biobanks and researchers[147]. Concluding the results of this research, several specific restrictions can be named when accessing data or samples in biobanks:

1. Geographical restriction. Data/samples cannot leave the country of origin (applied by Canadian Health Measures Survey (CHMS), LifeLines Cohort Study & Biobank (LifeLines), Scottish Family Health Study (GS-SFHS))
2. Researchers limitations. I) Participation in the study – only researchers from the study can use data/sample (applied by Norwegian Women and Cancer Study postgenome cohort (NOWAC)); II) Researchers can be only from the public sector, nonprofit organizations or must conform with the *bona fide* requirement (Norwegian Women and Cancer Study postgenome cohort (NOWAC), European Prospective Investigation into Cancer and Nutrition (EPIC), Malmö Diet Cancer (MDC), Moli-Sani Project (Moli-Sani), LifeGene (LifeGene))
3. Research limitations. I) limited to particular projects (scope of the research, what questions the research wants to answer, e.g. only for cancel studies, heart diseases, etc.)
4. Data use limitations. Can be used only for academic, research purposes (NUgene project, No use by insurance companies, Scottish Family Health Study (GS-SFHS)). Excluded evidence collections, for surveillance purposes.

[147] Marco Capocasa and others, 'Samples and Data Accessibility in Research Biobanks: An Explorative Survey' [2016] PeerJ 13.

5. Need for additional approvals by scientific committees (requirement is applied to all public research biobanks)
6. Fees. Fees either to access data/samples or fees related to sending of samples (all biobanks apply at least a fee for the preparation and shipment of the samples).
7. Time scale. Approval of the scientific board(s) and preparation/shipment of the samples can take 2 to 6 months (not all biobanks indicate the time).
8. Return of research results. Samples, data and new data generated must be given back to the study (applied by GWAS, biochemical tests, Cohort of Swedish Men (COSM), Canadian Longitudinal Study on Ageing (CLSA), Canadian Health Measures Survey (CHMS), CARTaGENE (CaG)).
9. Restriction for generating IPR. I) Intellectual property rights resulting from the research using data/samples have to be negotiated with study representative. The publications (articles, presentation, etc) must be submitted to the study for review prior to public disclosure (applied by Cohort of Swedish Men (COSM), Canadian Longitudinal Study on Ageing (CLSA), Atlantic Partnership for Tomorrow's Health (The) (Atlantic PATH (The)), LifeLines Cohort Study & Biobank (LifeLines), LifeGene (LifeGene), KORA-gen - Cooperative health research in the Region of Augsburg, Japan Public Health Center-Based Study - Cohort II (JPHC Study - Cohort II), Banco Nacional de ADN Carlos III (BNADN), etc.).

For the benefit of science and the research, biobanks should be more readily available. It does not mean that all the mentioned barriers should be necessarily overcome thus leading to unrestricted access to biobank resources. In fact, some of these barriers guarantee some fundamental rights of donors (e.g., privacy, misuse prevention) so should be considered as 'necessary'[148]. However, today access to data and samples collected by biobanks is still too much restricted. In this work, I consider a biobank **open** if it does not have financial, technical, territorial, intellectual property rights or similar subjective limitations. Only legal restrictions that are not discriminatory for the researchers and are related to the protection of donors' privacy, human rights, can be justifiable. Bearing in mind the need to respect the donor's rights when trying to overcome the sharing barriers, the accessibility of biological resources should not be "unified" but rather go through standardized operating procedures[149]. Restrictions related with the ethical rules, national or international legal regulations, are not considered as a restriction to access data *per se*. Such requirements can be reasonably justified and usually has no impact to treat a biobank as a closed database.

[148] Ibid.
[149] Ibid.

III. Information stored in biobanks

1. Generalities

The core activities of research biobanks consist of a set of practices: to collect, store, distribute, and analyse a broad set of medical and biomedical materials and information[150]. A biorepository is a collection of biological material (e.g. animal, plant, human (skin, blood, organs, hair, saliva, etc.) cells, bacteria, yeast, molds etc.) together with corresponding documentation about it. As this research concentrates on biobanks collecting, storing and guarding cells from human donors, in this part, and later on in the text, I will mostly refer to the human samples or data.

The structured genetic resources that can be found in a biobank include: (a) human biological materials and information generated from the analysis of the same; and (b) extensive associated information[151]. Human biosamples may be collected through routine medical procedures or additional medical procedures when needed. Taking part in biobanking involves donating samples of body fluid and tissue.

The most common types of sample are blood and urine (for example in the UK Biobank) also saliva. Other types of the sample included samples from cancer tumors, spinal fluid, fat samples, and umbilical cord blood[152]. In cases of the deceased patients, whole organs can be collected in a biobank[153].

Apart from biosamples, which are very variable, biobanks also record and stores a huge amount of data. This data can be related to donor's personal information; such as height, weight and also epidemiological data about things that may have a bearing on health (e.g. family history and lifestyle)[154]. Medical data including specific biological data in connection to the stored biospecimen(s) and also all other medical conditions about the donor is also collected[155]. Such information may be recorded at the time when the sample is taken, to provide the context for the sample.

A donor fills a particular questioner when donating the bodily sample to a biobank, where he answers all the relevant questions. The genetic information from each human sample can

[150] BBMRI Project, 'Biobanks and the Public. Governing Biomedical Research Resources in Europe' (2013).
[151] OECD Guidelines on Human Biobanks and Genetic Research Databases (2009).
[152] DIPEx, 'Types of Biobanking Sample' <http://www.healthtalk.org/peoples-experiences/medical-research/biobanking/types-biobanking-sample> accessed 8 May 2018.
[153] Riegman P, Daidone MG and Hall J, 'Biobanking: FAQs' 7. Available at <http://www.ecpc.org/pressroom/news/projects/biobank-faq-eurocanplatform-wp10> accessed 8 May 2018.
[154] DIPEx, 'Types of Biobanking Sample'.
[155] Daniel Simeon-Dubach and Peter Watson, 'Biobanking 3.0: Evidence Based and Customer Focused Biobanking' (2014) 47 Clinical Biochemistry 300.

be linked to the individual's medical history and may be linked to his lifestyle data (e.g. diet, smoking etc.). Often the samples and the data are kept indefinitely or for several years so that long-term future research can be carried out[156].

Apart from providing access to human samples and their associated data, biobanks may offer access to a variety of medical information, including genomic data, population-genetic data and molecular data, which would be too expensive for many individual medical research laboratories to maintain[157]. Genomic data is a data derived from DNA using molecular biology techniques. The format of the data can be kept in many different ways depending on the technique used and can include the entire DNA sequence of organisms and fine-scale genetic mapping, single-nucleotide polymorphism (SNP), ribonucleic acid (RNA) molecules, complementary DNA[158], protein and other macromolecules.[159] Molecular data is another kind of data derived using molecular biology techniques for the study of molecular characteristics of cells and tissues (e.g. levels of genetic expression, biomarkers and protein structure and function) that are key to modern research.[160] This kind of data is not raw information, like samples. This kind of data is already processed by the researchers, from the use of samples. By using different techniques, researchers can extract information about the electronic structure, size, shape, dynamics, polarity, and modes of interaction of biological molecules[161]. Biobanking has reached an era where data and metadata extend far beyond the sample itself and now also include the full clinical history of the donors across primary, secondary and tertiary care, and the return of data about the samples generated by the researcher.[162]

2. Digitalization of the content

2.1. From samples to data

Biobanks have emerged as a new type of "Big Science" undertaking. The need for ever larger numbers of samples has raised the bar for investments into resource collections, from tens or hundreds of samples to tens or even hundreds of thousands of samples. Thus, over the

156 DIPEx, 'What Is Biobanking and Why Is It Important?' <http://www.healthtalk.org/peoples-experiences/medical-research/biobanking/what-biobanking-and-why-it-important> accessed 8 May 2018.

157 Riegman, Daidone and Hall 7.

158 Complementary DNA (cDNA) is double-stranded DNA synthesized from a single-stranded RNA (e.g., messenger RNA (mRNA) or microRNA (microRNA)) template in a reaction catalysed by the enzyme reverse transcriptase.

159 Riegman, Daidone and Hall 4-6.

160 Ibid.

161 Biophysical Society, 'Biophysical Techniques' <http://www.biophysics.org/education-careers/education-resources/selected-topics-in-biophysics> accessed 8 May 2018.

162 Philip R. Quinlan, Stephen Gardner, Martin Groves, Richard Emes, and Jonathan Garibaldi 'Data-Centric Strategy for Modern Biobanking' in Feridoun Karimi-Busheri (ed), *Biobanking in the 21st Century* (Springer International Publishing Switzerland 2015).

past few years, funding agencies have started to look at biobanks as an important common infrastructure for biomedical research—thus, the emergence of increasingly sizeable "infrastructure" biobanks that collect, store, and distribute large quantities of human blood and tissue samples potentially useful to many different investigative strategies and research purposes.[163] Biobanks today are increasingly turning into sizeable facilities with large numbers of tanks for cryopreservation, large sequencing or proteomics pipelines, and increasingly large computer rooms to store and analyse genomic and proteomic data.[164] According to a report from International Data Corporation, in 2011, the overall created and copied data volume in the world was 1.8ZB (≈ 1021B), which increased by nearly nine times within five years[165]. This figure will double at least every other two years shortly.

As the understanding of diseases increases, researchers require a far more vibrant data set about the donors from which the sample originate and also, to have access to previous research based on the same genetic data. Therefore, not only the specimens but also the associated data must be collected and stored. Biobanks are providing not just the biological samples, but also accumulating and creating an immense amount of data, related either to the information about the donor or new finding in gene sequences. Biology, like most scientific disciplines, is in an era of accelerated information accrual and scientists increasingly depend on the availability of each others' data.

Large-scale sequencing centres, high-throughput analytical facilities and individual laboratories produce vast amounts of data such as nucleotide and protein sequences, protein crystal structures, gene-expression measurements, protein and genetic interactions and phenotype studies[166]. It increases the scope of the biobank. As the costs of sequencing and analysis decrease, and with the increasing amount of data being stored at biobank facilities, many large biobanks are effectively turning into data centre facilities. Such biobanks are not only traditional cell or tissue banks, but also having great data storage equipment substituting liquid nitrogen tanks with samples[167]. The data in biobanks correlated with specimen increases explosively nowadays, not only because of the larger number of the basic specimen's information, but also because the development of high-throughput technologies which accumulate tons of original data for further analysis and application (composing of the information of genome, transcriptome, proteome, metabolome, and epigenome)[168] This shift

163 CORDIS European Commission, 'BBMRI Report Summary'.
164 Ibid.
165 Min Chen, Shiwen Mao and Yunhao Liu, 'Big Data: A Survey' [2014] Springer Science+Business Media New York 171–209.
166 Doug Howe and Seung Yon, 'The Future of Biocuration' (2008) 455 Nature 47.
167 CORDIS European Commission, 'BBMRI Report Summary'.
168 Massimiliano Izzo and others, 'A Digital Repository with an Extensible Data Model for Biobanking and Genomic Analysis Management.' (2014) 15 Suppl 3 BMC genomics S3.

from biological materials to information as the main ingredient of biobanks, while gradual, is already well underway.[169]

Biobanks have started so-called 'gene hunting', that gave way to a much more systematic and data-driven approach. 'Data-driven' describes a form of research that, rather than using the experiments and testing hypotheses, better relies on accumulating large amounts of data that can be systematically analysed, browsed, and systemized with the help of computer programs looking for models and connections.[170] Enormous amounts of sequencing data are assembled in large-scale databases, allowing for a more comprehensive analysis of living systems.

The role of the sample is a substrate to allow generation of data and annotations that are currently missing (such as protein or genetic information) and that researchers will use to select tissues that are relevant to their study according to such data. But samples may not always be appropriate, and future research can be based on previous studies that used same biological information. Therefore, today biobanks put a greater focus on data and the needs of the researchers.

To retain a sample-centric strategy in a research environment that is increasingly dictated by data will place a biobank at a significant disadvantage and even result in the samples collected going unused. As result biobanking is required to change strategic focus from a sample dominated perspective to a data-centric strategy.[171] In fact, it is quite conceivable that the biobanks shortly may well have more in common with large server farms and data centres, processing and storing vast amounts of genomic and medical data—rather than the cryopreservation facilities they are today.[172] Increasingly, what biobanks will provide to researchers is not a blood or tissue sample, but rather a data set for further analysis. It is also visible from the numbers given by the biobanks. The UK Biobank counted that from 762 preliminary applications to use biobank's resources during the year 2012-2016, 668 applications (so 87,7 %) requested only data without samples[173]. While samples need to be physically shipped to an end user, data is much more versatile. Large quantities of data can be easily downloaded over a fast network and replicated at many locations across the Internet.[174] As the number of population-based and large size biobanks is increasing throughout the

169 CORDIS European Commission, 'BBMRI Report Summary'.

170 Hub Zwart, 'Human Genome Project: History and Assessment' in James Wright (ed.) *International Encyclopedia of the Social & Behavioral Sciences (2nd Edition)* (Oxford: Elsevier 2015) 311-317.

171 Philip R. Quinlan, Stephen Gardner, Martin Groves, Richard Emes, and Jonathan Garibaldi 'Data-Centric Strategy for Modern Biobanking' in Feridoun Karimi-Busheri (ed), *Biobanking in the 21st Century* (Springer International Publishing Switzerland 2015).

172 CORDIS European Commission, 'BBMRI Report Summary' <https://cordis.europa.eu/result/rcn/162431_en.html> accessed 8 May 2018.

173 UK Biobank Ethics and Governance Council, 'Annual Review 2016 / 17 UK Biobank Governance' 3.

174 CORDIS European Commission, 'BBMRI Report Summary'.

world, sharing and ability to access metadata for anyone interested in most available possible means[175].

There are already examples, how biobanks are moving towards data-centric approach. The GenBank[176] is a comprehensive database that contains publicly available nucleotide sequences for almost 260 000 formally described species.[177] On 30 June 1982, the contract establishing of a public and free nucleic acid sequence databank (soon called GenBank) was signed[178]. The database comprises data from DNA DataBank of Japan (DDBJ), the European Molecular Biology Laboratory (EMBL), and GenBank at the National Center for Biotechnology Information (NCBI). These three organisations exchange data on a daily basis.[179]

In 2012 GenBank contained over 451 billion nucleotide base pairs, with the annual increase of 33%[180]. The information in GenBank contains data from the major DNA and protein sequence databases along with taxonomy, genome, mapping, protein structure and domain information, and the biomedical journal literature. While having its headquarters in Maryland state (USA), NCBI makes the GenBank data available at no cost over the Internet, through FTP and a wide range of web-based retrieval and analysis services[181]. NCBI places no restrictions on the use or distribution of the GenBank data. Funding for open access comes from Intramural Research Program of the National Institutes of Health and the National Library of Medicine.[182] What is also important from intellectual property rights perspective, GenBank also collaborates with US Patent and Trademark Office (US PTO), where US PTO contributes the sequences from issued patents. In the report of 2012, the number of patented sequences was more than 12 billion.[183]

Biomedical Big Data is not a new concept in biotechnology anymore. GenBank is a clear example of big data database in the biotechnology field. Future biobanking in the age of New Biology would be a powerful resource to solve many questions regarding the incredible diversity and the dynamic complexity of human beings; including, evolution, human behavior, and cutting-edge research on anti-ageing and longevity. This is not a futuristic vision considering what biobanking is forming even now. Biobank can potentially store the vast

175 Feridoun Karimi-Busheri and Aghdass Rasouli-Nia 'Integration, Networking, and Global Biobanking in the Age of New Biology' in Feridoun Karimi-Busheri (ed), *Biobanking in the 21st Century* (Springer International Publishing Switzerland 2015).

176 National Center for Biotechnology Information, 'Welcome' <https://www.ncbi.nlm.nih.gov/> accessed 8 May 2018.

177 Dennis A Benson and others, 'GenBank' (2013) 41 Nucleic Acids Research 36.

178 Bruno J Strasser, 'GenBank-Natural History in the 21st Century?' (2008) 322 Science 537 LP.

179 NCBI, 'GenBank Overview' <https://www.ncbi.nlm.nih.gov/genbank/> accessed 8 May 2018.

180 Benson and others 38.

181 NCBI Resource Coordinators. (2013) Database resources at the National Center for Biotechnology Information. Nucleic Acids Res., 41, D8–D20.

182 Benson and others 36.

183 Ibid 38.

amount of data and information around the world generated from DNA, blood, saliva, tissue and tumors, umbilical cord, urine, physical measures, hair, teeth, MRI and other scans.[184]

Other examples of big data biobank projects are 1000 Genomes Project and International HapMap Project. 1000 Genomes Project ran between 2008 and 2015. It created the largest public catalogue of human variation and genotype data. The goal of the 1000 Genomes Project was to find most genetic variants with frequencies of at least 1% in the populations studied. The 1000 Genomes Project took advantage of developments in sequencing technology, which sharply reduced the cost of sequencing. It was the first project to sequence the genomes of a large number of people, to provide a comprehensive resource on human genetic variation. Data from the 1000 Genomes Project was quickly made available to the worldwide scientific community through freely accessible public databases. The project generated over 84.4 million variants of data sequences. [185] All cell culture and DNA samples from the project can be accessed as well, however, a fee must be paid.[186]

In 2001 the International HapMap Consortium launched the project called the International HapMap Project, that developed a haplotype map ("HapMap") of the human genome – a resource that describes the general patterns of human DNA sequence variation. The HapMap has become an essential tool for researchers to find genes that affect health, disease, and response to drugs or environmental factors. All HapMap data are freely available to the public through the particular database. [187]

Big data is an abstract concept. But it can be described, as a large-volume, complex, growing data sets with multiple, autonomous sources[188]. Apart from masses of data, Big Data also has some other features. Riccardo Bellazzi describes Big Data in biomedicine by four most relevant elements, namely: Volume, Variety, Velocity, and Veracity. Other authors add Value to this description[189]. Volume means that the data must be large, sizable, massive. Variety means that the data stored are unstructured and structured texts, images, signals and streams, point-based numerical values, meta-data – all kinds of different information. Data may refer to different dimensional scales, from the molecular to the population one, and span over different time scales, from milliseconds to years. The third element – velocity, i.e. the speed of analytical processing. Data must be accessed quickly, timely and by the speedy

[184] Feridoun Karimi-Busheri and Aghdass Rasouli-Nia 'Integration, Networking, and Global Biobanking in the Age of New Biology', in Feridoun Karimi-Busheri (ed), *Biobanking in the 21st Century* (Springer International Publishing Switzerland 2015).

[185] EMBL-EBI, 'About IGSR and the 1000 Genomes Project' <http://www.internationalgenome.org/about> accessed 8 May 2018.

[186] Coriell Institute, '1000 Genomes Project' <https://www.coriell.org/1/NHGRI/Collections/1000-Genomes-Collections/1000-Genomes-Project> accessed 8 May 2018.

[187] Coriell Institute, 'International HapMap Project' <https://www.coriell.org/1/NHGRI/Collections/HapMap-Collections/HapMap-Project> accessed 8 May 2018.

[188] Xindong Wu and others, 'Data Mining with Big Data' (2014) 26 IEEE Trans. on Knowl. and Data Eng.

[189] Baro Emilie and others, 'Toward a Literature-Driven Definition of Big Data in Healthcare' [2015] BioMed Research International 9.; Vivien Marx, 'The Big Challenges of Big Data' (2013) 498 Nature 259.

broadband connection. Fourth it's veracity – or the uncertainty of the data. Extensive data collections may often combine various sources of variable reliability and trust.[190] Value means that due to the amount of data, the analyses in great volumes can lead to new insights and substantially increase the value of the data[191].

Biomedical Big Data is diverse and complex. It includes imaging, phenotypic, molecular, exposure, health, behavioral, and many other types of data, any data that could be used to discover new drugs or to determine the genetic and environmental causes of human disease[192]. Biobanks are the most precious source of material available in the post-genomic era. An increasing source of data from blood to tissues, DNA, saliva, and other sources has generated a tremendous amount of information that is useful to all aspects of omics, arrays, and next-generation sequencing[193]. Biobanks have already entered the area of "Big Data" and are increasingly turning into large data centre facilities or "cloud" environments[194]. With the fast development of networking, data storage, and the data collection capacity, Big Data are now rapidly expanding in all science and engineering domains. Biobanks are no exception. What is created today will be the largest ever library of biological materials. Data, produced or published in accordance to a high standard, and made accessible as soon as it becomes available, would allow biological research to be conducted much faster. The challenges concerning location, integration and access of Big Data so far has to be overcame[195], however the collections already stored is a big step towards more individualized and improved medicine. Digesting information and generating hypotheses at the computer screen will be so much faster, experiments will be designed with more insight increasing exponential growth in knowledge.

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190 R Bellazzi, 'Big Data and Biomedical Informatics: A Challenging Opportunity.' (2014) 9 Yearbook of medical informatics 8.

191 Amir Gandomi and Murtaza Haider, 'Beyond the Hype: Big Data Concepts, Methods, and Analytics' (2015) 35 International Journal of Information Management 137.

192 National Institutes of Health, 'What Is Big Data?' <https://datascience.nih.gov/bd2k/about/what> accessed 8 May 2018.

193 Feridoun Karimi-Busheri and Aghdass Rasouli-Nia 'Integration, Networking, and Global Biobanking in the Age of New Biology', in Feridoun Karimi-Busheri (ed), *Biobanking in the 21st Century* (Springer International Publishing Switzerland 2015) 5.

194 BBMRI Project, 'Biobanks and the Public. Governing Biomedical Research Resources in Europe' (2013) 58.

195 One of the most challenging issues in modern biobanking is the ever increasing complexity of data management and integration. Advanced high throughput profiling machines are constantly adding several hundred gigabytes of data into the biobanks. Biobanks and repositories are no longer limited to one laboratory or department and facility, as heterogeneity of the collected data is so immense that no single standardization could handle the extensive metadata. For more information please see Feridoun Karimi-Busheri and Aghdass Rasouli-Nia, "Integration, Networking, and Global Biobanking in the Age of New Biology", in Feridoun Karimi-Busheri (ed), Biobanking in the 21st Century; Min Chen et al. "Big Data: A Survey", Springer Science+Business Media New York (2014); Vivien Marx "The Big Challenges of Big Data", Nature Vol. 498 (2013); Doug Howe et al. "Big data:The future of biocuration", Nature 455 (2008).

2.2. Data storage: from cloud computing to synthetic DNA

With the increase of the information in the biobanks and the need to access such information quickly, much of the construction in big-data biology is virtual, focused on cloud computing. High throughput analysis, such as next-generation sequencing (NGS), generates terabytes of data. Data of the biobanks is situated in huge, off-site centres that users can access on demand through the network connection (in the Internet, or local network). Labs can create virtual spaces for data, software and result that anyone can access, or they can lock the spaces up behind a firewall so that only a select group of collaborators can get to them[196]. Big data in biology adds the possibilities for scientists to make discoveries on already discovered information. New findings can be done composing prior facts and knowledge, using under-analysed data available in databases all over the world.

In this context, it is much more useful to think of modern biobanking as an informatics project supported by a high-quality, scientifically driven tissue collection and storage strategy, rather than as a high-quality tissue collection and storage strategy supported by an IT system[197]. The reason is to promote the use of a biobank, to make biospecimen available on demand and at the most affordable cost. It is of general importance in the biobank networks, where accompanying sample information is uploaded onto a central database, and researchers can identify collections of interest and access them from the multiple collection sites[198].

Cloud computing becomes vital to ensure the easier access to information and faster means to share the data. Cloud storage may occur either in public or private clouds, but the essence remains the same, which is scaling storage capacity and performance, and providing shared access via a standard network[199]. Many scientists access databases and software tools on the Web and through clouds. One heavily used resource is the Ensembl Genome Browser, run jointly by the EBI and the Wellcome Trust Sanger Institute in Hinxton. Life scientists use it to search through, down- load and analyse genomes from armadillo to zebrafish.[200] Clouds are the solution, but they also throw up fresh challenges. Some companies are avoiding clouds because of security problems. Information can be leaked; the data may not be secure when transiting it to the cloud, the uploaded data must be encrypted with adequate encryption tools. As biobanks collect and store sensitive information about the research participants, all such security issues must be properly solved.

196 Vivien Marx, 'The Big Challenges of Big Data' (2013) 498 Nature 255.
197 Philip R. Quinlan and others, 'A Data-Centric Strategy for Modern Biobanking' (2015) 864 Advances in Experimental Medicine and Biology 165.
198 Karimi-Busheri and Aghdass Rasouli-Nia 19.
199 Ken Rubenstein, *Cloud Computing in Life Sciences R&D* (Cambridge Healthtech Institute 2010) 13.
200 Vivien Marx 259.

There are tools created that ensure the data safety in the cloud. For example, the DNAnexus cloud[201] has been created to be compliant with US and European regulatory guidelines. In the DNAnexus cloud, all data are encrypted, unencrypted data is transient, existing only in worker node memory. All data, tools, and workflows are tracked and controlled to ensure traceability and reproducibility.

When storing the medical information on the online platforms, the protection of patients personal medical information is critical. In accordance with the US Health Insurance Portability and Accountability Act (HIPAA)[202], the US Department of Health and Human Services (HHS) developed the Privacy Rule, which constitutes a broad-ranging federal health privacy regulations and generally restricts the use or disclosure of protected health information, except as permitted by the individual or as authorized or required by the Privacy Rule[203]. Biobanks, just like other individuals or organisations that electronically transmit health information, shall comply with the Privacy Rule regulations[204]. So, biobanks should be cautious about the information they store and information that is available for the researchers.

Similarly, to the US Privacy Rule, European law also regulates the protection of personal information. The Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation) protects fundamental rights and freedoms of natural persons and in particular their right to the protection of personal data. Biobanks must respect the rules of the General Data Protection Regulation to the extent they collect, store and process human biological materials, in combination with other forms of personal data, such as genetic and health data.

There are other problems that can be caused by cloud storage. Clouds' proliferation can cause a bottleneck if data end up parked on several clouds and thus still need to be moved to be shared. Using cloud storage could mean entrusting valuable data to a distant service provider who may be subject to power outages or other disruptions[205]. Therefore, mainly because the amount of data generated increases daily, new possibilities to store information are searched.

In 2012 George M. Church with his team developed a strategy to encode arbitrary digital information stored in a DNA by using a novel encoding scheme that uses next-generation

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201 DNA Nexus, 'PRODUCT OVERVIEW' <https://www.dnanexus.com/product-overview> accessed 8 May 2018.

202 The Health Insurance Portability and Accountability Act of 1996 (HIPAA).

203 SJ Nass and O Lawrence Levit, L. A. Gostin, *Beyond the HIPAA Privacy Rule: Enhancing Privacy, Improving Health Through Research* (National Academy of Sciences 2009).

204 National Institutes of Health, 'Summary of the HIPAA Privacy Rule' <https://www.hhs.gov/hipaa/for-professionals/privacy/laws-regulations/index.html> accessed 8 May 2018.

205 Vivien Marx, 255–259.

DNA synthesis and sequencing technologies[206]. The technology leverages next-generation technologies in both DNA synthesis and sequencing to allow for encoding and decoding of large amounts of information[207]. A DNA storage system consists of a DNA synthesizer that encodes the data to be stored in DNA, a storage container with compartments that store pools of DNA that map to a volume, and a DNA sequencer that reads DNA sequences and converts them back into digital data[208].

How it works, is that information is coded into four DNA bases: adenine, guanine, cytosine, and thymine. The information is inserted into a cell and can be decoded using gene sequencing technologies. Reading the DNA pairs, the information can be restored to a form that is understandable to a person – imagine, script, video. Recently the scientists from Harvard University used the CRISPR genome-editing tool to store an animation of a running horse adapted from Eadweard Muybridge's 1878 photographic study *Human and Animal Locomotion* in the genome of *E. coli* bacteria[209]. And later they successfully decoded this information from the DNA.

A single gram of DNA can store almost one trillion gigabytes (almost a zettabyte) of digital data. DNA-based storage has the potential to be the finest archival storage solution because it is incredibly dense and permanent[210]. The volume of data that can be synthesized in DNA today is limited mostly by the cost of synthesis and sequencing. But with the growth of data in the biotechnology industry and the interest in DNA storage from other sectors (information technology), the costs have dropped down evidently and the efficiency of DNA storage has been improved.

206 George M Church, Y Gao and Sriram Kosuri, 'Next-Generation Digital Information Storage in DNA' (2012) 337 Science 1628.

207 Ibid.

208 James Bornholt and others, 'A DNA-Based Archival Storage System' [2016] Proceedings of the 21st International Conference on Architectural Support for Programming Languages and Operating Systems (ASPLOS'16) 637.

209 Ian Sample, 'Harvard Scientists Pioneer Storage of Video inside DNA' *The Guardian* (2017). Available at https://www.theguardian.com/science/2017/jul/12/scientists-pioneer-a-new-revolution-in-biology-by-embeding-film-on-dna accessed 2018 May 8.

210 Bornholt and others, 639.

CHAPTER II

INTELLECTUAL PROPERTY RIGHTS IN BIOBANKING. CURRENT LEGAL STATUS

I. Overview of biobanks regulations

1. International legal instruments

This part of the chapter by no means is going to talk profoundly about the complexity of the general legal regulations of the biobanks. Taking into account social differences in the countries, disparate legal backgrounds and doctrines, it would be out of the scope of this thesis to look and analyse all of them. However, a basic understanding of the legislative grounds helps to proceed a decent analysis on the topic and assists the reader to have a better image on the biobanks regulation in general.

Although biobank research takes place on a global scale, there is no internationally binding framework for its ethical or legal regulation, rather just a scarce legislative action or soft laws. The establishment and functioning of the biobanks are mostly regulated by national laws, secondary acts or biobank's internal rules. However, there are few international or regional instruments that regulate the protection of donor's right, requirements for the scientific research in the field of biology and genetic investigations. Such legal acts as the Council's of Europe 1997 Convention on Human Rights and Biomedicine[211] can be mentioned or 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.[212]

The Convention on Human Rights and Biomedicine lay down a series of principles and prohibitions concerning bioethics, medical research, consent, rights to private life and information, organ transplantation, public debate. Directive 2004/23/EC lays down the standards for the collection and storage of the human biological samples. It must be implemented by all the Member States in its national legislation. This Directive does not

[211] Convention for the protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine 1997. (adopted 04 April 1997, entered into force 01 December 1999) ETS No.164 (Convention on Human Rights and Biomedicine)

[212] Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells., OJ L 102, 7.4.2004, p. 48–58.

cover research using human tissues and cells, such as when used for purposes other than the application to the human body, e.g. *in vitro* research,[213] however, it establishes fundamental principles and requirements that by analogy could also be applied to the collection of human samples for the research performed outside a living organism.

More frequently the rules for the biobanks are presented in the form of recommendations or declarations. Some authors count more than thirty international documents concerning privacy, consent, anonymisation, access, security, and governance in biobanking.[214] However, most of these sources are dealing with the protection of donor's rights and only a few talks about biobank's governance. Without indicating international instruments related solely with the protection of human rights and fundamental freedoms,[215] I consider the following international sources most relevant in the biobanks regulation:

- International Declaration on Human Genetic Data[216] (UNESCO) (2003)
- Universal Declaration on the Human Genome and Human Rights (UNESCO) (1997)
- Universal Declaration on Bioethics and Human Rights (UNESCO) (2005)
- Recommendation on research on biological materials of human origin[217] (the Council of Europe's Committee of Ministers') (2006)
- Guideline for obtaining informed consent for the procurement and use of human tissues, cells and fluids in research (WTO Scientific and Ethical Review Group) (2003)
- OECD Recommendation on Human Biobanks and Genetic Research Databases (2009)
- OECD Principles and Guidelines for Access to Research Data from Public Funding (2007)
- The opinion of the European Group on Ethics in Science and New Technologies on Ethical Aspects of Human Tissue Banking[218] (1998).

213 Recital 11 of the Directive 2004/23/EC.

214 Adrian Thorogood and Ma'n H Zawati, 'International Guidelines for Privacy in Genomic Biobanking (or the Unexpected Virtue of Pluralism)' (2015) 43 Journal of Law, Medicine and Ethics 691.

215 From these sources the UN General Assembly, Universal Declaration of Human Rights (1948), UN General Assembly, International Covenant on Civil and Political Rights (1966), UN General Assembly, Convention on the Rights of the Child (1989) can be mentioned. However, these sources do not deal with the bioethics or biobanks directly, therefore, for the scope of this research they will not be analysed or mentioned in depth.

216 UNESCO, 'International Declaration on Human Genetic Data' (2003).

217 Council of Europe Committee of Ministers, 'Recommendation Rec(2006)4 of the Committee of Ministers to Member States on Research on Biological Materials of Human Origin and Its Explanatory Memorandum' (2006).

218 Opinion of the European Group on Ethics in Science and New Technologies No. 11 on Ethical Aspects of Human Tissue Banking (1998).

There are also several international associations or projects (such as WMA,[219] HUGO,[220] GA4GH,[221] ISBER,[222] CIOMS,[223] BBMRI[224]) that have published different recommendations, frameworks or best practices regarding the gene research, DNA sampling of biobanks governance.

2. National legislation

In the national jurisdictions, the instruments regulating establishment and functioning of the biobanks varies. Some countries have national laws governing role and working methods of the biobanks. For example, in Spain the Royal Decree 1716/2011[225] establishes the basic requirements for the authorisation and operation of biobanks for biomedical research purposes as well as for the treatment of human biological samples.[226] It also regulates the operation and organisation of the National Biobanks Registry. The Spanish Law 14/2007 on Biomedical Research (LBR),[227] establishes requirements for biomedical research, including requirements for informed consent, evaluation and authorisation of the research, management of personal genetical data.

Similarly, biobanks are regulated in northern European countries. Estonia,[228] Finland,[229] Iceland,[230] Sweden,[231] Norway,[232] all these countries have specific laws on the establishment of biobanks and the use of human samples in research studies.

In the UK, there is no public law regulating the establishment and functioning of a biobank. The UK Biobank has its own internal rules – Ethics and Governance Framework,[233] Protocol for a large-scale prospective epidemiological resource.[234] The national UK law,

219 World Medical Association, 'WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects' (1964).
220 Statement on DNA sampling control and access (1999) 8.
221 Constitution of the Global Alliance for Genomics and Health (2018) 1.
222 Lori D Campbell and others, 'BEST PRACTICES: Recommendations for Repositories' [2018] ISBER.
223 Council of International Organizations of Medical Sciences, 'International Ethical Guidelines for Epidemiological Studies' (2009).
224 BBMRI Project, 'Biobanks and the Public. Governing Biomedical Research Resources in Europe' (2013).; BBMRI-ERIC, 'Comments to the Public Consultation on the Council of Europe Recommendation (2006) 4 on Research on Biological Materials of Human Origin'.
225 Real Decreto 1716/2011, de 18 de noviembre, por el que se establecen los requisitos básicos de autorización y funcionamiento de los biobancos con fines de investigación biomédica y del tratamiento de las muestras biológicas de origen humano, y se regula e 2011 128434.
226 Pilar Nicolás, 'Spanish Regulation of Biobanks' (2015) 43 Law, Medicine and Ethics 801.
227 Ley 14/2007, de 3 de julio, de Investigación biomédica 2007 (BOE nú m) 28826.
228 Estonian Human Genes Research Act of 2000 December 13, published RT I 2000, 104, 685 2000.
229 Finnish Biobank Law 688/2012 of October 2, 2012.
230 Iceland Biobanks and Health Databanks Act No. 110/2000, as amended by Act No. 27/2008, No. 48/2009 and No. 45/2014.
231 Biobanks in Medical Care Act (2002:297) 2002.
232 Norwegian Act Relating to Biobanks 2003 1.; subsequently replaced by the Act on medical and health research of ACT 2008-06-20 no. 44: Act on medical and health research (the Health Research Act) 2008.
233 UK Biobank Ethics and Governance Framework 2007.
234 UK Biobank: Protocol for a large-scale prospective epidemiological resource UK Biobank Coordinating Centre Stockport.

however, regulates the use of human samples and protection of donor's personal information. The national law – Human Tissue Act 2004 – regulates the removal, storage and use of human organs and other tissue for research purposes.[235] Another legal act, Research Governance Framework for Health and Social Care, prepared by the UK Department of Health, sets national standards for the protection of research participants' rights,[236] responsibilities of people involved in the research.[237] UK Biobanks' internal rules assure the respect and compliance with the above-mentioned laws.[238]

Creation and operation of biobanks in Italy are subject to rules mainly derived from guidelines and "soft laws" instruments, such as non-binding recommendations issued by ethics committees and scientific associations.[239] As well in Germany, there are no laws regulating biobanks. The general legal framework for biobanking in Germany is a collection of abstract norms, applied specifically to the procurement, storage, and use of human tissues and cells (and associated data).[240] Germany regulates some issues related to the use of human material through the German Drug Law and the Medical Devices Law.[241] France also has decided to regulate biobanks under the umbrella of various laws and it does not have a specific act on biobanks.[242]

The US has not enacted laws explicitly regulating biobank creation or governance.[243] Instead, legal regulation focuses on biobank activities: genomic research, informed consent and protection of privacy. Furthermore, different states in the country have different rules regulating genetic research. Genetic-specific laws in a single state may address discrimination based on genetic information, concerns about autonomy in and understanding of genetic testing (informed consent, direct-to-consumer advertising), or related privacy issues.[244] Such disparities make biobanking laws highly confusing and very complicated.

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235 UK Human Tissue Act 2004. Part 1 "Removal, storage and use of human organs and other tissue for scheduled purposes"

236 UK Department of Health, Research governance framework for health and social care (Second edition, 2005). Part 2 "Standards"

237 Ibid. Part 3 "Responsibilities and accountability"

238 UK Biobank Ethics and Governance Framework.

239 Alessia Calzolari, Mariarosaria Napolitano and Elena Bravo, 'Review of the Italian Current Legislation on Research Biobanking Activities on the Eve of the Participation of National Biobanks' Network in the Legal Consortium BBMRI-ERIC.' (2013) 11 Biopreservation and biobanking 124.

240 Nils Hoppe, 'Privacy Laws and Biobanking in Germany' (2016) 44 The Journal of Law, Medicine & Ethics 35.

241 Christian Lenk, 'Medical Ethicists: Biobanks Need Harmonization rather than New Laws' [2011] BIOPRO Baden-Württemberg GmbH 1.

242 Emmanuelle Rial-Sebbag and Anna Pigeon, 'Regulation of Biobanks in France' (2015) Winter Journal of Law, Medicine and Ethics 754–765.

243 Heather L Harrell and Mark A Rothstein, 'Biobanking Privacy Laws in the United States' (2016) 44 Journal of Law, Medicine and Ethics 121.

244 ibid 118–119.

From the most important federal acts regulating biological research, the Federal Policy for the Protection of Human Subjects[245] (generally titled as the Common Rule) must be mentioned. The Common Rule outlines the basic provisions for Institutional Review Boards (IRBs), informed consent, and Assurances of Compliance. The US Food and Drug Administration (FDA) created its regulations addressing the same core components of research, and the FDA regulations apply to research performed in contemplation of submission to the FDA.[246] Biobank research, if conducted through an institution that has signed onto the Common Rule, must comply with the Common Rule regardless of its funding source.[247] FDA regulations apply to research on specimens, not data. Therefore, biobanks are subject to FDA regulations if they are engaged in research with their specimens, or researchers are using biobank specimens in their studies if the research studies an investigational drug or medical device.[248]

For the research biobanks, United States' National Institute of Health (NIH) is an vital institution providing guidelines and recommendations. US NIH has issued a policy on genomic data sharing[249] and also has published information about intellectual property policies in genetic research.[250] The Policy applies to researches funded in part or in total by the NIH if the NIH funding supports the generation of the genomic data.[251]

All of these mentioned rules vaguely mention intellectual property rights or regulates its creation in the biobanks. Understandably, when international instruments regulating intellectual property rights exist in the world, specific biobank rules do not wish to intervene or duplicate such regulations. Nevertheless, there are some allusions in the above-mentioned rules about the intellectual property rights created in the biorepositories.

II. IPR regulation in biobanks

Despite efforts to simplify the process of securing intellectual property rights (IPR) (e.g. international treaties, centralized patent offices), such rights are still registered and protected

245 US Federal Policy for the Protection of Human Subjects ('Common Rule') 1981. Available at http://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/ accessed 2018 May 8.
246 FDA Regulations Relating to Good Clinical Practice and Clinical Trials. Available at <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/ucm155713.htm> accessed 2018 May 8.
247 Harrell and Rothstein 111.
248 ibid 113.
249 NIH, 'National Institutes of Health Genomic Data Sharing Policy, Notice Number NOT- OD-14-124'. Available at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-124.html accessed 2018 May 8.
250 NIH, 'NIH Grants Policy Statement States the NIH Policy Regarding IPR' (2015). Available at: http://grants.nih.gov/policy/nihgps/index.htm accessed 2018 May 8.
251 Federal Register Notices, Vol. 79, No. 167, August 28, 2014, p. 51345.

by national laws and is valid only in the countries that grant them (principle of territoriality)[252]. As there is a weak international regulation of the biobanks, unlikely any guidance regarding IPR protection in this field can be found.

Some national biobank laws or international soft law instruments mentions intellectual property rights or patent rights concerning the dissemination of the research results. Spanish legislation[253] establishes that researchers must take into account the intellectual and industrial property rights once publishing the results of the investigation.

Norway's legislation foresees that

> "The person or body responsible for the research and the project manager can apply to the regional committee for medical and health research ethics for deferred publication in cases where this is necessary to protect legitimate interests linked to patents or competition <...>.[254]"

Section 27 of the Finish biobanks law[255] states that a biobank may restrict the granting of access to samples and information if it may interrupt with intellectual property rights. Estonian Human research act[256] section 19, directs all the IPR questions to the basic IP laws. However, same section imperatively states, that the descriptions of DNA or parts thereof shall be unconditionally delivered to the chief processor[257].

WTO guidelines for obtaining informed consent for the procurement and use of human tissues, cells and fluids in research[258], advice to inform the research subjects in advance about possible commercial value of the research and if they would receive any money or other benefits of intellectual property rights that may result from commercial applications of the research.

The biobank's institutions can of cause regulate the IPR questions in its internal documents, as the UK Biobank does it. In its Ethics and governance framework[259], the UK biobank states that its primary aim to become a valuable shared resource for research. Therefore, it is not expected in itself to lead to patentable inventions that return significant income either to researchers or UK Biobank. Furthermore, UK biobank indicates that no IPR

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252 Edward S Dove and Yann Joly, 'The Contested Futures of Biobanks and Intellectual Property' (2012) 11 Teoría y derecho 132–146.

253 Ley 14/2007, de 3 de julio, de Investigación biomédica. Article 27(3).

254 ACT 2008-06-20 no. 44: Act on medical and health research (the Health Research Act). Chapter 8 para. 45.

255 Finland Biobank Law 688/2012 2012.

256 Estonian Human Genes Research Act of 2000 December 13, published RT I 2000, 104, 685.

257 Estonian Human Genes Research Act § 3, establishes the chief processor of Gene Bank: (1) The chief processor of the Gene Bank is the University of Tartu whose objective as the chief processor of the Gene Bank is to: 1) promote the development of genetic research; 2) collect information on the health of the Estonian population and genetic information concerning the Estonian population; 3) use the results of genetic research to improve public health.

258 Guideline for obtaining informed consent for the procurement and use of human tissues, cells and fluids in research 2000.

259 UK Biobank Ethics and Governance Framework.

generated by UK biobank can be used in any way that inappropriately constrains use by others. It also imperatively states that all research users must put results from all analyses made on participants' data and samples, and any relevant supporting information in the UK Biobank database, so that they are subsequently available to all researchers with appropriate scientific and ethics approval. There is also a requirement for all research users to place the findings (whether positive or negative) from all research based on UK Biobank in the public domain so that people can benefit from them. On the other hand, similarly as Spanish and Norwegian[260] acts, internal UK Biobank rules allow to keep results confidential for a limited and reasonable period because of IP related matters (for example, while researchers prepare papers for publication, file patent applications or otherwise pursue reasonable competitive advantage for their efforts).

There is no restriction for the biobanks to own intellectual property rights. As legally established entities, biobanks can apply for patents, trademark registrations or claim copyrights. Even if established for research purposes, a biobank can apply for IPR protection. UK Biobank regulates in its policies that it has no objective to acquire IPR, but it does not prohibit the researchers to do so. What can be summarised from the above-mentioned legislation is that IPR in biobanks is referred not only as the revenues generating tools, providing commercial gain to a biobank but also as a possible restriction to use the genetic resources for others. Therefore, biobanks quite clearly express the need to disseminate the research outcomes and return the research results back to the biobank. Too much intangible protection to biobank's materials might be a burden for other forthcoming research. Future uses of the information might be banned if monopoly rights over such information are given to a single enterprise. However, biobanks cannot forbid researchers to gain IPR. IPR are well established legal rights and must be respected by all the states and persons, including such legal entities as biorepositories. Therefore, even if biobanks would believe, that no IPR in this field is better for the society, it could never declare going against or preventing researchers to apply for IPR, and no matter in which form such rights would arise – copyright or patent.

[260] ACT 2008-06-20 no. 44: Act on medical and health research (the Health Research Act)., para 45.

CHAPTER III

COPYRIGHT AND DATABASES IN BIOBANKS

I. Copyright of the genomic data

Biobanks not only collect and stores biological data, bus also, as concluded in the previous part of this thesis, one of the primary missions of the biobanks is to perform research. Participants and researchers at the biobanks are working every day with the specimen's collections or relevant data to make new findings of a disease, its roots, causes. Researchers are sequencing new genes, discovering new genetic information. Naturally, research leads to publications, which are the objects protected by copyright law.

Article 2 of the Berne Convention for the Protection of Literary and Artistic Works[261] states that protected literary and artistic works include:

> *"every production in the <...> scientific <...> domain, whatever may be the mode or form of its expressions, such as books, pamphlets and other writings; lectures, addresses, sermons and other works of the same nature."*

There is no doubt that fixed in a material form biobank's studies and other research outcomes are automatically protected by copyright. The question however is, can the genomic data, such as gene sequences, single-nucleotide polymorphism (SNP), ribonucleic acid (RNA) molecules, complementary DNA and similar, be protected by copyright law?

The *sine qua non* for statutory copyright protection under any legal system is that the work must be original and fixed in a tangible form. An author's work can be copyrighted only if it fits within the statutory definition of copyrightable subject matter; otherwise, it falls into the public domain and can be used by all.[262] For example, Directive 2009/24/EC[263] on the legal protection of computer programs states that a computer program shall be protected if it is original in the sense that it is the author's intellectual creation and expressed in any form of a computer program.[264] Another Directive 2006/116/EC[265] harmonising the term of protection of copyright and certain related rights protects works which are original creation.[266] US law

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261 Berne Convention for the Protection of Literary and Artistic Works 1886.
262 Jessica D Litman, 'The Public Domain' (1990) 39 Emory Law Journal 965–1023.
263 Directive 2009/24/EC of the European Parliament and of the Council of 23 April 2009 on the legal protection of computer programs 2009.
264 Article 1(2) and Article 1(3).
265 Directive 2006/116/EC of the European Parliament and of the Council of 12 December 2006 on the term of protection of copyright and certain related rights 2006.
266 Ibid. Article 6.

declares that "copyright protection subsists <...> in original works of authorship fixed in any tangible medium of expression".[267]

1. Fixation requirement

When looking at the gene sequences, DNA codes and other biological information stored in the biobanks, the question if such information is fixed in the tangible form must be answered. Some authors argue that DNA fragments should be copyrightable. One of the supporting arguments are that DNA fragments and cultures of engineered cells are fixed in a tangible form which is permanent (DNA sequence can be coded and recorded in an electronic form,[268] genetic works are fixed in a cells and cell cultures, sequence of the base pairs in DNA is fixed in the DNA itself), they can be reproduced, as the fissions of the cell is the entire point of genetic engineering, and the information from such data can be recognized by particular machine or device.[269]

Fixation, on the other hand, is losing its statutory provisions and depending on a country's national laws can be not such a strict requirement. It is proposed by the scientific community that fixation requirement is too strict and does not correspond to the current social needs (for example, to protect the rights of the contemporary artists[270] or playwright directors[271]). Such countries as France or Great Britain does not implicitly require fixation of the work to be a precondition of protection.[272] The TRIPS Agreement does not require that copyrightable works be fixed in some way.[273] Some authors[274] state, that fixation requirement is in reality motivated by evidentiary concerns and helps to distinct the expression – that is copyrightable, from the idea – that is not. The whole point of the idea/expression dichotomy is to recognise rights in the specific expression an author uses to write, sing, or code his inspiration, all without granting rights to the abstract ideas communicated thereby.[275] Without substantial evidence, authors point, expression can blur into an idea.

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267 17 U.S.C. § 102: US Code. - Section 102: Subject matter of copyright.

268 Protein Information Management System, 'DNA Sequence Help' <https://www.oppf.rc-harwell.ac.uk/pims/help/target/HelpRecordDNASeq.jsp#codingSequence> accessed 8 May 2018.

269 Irving Kayton, 'Copyright in Living Genetically Engineered Works' (1982) 191 George Washington Law Review 198.

270 Megan Carpenter and Steven Hetcher, 'Function Over Form: Bringing the Fixation Requirement into the Modern Era' (2014) 82 Fordham Law Review 2221.

271 Carrie Ryan Gallia, 'To Fix, or Not To Fix: Copyright's Fixation Require Ment and the Rights of Theatrical Collaborators' (2007) 92 Minnesota Law Review 1.

272 Paul Goldstein and P Bernt Hugenholtz, *International Copyright. Principles, Law, and Practice* (Third edit, Oxford University Press 2013) 233.

273 Carrie Ryan Gallia 16.

274 Douglas Lichtman, 'Copyright as a Rule of Evidence' (2003) 52 Duke Law Journal 683.; Carpenter and Hetcher.

275 Lichtman 731.

The main rule is that copyright does not protect ideas, but only their expressions. In the copyright law, the idea-expression dichotomy was explained back then in the year 1879, where the US Supreme Court ruled in the case *Baker v. Selden:*[276]

> *"*<...> no one would contend that the copyright of the treatise would give the exclusive right to the art or manufacture <...>. The copyright of the book, if not pirated from other works, would be valid without regard to the novelty, or want of novelty, of its subject matter. The novelty of the art or thing described or explained has nothing to do with the validity of the copyright. To give to the author of the book an exclusive property in the art described therein when no examination of its novelty has ever been officially made would be a surprise and a fraud upon the public*"*.

The court explicitly separated novelty (or idea, so to say), from the expression. A work whose form is dictated solely by a function is uncopyrightable.[277] What is new, is a question of patent law – the court rules – and copyright does not protect new ideas, but just the expressions, regardless if what is expressed is a new or old discovery or an invention.

This court decision was later implemented in the law. US law states that "In no case does copyright protection for an original work of authorship extend to any idea, procedure, process, system, method of operation, concept, principle, or discovery, regardless of the form in which it is described, explained, illustrated, or embodied in such work".[278]

A separation between the ideas *per se* and protected expressions is also implicitly stated in a majority of international or national legal instruments regulating copyright. For example, Article 2 of the WIPO Copyright Treaty[279] states that "Copyright protection extends to expressions and not to ideas, procedures, methods of operation or mathematical concepts as such". EU law also notes the necessity to express the work in a tangible form: "Copyright protection <...> includes the exclusive right to control distribution of the work incorporated in a tangible article "[280]. The question in our case is if a pure DNA sequence (which by pure I mean not altered or changed by human intervention) should be treated as an expression or as an idea?

DNA, a deoxyribonucleic acid, is the building block of every life form. It contains the information the cell requires to synthesize protein and to replicate itself. Explaining in few words, it is the storage repository for the information that is required for any cell to

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276 *Baker v Selden [1879], 101 US 99*., page 102.
277 Andrew W Torrance, 'DNA Copyright' (2011) 46 Valparaiso University Law Review 35.
278 17 U.S.C. § 102(b).
279 WIPO Copyright Treaty 2002.
280 Recital 28 of the Directive 2001/29/EC of the European Parliament and of the Council of 22 May 2001 on the harmonisation of certain aspects of copyright and related rights in the information society 2001., OJ L 167, 22.6.2001.

function.[281] There are four nucleotide bases, which make up the DNA. Adenine (A), Guanine (G), Thymine (T) and Cytosine (C). A DNA sequence looks something like this "ATTGCTGAAGGTGCGG".[282] Sequencing a DNA has several purposes: to find genes, segments of DNA that code for a specific protein or phenotype; to establish a homologous DNA sequences of different organisms can to compare them for concluding evolutionary relationships between species; gene sequence can be screened to determine its functionalities.[283] Scientists are now able to quickly sequence entire genomes (so-called the whole genome sequencing) of organisms and to discover genes involved in disease, to better understand genomic structure and diversity between species in general.[284]

So, the information about a gene or its sequence is mainly used to show the functionality of that gene. The gene's sequence is like language that instructs the cell to manufacture a particular protein.[285] Therefore, the disclosed gene sequence only gives the information about the DNA itself and how it functions. There is only an idea in the gene sequence, or similar genomic data, such as variation of a single nucleotide, ribonucleic acid molecules, complementary DNA. All this information about gene is given in technically processed codes, which are expressed by different alphabetical elements (A-G-T-C). Therefore, the idea about the general functionality of the gene or another biological molecule, and its expression in a tangible form are always identical and equal. So, to say, there is no creativity in genetic sequencing, the disclosed data shows the elements of a gene. Even if a gene sequence is presented in a scientific paper, or in the database of a biobank, no copyright should apply to such sequenced code as it is a mere idea that exists in nature and is not created by a person.

If the expression of an idea in an otherwise copyright-eligible work is entirely determined by functional considerations, copyright protection is not appropriate because expression and idea may have impermissibly merged.[286] Moreover, this is the case of the genomic data – the information processed from that data, even if disclosed using human intervention, labor, skill and understanding, is functional and determined by the functionalities of a particular gene.

2. Originality requirement

To comprehensively look at the question of copyrightability of a genomic biobank's information, one shall also answer the question about the originality of it. Originality is

281 G.Osuri, 'Bioinformatics Tutorial' <http://www.bioinformatics.org/tutorial/1-1.html> accessed 8 May 2018.
282 G.Osuri.
283 Anthony JF Griffiths, 'DNA Sequencing' Encyclopedia Britannica.Available at https://www.britannica.com/science/DNA-sequencing accessed 2018 May 8.
284 Ibid.
285 G.Osuri.
286 Andrew W Torrance, 'DNA Copyright' (2011) 46 Valparaiso University Law Review 35. It is known as "idea-expression merger" doctrine under which no one may claim copyright in that single manner of expression or depiction because that would evict everyone else from the right to express or depict that idea.

perceived by common law and civil law countries slightly different. While common law countries phrase the test in terms of originality, to suggest that the work originated with its author and no one else,[287] civil law countries understand originality as being tantamount to the author's own intellectual creation.[288] Therefore, the legal tradition in the civil law countries, confer not only economic but also moral rights to the author.[289] But no copyright law, whether national or international, has provided any sort of definition or meaning what the term 'original' in the context of copyright means. The task of evaluating the originality of the work has been left for the court practice to decide.

The US Supreme Court in the case *Feist Publications, Inc. v. Rural Telephone Service Co.,*[290] held that creativity was an absolute prerequisite to copyright protection. In this case the Rural Telephone Service Company, Inc. provided telephone service to several communities. It had issued an annual telephone directory, which the Feist Publications, Inc. used without the Rural's agreement. Therefore, the Rural sued for copyright infringement.

In the decision, the Supreme court stated that "time, effort, and expense were not enough, nor was skill, nor, presumably, those random variations caused by bad eyesight or claps of thunder".[291] Originality was a prerequisite to have copyright protection:

> *The constitutional requirement necessitates independent creation plus a modicum of creativity. Since facts do not owe their origin to an act of authorship, they are not original, and thus are not copyrightable. Although a compilation of facts may possess the requisite originality because the author typically chooses which facts to include, in what order to place them, and how to arrange the data so that readers may use them effectively, copyright protection extends only to those components of the work that are original to the author, not to the facts themselves.*[292]

The court also ruled that "facts do not emerge from scientists' efforts, but rather they copy them from the world around them. Raw facts may be copied at will. This result is neither unfair nor unfortunate. It is the means by which copyright advances the progress of science."[293]

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287 Goldstein and Hugenholtz 192.

288 Eleonora Rosati, *Originality in EU Copyright. Full Harmonization through Case Law* (2013) 69–72.

289 Under American Law, moral rights also can receive protection through judicial interpretation of several copyright, trademark, privacy, and defamation statues, and through 17 U.S.C. §106A, known as the Visual Artists Rights Act of 1990 (VARA). VARA applies exclusively to visual art. However, in Europe and elsewhere, moral rights are more broadly protected by ordinary copyright law. See Betsy Rosenblatt, 'Moral Rights Basics' [1998] Harvard Law School. Available at https://cyber.harvard.edu/property/library/moralprimer.html accessed 2018 May 8.

290 *Feist Publications, Inc., v. Rural Telephone Service Co., 499 U.S. 340.* (1991).

291 Lichtman 697.

292 *Feist Publications, Inc., v. Rural Telephone Service Co., 499 U.S. 340.* Syllabus 344-351, emphasis added.

293 Ibid. Syllabus 350.

In the decision the raw data did not satisfy the originality requirement. Therefore, the names, towns, and telephone numbers were not protected by copyright. "Such information is uncopyrightable facts; they existed before Rural created a telephone directory, and would have continued to exist if Rural had never published a telephone directory"[294] - continued the court. The copyright protection is given only to those constituent elements of a work that possess more than a *de minimis* level of creativity.[295]

The court also ruled that the raw data is uncopyrightable fact, and if the way how the facts are selected, coordinated, and arranged is not original, no copyright protection applies to the work.[296] The distinction is one between creation and discovery: the first person to find and report a particular fact has not created the fact; he or she has merely discovered its existence, one who discovers a fact is not its "maker" or "originator."[297]

In Europe, the Court of Justice of the European Union (CJEU) forms legal precedents to all EU Member States. A relevant case, regarding originality requirement in copyright, is the Infopaq judgment.[298] In the case the company called Infopaq used a partially automated process and was summarising the relevant articles that have been printed in Denmark's newspapers and periodicals. In 2005, the Association of Danish Daily Newspapers learned of Infopaq's activities. Since it had not consented to such a use of the newspaper articles, it made a claim to the court for the copyright infringement. In the judgment the court ruled that:

> *"the possibility may not be ruled out that certain isolated sentences, or even certain parts of sentences in the text in question, may be suitable for conveying to the reader the originality of a publication such as a newspaper article, by communicating to that reader an element which is, in itself, the expression of the intellectual creation of the author of that article."*[299]

In the decision, the court lowered the threshold of originality, as it ruled that even a sentence not exceeding 11 words, can be copyrightable.[300] Can this judgment be relevant to the protection of a genomic data?

Even if in the decision the court lowered the requirements of originality, saying that even the short phrases can have copyright protection, it still leaves a prerequisite, that any copyrightable work must be an expression of the author's own intellectual creation. As already explained, the DNA fragments and sequences, amino acid groups, complementary DNA, all this is a raw data. Such information is extracted by special techniques from the

294 Ibid., 499 U.S. 340, para 361.
295 Ibid., 499 U.S. 340, para 363.
296 Ibid., 499 U.S. 340, paras 361-364.
297 James G Silva, 'Copyright Protection Of Biotechnology Works: Into The Dustbin Of History?' (2000) 28 Boston College Intellectual Property and Technology Forum 5.
298 *Infopaq International A/S v Danske Dagblades Forening (C-5/08) [2009] ECLI:EU:C:2009:465.*
299 Ibid. para 47.
300 Ibid. para 51.

human body's samples. There is no independent creation, no originality in the sequencing of the genome. It is a simple fact, which one kind of DNA has one kind of sequence, performs one kind of function, leads to a particular disease and so on. DNA is performing different functions, will have differently expressed sequence. If we follow the rules established by the court precedent, the disclose of such a raw data, without adding any creative additional explanations, comments or presentations, gives no copyright protection to the scientist who discovered it. It is quite arguable, if a DNA sequence can be regarded as an intellectual creation, because it is found in nature and is not created by a human being. The pure expression of a work done is not equal to the concept of originality.

CJEU ruled that significant labour or skill as such is not enough if there is no creativity[301]. In the case *Football Dataco and Others v Yahoo UK! and Others*, the CJEU ruled that "the fact that the setting up of the database required, irrespective of the creation of the data which it contains, significant labour and skill of its author, <…> cannot as such justify the protection of it by copyright under Directive 96/9, if that labour and that skill do not express any originality in the selection or arrangement of that data"[302].

Labour is not a substitute for originality. Sequences obtained from nature (e.g., the sequence for a gene of some sort) are not original. The biologist who sequences a gene is merely discovering facts. There is no independent creation as is required for originality. The biologist is merely copying from nature the genetic sequence that codes for proteins. Thus, there is no minimum creativity. So long as a researcher constructs a DNA sequence based on a sequence discovered in nature, there is no independent creation, no minimum creativity and thus no originality[303].

Furthermore, in the BSA[304] judgment the CJEU found that "<...> Where the expression of the components is dictated by their technical function, the criterion of originality is not met, since the different methods of implementing an idea are so limited that the idea and the expression become indissociable"[305]. As information about the DNA is extremely functional, following this decision, it would not be protected under the copyright regime. There are no two ways to express same DNA sequence. There is only one sequence that can describe and show how the gene is functioning, what actions it performs, where is the difference between the normal gene and affected one. The DNA contains the genetic information that synthesizes a particular protein. If the sequenced code were changed, it would not give factual information about the DNA or that information would be perverse. A biologist can

301 *Football Dataco and Others v Yahoo UK! and Others (C-604/10) [2012] ECLI:EU:C:2012:115.*
302 Ibid. para. 42.
303 Silva 5.
304 *Bezpečnostní softwarová asociace – Svaz softwarové ochrany v Ministerstvo kultury (C-393/09) [2010] ECLI:EU:C:2010:816.* (further referred to as BSA).
305 Ibid. para. 49.

independently create an "artistic" string of nucleotides based on his imagination and not based on a sequence he knows of in nature, but very unlikely such an artistically conceived DNA sequence could code for any protein or have any use other than as art[306].

And to conclude, to my knowledge, there are very few court rulings dealing with the question of copyright protection of DNA sequences. One ruling was given by an Indian court. The case was related to the genetic information stored in the plant, and not human tissue, however, I found it essential to make a short description of the case.

On 2 August 2011, the High Court of Delhi at New Delhi in the case *Emergent Genetics India Pvt. Ltd. v. Shailendra Shivam and Ors*[307], ruled that DNA sequences do not have copyright protection. The factual background of the case was that plaintiff alleged that defendant's product (particular seeds) are a genotypical similarity to his product. It found that defendant's seed varieties were similar to its own seed varieties having subjected the latter's seeds to a DNA Fingerprinting Test (a test whereby the genetic makeup of two seeds is compared). It, therefore, sought a permanent injunction from the court restraining the defendants from manufacturing, selling or offering to sell their seeds.

In this case, the arguments of the court were similar to the ones made by the academic scholars. The court ruled that "DNA cannot have copyright protection because it is not an original work (the microbiologist or scientist involved in gene sequencing "discovers" facts. There is no independent creation of a "work", essential for matching the originality requirement)".[308] Court also applied an "idea-expression merger" doctrine:

> "*Combination of gene sequences, the selection of genetic components, mostly has no minimal creativity because the creator is only considering what is scientifically known and necessary. If such selection were original, it would still fall foul of the merger doctrine. The idea of combining various gene components or constituents, is expressible in limited ways. Granting copyright protection would mean that others are precluded from expressing such ideas. Therefore, there is merger; with the resultant lack of copyright protection.*" [309]

Transcription of a DNA sequence or other biological data, expressed in a pure and clear way, without adding new interpretations, but merely providing information about the genetic component, should not be protected by copyright, because it is a simple use of intellectual effort and labour. As rightly said, some skills involve creativity, some not and choice is not

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306 Silva 6.

307 *Emergent Genetics India Pvt Ltd vs Shailendra Shivam And Ors*. Case available at <https://indiankanoon.org/doc/183763759/> accessed 2018 May 8.

308 Ibid. para. 28.

309 Ibid. para. 29.

equivalent to creativity.[310] To have copyright protection it is irrelevant, whether or not the selection or arrangement of that data includes additional significance to the data, and also the significant labour and skill required for setting up such information cannot justify protection by copyright if there is no original expression.

II. Scientific publications and authorship

Access to biobank's resources policies generally contains publication requirements. A publication policy is aimed at encouraging researchers to share their results and acknowledge the contribution of the biobank, some may also seek to have a reward for the creativity.[311] Publications and acknowledgements are also meant to increase a biobank's visibility within the scientific community. The literary works created by using biobank's information, should be related to the biobank itself. For example, Publication guidelines for EPIC related studies[312] indicate that publications based on laboratory analysis of material gained from the biobank (e.g. plasma, serum, red blood cells or DNA samples), or its data: are planned and supervised by the Steering Committee. The analysis of the data and preparation of manuscripts for publication is trusted to an ad hoc working group. Also, the biobank's Steering Committee has the authority to decide whether specific papers shall be published with the complete author list, or under the EPIC acronym with the individual names in proper electronic forms or notes. The above-mentioned approval means, that the biobank's body can decide how the research must be performed and also, who will be the author of the publication (an individual scientist or an organisation). Also, these guidelines state, that apart from the leading group of researchers, the representatives of the individual centres, that assisted in submitting the samples or data, should also be listed in the publication next to the authors.

It is clear that the guidelines wish to increase the awareness of the biobank. However, they do not answer the question, to whom belong the economic benefits that might be received from the publication? If a publisher wishes to publish an article, must he have the consent of the biobank? Moreover, shall the primary authors and researchers split the revenues with the biobank if they have used biobank's resources?

There is a widely accepted rule that only substantive intellectual contributions to a paper give a credit to a person to be named as an author. The International Committee of Medical

310 Estelle Derclaye, 'Assessing the Impact and Reception of the Court of Justice of the European Union Case Law on UK Copyright Law : What Does the Future Hold ?' [2014] Revue Internationale du Droit d'auteur 9.

311 Ariane Mallette and Anne Marie Tassé, 'P3G Model Framework for Biobank Access Policy: Core Elements' 10.

312 EPIC, 'Publication Guidelines for EPIC Related Studies' 1. (V3, 2013), revised 29 January 2014, available at https://epic.iarc.fr/docs/EPIC_Publication%20Guidelines.pdf accessed 2018 May 8.

Journal Editors,[313] in its recommendation writes that authorship should be based on the following 4 criteria: 1) Substantial contributions to the conception or design of the work; or the addition, analysis, or interpretation of data for the work; 2) Drafting the work, revising it critically for important intellectual content; 3) Final approval of the version to be published; 4) Accountability for all aspects of the work to ensure that questions related to the precision or sincerity of the work are competently investigated and resolved.[314] Those who do not meet all the four criteria, but have contributed for the work to some extent, should be acknowledged merely.

The traditional form of acknowledgement is through a publication. Guidelines for many journals require that data production should be acknowledged, but how this is done is largely left up to individuals following the norms that exist within different disciplines.[315] The above mentioned EPIC guidelines indicate that: "In all publications, due acknowledgment will be made of funding bodies, as applicable. In publication of pooled data, due acknowledgment will be made of national funding sources".[316] Paragraph 9.5 of OECD Guidelines on Human Biobanks and Genetic Research Databases[317] reads as follows: "In publications and presentations, researchers should acknowledge the HBGRD (Human Biobanks and Genetic Research Databases) whose resources they have used or relied on, and the HBGRD should provide researchers with guidance on how it wishes to be acknowledged". Similarly states the UK Biobank's rules: users are required to undertake to notify UK Biobank in advance of publishing findings of their research, to acknowledge the contribution of the resource, and to provide a copy of any published reports.[318] The National Institute of Health (NIH) in its policy regulation implies "acknowledging in all oral or written presentations, disclosures, or publications the contributing investigator(s) who conducted the original study, the funding organization(s) that supported the work, the specific dataset(s) and applicable accession number(s), and the NIH-designated data repositories through which the investigator accessed any data".[319] The Telethon Network of Genetic Biobanks[320] gives an exact wording of the

313 International Committee of Medical Journal Editors, 'About ICMJE' <http://www.icmje.org/about-icmje/> accessed 8 May 2018.

314 ICMJE, 'Defining the Role of Authors and Contributors' <http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html> accessed 8 May 2018.

315 Jane Kaye and others, 'Data Sharing in Genomics – Re-Shaping Scientific Practice' (2009) 10 Nat Rev Genet 333.

316 Second part of the Guidelines Publication Policy.

317 Organisation for Economic Cooperation and Development, 'Guidelines on Human Biobanks and Genetic Research Databases' (2009).

318 UK Biobank: Protocol for a large-scale prospective epidemiological resource UK Biobank Coordinating Centre Stockport 2007, 99.

319 NIH, 'National Institutes of Health Genomic Data Sharing Policy, Notice Number NOT- OD-14-124' 8.

320 The Telethon Network of Genetic Biobanks (TNGB) has been founded in 2008 by 7 Biobanks supported by Telethon Foundation, whose purpose is to collect, preserve and offer to the Scientific Community biological samples and related clinical data from individuals affected by genetic diseases, from their relatives or from healthy control individuals. More information at http://biobanknetwork.telethon.it/ accessed 2018 May 8.

acknowledgement: "The [name of the Biobank which provided the service], member of the Telethon Network of Genetic Biobanks (project no. GTB12001), funded by Telethon Italy, provided us with specimens".[321] Da Vinci European BioBank,[322] not only wishes to be cited in all the publications resulting from the use of its samples, but also asks the researcher to provide a copy of the published paper to the biobank.

In general, biobank does not seek to publish articles, neither has a goal be named as an author of the paper. For the biobanks, the most important aspect is that they would be known and that they would be used for the purpose they have been established – to provide the scientific community with information needed for the research so to improve the well-being of the whole population. Following this logic, biobank's should not withhold the information they have discovered. And in most situations, they do not. Biobanks are willing to share the information with each other and with the scientific community. I will talk about the data sharing policy of the biobanks in the next chapter. Now, I would like to cover the question if biobanks can claim database protection right, as obviously, they do have a massive storage of data collected.

III. Database rights v. "sweat of the brow" doctrine

In Europe, the database rights were established by the Directive 96/9/EC on the legal protection of databases[323] (Database directive). After the implementation of the directive, non-original compilations of data, the collection of independent works, data or other materials arranged in a systematic or methodical way and individually accessible by electronic or other means[324] are legally protected as valuable intellectual property. While original databases require an element of intellectual creation, the non-original databases are protected as long as there has been "qualitatively or quantitatively a substantial investment in either the obtaining, verification or presentation of the contents" of a database.[325] The *sui generis* form of protection for non-original databases was introduced as an entirely novel form of intellectual property. The Directive provides a two-tier protection: first, a harmonised level of protection

321 FONDAZIONE TELETHON, 'INSTRUCTIONS FOR REQUESTING THE SAMPLES' <http://biobanknetwork.telethon.it/Pages/View/Instructions> accessed 8 May 2018.

322 The da Vinci European BioBank (daVEB) is a research infrastructure which belongs to the Farmacogenomics Foundation FiorGen Onlus. The da Vinci European BioBank is a multicenter biobank with a centralised IT infrastructure and a central repository located at the Polo Scientifico (Scientific Campus of the University of Florence) in Sesto Fiorentino (Florence, Italy), hosted by CERM (Magnetic Resonance Center), focused on protein structure and metabolomics.

323 Directive 96/9/EC of the European Parliament and of the Council of 11 March 1996 on the legal protection of databases OJ L 77, 27.3.1996, p. 20–28.

324 Art. 1 (2) of Directive.

325 Commission of the European Communities, DG Internal Market and Services Working Paper 'First evaluation of Directive 96/9/EC on the legal protection of databases', Brussels, 12 December 2005, 4.

of original databases under copyright law (Articles 3-5) and second, the protection of *sui generis* right to protect investments in non-original databases (Articles 7, 10 and 11). The approach chosen in the Database Directive was to harmonise the threshold of "originality". Those "non-original" databases that did not meet the threshold would be protected by a newly created right.[326]

Article 1 of the Database directive defines a "database" as a collection of independent works, data or other materials arranged in a systematic or methodical way and individually accessible by electronic or other means. For the purposes of the directive, this definition applies to both original and non-original databases.

The Database directive had several overall and specific objectives,[327] from which the most important for the subject of this thesis is:

- Ensure an attractive environment for investment in databases;
- Balance the legitimate interests of manufacturers and users of databases;
- Close the gap between the EU and US information markets (emphasis added).

Commission's argument, when proposing the text of the directive, was that current copyright law does not give sufficient investment to create databases in Europe. The Commission recognised that copyright protection based on the standard of originality alone might not be an adequate tool to protect these often considerable investments. Therefore, to protect the selection or arrangement of the contents of a database which did not meet the standard of being original, the Commission considered it appropriate to provide a form of *sui generis* protection for the investment involved in the making of a database.[328]

When we talk about biobanks, we talk about collecting biological samples (blood, saliva, etc.) and also about collecting the information generated from such samples and information about the donor or research participant. As I have separated these different categories before, I find it essential to deal with each of them when applying database protection rules.

Firstly, the dictionary definition of a word data is "facts and statistics collected together for reference or analysis."[329] Data can also be described as "information, especially facts or numbers, collected to be examined and considered and used to help decision-making or information in an electronic form that can be stored and used by a computer."[330] So data is information. A mere specimen of blood or saliva can be treated as data because it does contain relevant information in it. A person skilled in the art can read this information from the

326 Ibid. 3.

327 For the full list see the Figure 1 of the Commission of the European Communities, DG Internal Market and Services Working Paper 'First evaluation of Directive 96/9/EC on the legal protection of databases'.

328 Ibid. 8–9.

329 Oxford Dictionaries, 'Definition of Data in English' <https://en.oxforddictionaries.com/definition/data> accessed 8 May 2018.

330 Cambridge Dictionary, 'Meaning of "data" in the English Dictionary' <http://dictionary.cambridge.org/dictionary/english/data> accessed 8 May 2018.

sample, using specific tools and techniques (such as gene sequencing machines). A sample is a tangible object as any other tangible objects, but for those who can read it, a sample can give a lot of facts and information about that specific tissue. It can tell the information from which source the samples are received, what disease that source had or is having, and other information. Of cause, you cannot protect the alphabetical storage of samples *by sui generis* right, as it is the most common way to arrange significant amounts of data. But the information that is contained in the samples, when it is examined, studied and disclosed, is a clear data that can fall under the definition Database Directive.

The Directive's definition of a "database" seems to be very broad. Any collection of independent works, data or other materials arranged in a systematic or methodical way and individually accessible by electronic or other means can be a protected under this legal act (emphasis added). National case-law shows that the notion of "database" has been interpreted widely so as to include listings of telephone subscribers; compilations of case-law and legislation; websites containing lists of classified advertisements; catalogues of various information; lists of headings of newspaper articles.[331] From the first Commission's proposal, is clear that database *sui generis* right arose as a backup of the copyright (that is, when the novelty of an artistic work is missing, then *sui generis* right might be applicable) and is closely related to the copyrightable subject matters. This was also indirectly stated in the CJEU decision in OPAP case.[332]

In the OPAP case, the organisers of English and Scottish league football retained a company, Football Fixtures Limited, to handle the exploitation of the fixture lists outside the United Kingdom through licensing. Fixtures were assigned the right to represent the holders of the intellectual property rights in those fixture lists. In Greece, OPAP has a monopoly on the organisation of gambling. In its activities, it used information from the fixture lists for the English and Scottish football leagues. Fixtures brought an action against OPAP on the ground that OPAP's practices were precluded by the *sui generis* right. In the case the court noted that "According to the 17th recital of the preamble to the directive, the term "database" should be understood to include literary, artistic, musical or other collections of works or collections of other material such as texts, sound, images, numbers, facts, and data" (para 23).

According to such interpretations, biobank's data available in the electronic databases, where the "metadata" relating to the sample (e.g., tissue type, date of sampling, assigned barcode) are indexed, as well as the data derived from the analysis performed on the same

331 Commission of the European Communities, DG Internal Market and Services Working Paper 'First evaluation of Directive 96/9/EC on the legal protection of databases', Brussels, 12 December 2005, 12.

332 *Case C-444/02 Fixtures Marketing Ltd v. Organismos prognostikon agonon podosfairou AE -'OPAP' [2004] ECLI:EU:C:2004:697*.

biomaterial,[333] can be protected by *sui generis* right. Such data can consist of measurements, observations, images, genetic analysis, and phenotypic or genotypic information – which can be considered facts and statistics, as defined by the Directive. Biobanks store in their databases the sequence identifiers and annotations, publications, scientific literature. Such information and data collected, therefore, fall within the definition of Article 1 of the Database Directive.

1. Should biobanks fall under the sui generis exceptions?

Article 9(b) of the Database Directive foresees the possibility for the national law to stipulate that lawful users of a database which is made available to the public in whatever manner could, without the authorization of its maker, extract or re-utilize a substantial part of its contents for the scientific research, as long as the source is indicated and to the extent justified by the non-commercial purpose to be achieved. If implemented in the national laws, this exception would give the researchers in the genetic field a possibility to use biobank's information without any fear to infringe a *sui generis* right. However, as this exception is not obligatory and is left to each Member State to decide if to implement it in the national legislation, not all EU countries have done it. For example, France and Italy have not taken advantage of the directive's optional exemptions for scientists who download data for educational or research purposes.[334]

Some authors (Derclaye and Ducato) proposes that irrespective of the nature of the data, and notwithstanding of a substantial investment made in the obtaining, verification or presentation of the data, the database should not receive protection if it is a state databases.[335] One of the arguments is that the investment in the creation of a database has been recouped since the taxpayer has already paid for the data. Therefore, a person should not pay a second time for such information. When the resources for the creation of data is allocated by governmental resolutions and not by the market processes, intellectual property protection has no economic justification.[336]

I would agree very strongly with the rationale of such statement. Unfortunately, there is no such exception in the Database Directive. The directive does not implicitly allow the users to extract or re-utilise information stored in the public database. Such concerns were also

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333 Rossana Ducato, '"Adiós Sui Géneris" a Study of the Legal Feasibility of the Sui Generis Right in the Context of Research Biobanks'.

334 Stephen M Maurer, Arti Rai and Andrej Sali, 'Finding Cures for Tropical Diseases: Is Open Source an Answer?' (2004) 1 PLoS Medicine 183-184.; Ducato 11.

335 Derclaye, 'Databases "Sui Generis" Right: Should We Adopt the Spin-off Theory' 408.; Ducato 16–17.

336 WIPO Standing Committee on Copyright and Related Rights. Study prepared by Thomas Riis, 'Economic Impact of the Protection of Unoriginal Databases in Developing Countries and Countries in Transition' (2002) 31.

raised during the Commission's evaluation report.[337] The Commission did not give a clear answer to this question but indicated that the re-use of public sector information is a subject matter of another Directive. Indeed, Directive 2003/98/EC on the re-use of public sector information[338] (hereinafter the PSI Directive), establishes a minimum set of rules governing the re-use and the practical means of facilitating re-use of existing documents held by public sector bodies of the Member States (Article 1). The Directive obliges public sector bodies to exercise their copyright in a way that facilitates re-use (Recital 22).

Article 2(1) of the PSI Directive describes "public sector body" as the "State's, regional or local authority, body governed by public law and associations formed by one or several such authorities or one or several such bodies governed by public law". Article 2(2) also defines a "body governed by public law". It must be a body established for the specific purpose of meeting needs in the general interest, not having an industrial or commercial character; and having legal personality; and financed, for the most part by the State, or regional or local authorities, or other bodies governed by public law; or subject to management supervision by those bodies; or having an administrative, managerial or supervisory board, more than half of whose members are appointed by the State, regional or local authorities or by other bodies governed by public law.

Most of the public biobanks operating in Europe would meet the criterion of a public sector body. For example, Estonian Genome Center of the University of Tartu (Estonia biobank) was founded by the Human Genes Research Act and is funded by the Estonian Government.[339] The Regional Biobank of Central Norway was established in collaboration between the Central Norwegian Regional Health Authority (data management and administration) and the Faculty of Medicine at the Norwegian University of Science and Technology. It is owned and operated by official authorities.[340] CNIO Biobank in Spain is defined as a public, non-profit organisation. The Biobank has been authorised by the Health Authorities of the Community of Madrid – in accordance with the regulation established by RD1716/2011.[341]

Therefore, if we would agree that public biobanks do fall under the regulation of the PSI Directive, they should ensure that relevant information ("documents" according to the

337 Commission of the European Communities, 'DG Internal Market and Services Working Paper. First Evaluation of Directive 96/9/EC on the Legal Protection of Databases' (2005), 21.

338 Directive 2003/98/EC of the European Parliament and of the Council of 17 November 2003 on the re-use of public sector information OJ L 345. As amended by Directive 2013/37/EU of the European Parliament and of the Council of 26 June 2013, OJ L 175, 27.6.2013, p. 1–8.

339 The Estonian Biobank, 'Estonian Genome Center, University of Tartu' <https://www.geenivaramu.ee/en/about-us> accessed 8 May 2018.

340 Norwegian University of Science and Technology, 'The Regional Biobank of Central Norway' <https://www.ntnu.edu/lbk/biobank> accessed 8 May 2018.

341 CNIO Biobank, 'About' <https://www.cnio.es/ES/grupos/plantillas/presentacion.asp?grupo=50004308> accessed 8 May 2018.

definition of the PSI Directive) shall be re-usable for commercial or non-commercial purposes in accordance with the conditions set out in the PSI Directive (Article 3(1)) and the charges required for the re-use of documents shall be limited to the marginal costs incurred for their reproduction, provision and dissemination (Article 6(1)).

The other problem is, that biobanks, even if getting public finding, not necessarily is a public body. Much funding is given from the national funds to the researchers or institutions that are not considered public, therefore, for the information stored in such kind of biobanks PSI Directive's rules not apply automatically. Furthermore, PSI Directive explicitly excludes from its objects documents held by educational and research establishments, including organisations established for the transfer of research results, schools and universities (Article 1(2)(e)). It is quite a dilemma, as the most significant majority of projects and investigations done by the university are funded from the state (by ways of receiving state support, grants, etc.). The previously described universities' biobanks or state (population) biobanks are mostly funded from the state budget.

The PSI Directive also states that "The intellectual property rights of third parties are not affected by this Directive. For the avoidance of doubt, the term 'intellectual property rights' refers to copyright and related rights only (including *sui generis* forms of protection). <…> The Directive does not affect the existence or ownership of intellectual property rights of public sector bodies, nor does it limit the exercise of these rights in any way beyond the boundaries set by this Directive. The obligations imposed by this Directive shall apply only insofar as they are compatible with the provisions of international agreements on the protection of intellectual property rights, in particular, the Berne Convention and the TRIPS Agreement. Public sector bodies should, however, exercise their copyright in a way that facilitates re-use." (recital 22, Article 1(5)).

Therefore, the PSI Directive could be used to foster accessibility of the data in the biobanks only to some extent. Not to mention, that the information stored in the biobanks can be very sensitive, if, for example, it is related to the personal information about the donor. Therefore, for the reasons of protecting personal information, the PSI directive could be applied with limitations in the biobanks.

Concluding, there does not seem to be sufficient grounds to state that information stored in the biobanks should fall under the exception of the protection of *sui generis* right and should be freely available to any interested party according to the law, even if a biobank is strongly funded by the state.

2. Is a spin-off doctrine applicable to biobanks?

The database right should only protect investments that are directly related to the creation of a database, the presentation of the data in an intelligible form. A spin-off doctrine is a doctrine under which there should not be protection by the *sui generis* right for databases which are spin-offs or by-products of another or main activity.[342] The "spin-off" theory was developed by the doctrine and case law of several Member States (such as the United Kingdom, Sweden and Finland).[343]

The CJEU in its decisions established the criterion of when the spin-off doctrine can be applied, and the database would not have a *sui generis* protection. The CJEU ruled that „The expression 'investment in ... the obtaining ... of the contents' of a database in Article 7(1) of Directive 96/9 must be understood to refer to the resources used to seek out existing independent materials and collect them in the database. It does not cover the resources used for the creation of materials which make up the contents of a database."[344]

In another case C-203/02 *The British Horseracing Board Ltd and Others v. William Hill Organization Ltd* the court also pointed that, following the literal meaning of the 39th recital of the preamble of the directive, "<...> The aim of the *sui generis* right is to safeguard the results of the financial and professional investment made in 'obtaining and collection of the contents' of a database[345]". Therefore, if the creator of a database is also creator of its content, to gain a sui generis right protection, he or she must also show that independent substantial investment in quantitative or qualitative terms has been used in creation of a database and not only in creation of the database's content, and that the investment was different from the resources used to create the material as such[346].

Estelle Derclaye writes that as the primary rationale of the Directive is to promote investment in databases, encourage the production and dissemination of databases, there should be no reason to protect also databases deriving quasi-automatically from other activities. She also proposes that when evaluating if a spin-off doctrine should be applied to a database protection, one must establish if the primary activity (data creation) is distinct from the secondary activity (a database creation), and if the author can recoup its investment from the primary activity solely, or only also from the revenues gain from database. If the costs

342 Derclaye, 'Databases "Sui Generis" Right: Should We Adopt the Spin-off Theory' 408.
343 Commission of the European Communities, 'DG Internal Market and Services Working Paper. First Evaluation of Directive 96/9/EC on the Legal Protection of Databases' (2005) 8–9.
344 *Case C-444/02 Fixtures Marketing Ltd v Organismos prognostikon agonon podosfairou AE -'OPAP' [2004] ECLI:EU:C:2004:697* [53].
345 *Case C-203/02 The British Horseracing Board Ltd and Others v William Hill Organization Ltd [2004] ECLI:EU:C:2004:695 [32].*
346 Ibid [35].

incurred in performing the primary activity is recouped with the same activity, by asking a payment for the use a database would mean that consumers pay twice for the same data.[347]

The activity of the biobanks is to collect biological samples, related data and to provide the researchers with such information to perform accurate research. Recruiting of the sample donors, carrying out the maintenance of the biorepository and its cryopreservation system, preservation of the biological samples, procuring instruments for the management of special types of tissues, arranging for instruments for the quality control of the samples, making periodical checks for the maintenance of operating standards and procedures – all this work is done to collect the specimen and preserve of samples. The costs of the storage and maintenance of specimens (so that they could be used by researchers, shipped to different countries, would not lose its quality) are merely related to the samples themselves and not with the creation of a database.

However, as stated in the previous chapter of this thesis, biobanks are collecting and providing to the researchers not only the samples but also the data that is extracted from the samples. This data is equally relevant, if not more important to the scientific community. Therefore collecting and storing this information becomes one of the main activities of the biobank. The creation of a database in biobank might look like as a naturally-occurring fact, but it is not a straight forward answer. Without a systematic, clear, easily accessible representation of data, the differentiation of the samples according to their substance, the researchers would be extremely lost in finding an information or ordering the specimens. Therefore additional costs, so to quote CJEU "independent substantial investment", are also high in the creation of a biobank's information databases.

Such information databases, where a researcher can find disclosed sequenced genes, order samples, find other information: publications, comments, guidelines, information about performed researchers, are stored in the internet platforms. Researchers can access such platforms, search and download the information they need. Relevant IT tools are also created, constant support and supervision are provided. To name just a few biobank's online databases: the Ensembl database,[348] UK biobank's database,[349] The European Bioinformatics Institute's (EMBL-EBI) database.[350] These platforms provide data about nucleotide or protein sequences, DNA and RNA data. Not to mention, that when storing all this huge amount of data, the biobank is also responsible for managing a supercomputer system and IT tools.

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347 Derclaye, 'Databases "Sui Generis" Right: Should We Adopt the Spin-off Theory' para 407.

348 The goal of Ensembl is to automatically annotate the genome, integrate this annotation with other available biological data and make all this publicly available via the web. Ensembl, 'About' <http://www.ensembl.org> accessed 8 May 2018.

349 UK Biobank, 'Online Showcase of UK Biobank Resources' <http://biobank.ctsu.ox.ac.uk/crystal/> accessed 8 May 2018.

350 EMBL-EBI, 'Tools & Data Resources' <https://www.ebi.ac.uk/services> accessed 8 May 2018.

Sometimes such databases are created and managed independently for the biobank, like GenBank database,[351] but they exist in a very close collaboration with the biobanks. I would distinguish three largest databases storing and distributing biobanks' data: the first, the NCBI database,[352] the second, the European Molecular Biology Laboratory (EMBL) database,[353] and the third, DNA Database of Japan (DDBJ).[354] These databases collect all publicly available DNA, RNA and protein sequence data and make it available for free online.[355] They also belong to The International Nucleotide Sequence Database Collaboration (INSDC) foundational initiative that covers the spectrum of data raw reads, though alignments and assemblies to functional annotation, enriched with contextual information relating to samples and experimental configurations.[356] The National Institute of Genetics uses a large-scale computer utilisation site with genome analysis as its primary focus, which provides Supercomputing System Services comprising leading-edge, large-scale cluster-type computers, large-scale memory-sharing computers, and high-capacity, high-speed disk devices.[357]

Considering all the relevant aspects and the work biobanks perform in creating a database, the spin-off doctrine should not apply. Biobanks make a direct investment towards the creation of a database. It involves not only the financial investment into a data storage (individual databases or cloud storages) but also the creation of internet platforms, IT tools. The exception from such reasoning could be cases where private biobanks create databases just for their personal research and for its in-house resources. I agree with Rossana Ducato, that private biobanks "are not exclusively aimed at offering a service of "pure" collection and preservation of data for themselves", but instead such databases are the biobanks' in-house resource used for the biobanks' own research projects.[358] Therefore, in such cases, the investments are not primarily addressed to the creation of a database but merely is generated

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351 NCBI, 'GenBank Overview' <https://www.ncbi.nlm.nih.gov/genbank/> accessed 8 May 2018. GenBank is the NIH genetic sequence database, an annotated collection of all publicly available DNA sequences.

352 The National Center for Biotechnology Information database advances science and health by providing access to biomedical and genomic information. NIH, 'National Institutes of Health Genomic Data Sharing Policy, Notice Number NOT- OD-14-124' (2014).

353 The European Nucleotide Archive (ENA) provides a comprehensive record of the world's nucleotide sequencing information, covering raw sequencing data, sequence assembly information and functional annotation. EMBL-EBI, 'European Nucleotide Archive (ENA)' <https://www.ebi.ac.uk/ena> accessed 8 May 2018.

354 DDBJ Center collects nucleotide sequence data and provides freely available nucleotide sequence data and supercomputer system, to support research activities in life science. 'DDBJ Center' <https://www.ddbj.nig.ac.jp/index-e.html> accessed 8 May 2018.

355 Avril Coghlan, 'Sequence Databases' <http://a-little-book-of-r-for-bioinformatics.readthedocs.io/en/latest/src/chapter3.html> accessed 8 May 2018.

356 'International Nucleotide Sequence Database Collaboration' <http://www.insdc.org/> accessed 8 May 2018.

357 GeneBank database is supported by US National Institute of Health (so-called NIG Supercomputer). 'NIG Supercomputer System' <https://sc.ddbj.nig.ac.jp/en> accessed 8 May 2018.

358 Ducato 18.

as by-products of broader research activity. On the other hand, such situations seem to be limited, and it is more a rare exception than a basic rule.

3. EU database right v. US copyright

The database right as presented in this thesis is valid only in the European Union. The "sui generis" right is a Community creation with no precedent in any international convention. No other jurisdiction makes a distinction between "original" and "non-original" databases.[359] In the US no similar legislation exist,[360] and databases can only be protected by copyright as compilations. 17 US Code 101 defines a compilation as "a collection and assembling of preexisting materials or of data that are selected in such a way that the resulting work as a whole constitutes an original work of authorship."

One of the arguments, why at the first place, the *sui generis* right was established in the EU, was the unification of the copyright protection in continental and common law countries. In the United Kingdom or the US, databases were adequately protected by copyright because the level of originality was lower (sufficient skill, judgment and labour) and it protected not only the selection or arrangement of the database but also the content.[361] Sometimes called as the 'sweat of the brow' doctrine allowed to protect by copyright the expenditure of skill, labour or money and lowered the threshold of originality in common law countries.[362] Thus, a copyright was the reward for the hard labour that went into compiling facts.[363] The case was different in the *droit d'auteur* tradition countries, where in order to qualify for copyright protection work must constitute the author's own intellectual creation as regards its selection or arrangement. So the originality threshold was apparently higher.

In its proposal for a new directive, the European Commission followed the changes in the intellectual property field in the United States and suggested not to depart from the same rules as the US courts. One of the main purposes of the Database directive in Europe was to extend somehow the scope of copyright protection, so that the works (at that time) protected in the

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359 Commission of the European Communities, DG Internal Market and Services Working Paper 'First evaluation of Directive 96/9/EC on the legal protection of databases', Brussels, 12 December 2005, p. 5.

360 Two bills were introduced on this matter in the US in 1999: H.R. 354, Collections of Information Antipiracy Act and H.R. 1858, Consumer and Investor Access of Information Act. The bills were oriented towards database producers and prohibition of uses which could harm the primary or related market of the database and the exceptions and the legal uses of databases. The bills, however, have not been adopted (sources Library of Congress, 'Collections of Information Antipiracy Act' <https://www.congress.gov/bill/106th-congress/house-bill/354/all-actions-without-amendments> accessed 8 May 2018. and Library of Congress, 'Consumer and Investor Access to Information Act of 1999'.)

361 Estelle Derclaye, *The Legal Protection of Databases. A Comparative Analysis* (Edward Elgar Publishing 2008) 45.

362 Annemarie Christiane Beunen, 'Protection for Databases: The European Database Directive and Its Effects in the Netherlands, France and the United Kingdom' (Leiden University 2007) 83.

363 James G Silva, 'Copyright Protection Of Biotechnology Works: Into The Dustbin Of History?' (2000) 28 Boston College Intellectual Property and Technology Forum 4.

Common law countries under the "sweat of the brow" doctrine, would also have protection in continental Europe. Commission argued that the difference between the lower "sweat of the brow" copyright standard and the higher "intellectual creation" standard created distortion of trade in "database products".[364] The Database Directive, therefore, imposed higher originality criterion for copyright protected original databases, and the protection under newly created *sui generis* right was granted for non-original compositions.

However, while the European institutions were proposing and evaluating the needs for a new directive, the precedents in the United States changed. In already mentioned Feist Publications, Inc. v. Rural Telephone Service Co.[365] case, the United States Supreme Court rejected the "sweat of the brow" doctrine. The court ruled that:

> "It is not enough for copyright purposes that an author collects and assembles facts. To satisfy the statutory definition, the work must get over two additional hurdles. In this way, the plain language indicates that not every collection of facts receives copyright protection."[366]

The court clearly stated, that to be protected under the copyright law a database must be original and that "copyright is not a tool by which a compilation author may keep others from using the facts or data he or she has collected" and that "the facts contained in existing works may be freely copied, because copyright protects only the elements that owe their origin to the compiler - the selection, coordination, and arrangement of facts."[367]

According to the decision, the database containing unprotected facts can be protected under copyright only if the selection and arrangement of facts are not mechanical or routine but implies at least some level of creativity. The underlying data would be part of the public domain if not novel, and only the arrangement of the database would be protected.[368] In a protected database the uncopyrightable facts must be selected, coordinated, or arranged originally. If a database arranges the facts in alphabetical order or in another way that is practically inevitable, it cannot be regarded as original.[369]

The Feist decision protects from the monopolisation the information that is in the public domain. If we analyse how biobank's databases are created and agree that the primary biogenetic data (such as gene sequences) has no copyright as it is a naturally-occurring fact, then the question if a compilation of such data can be regarded as original, must be answered. The information in the biobank's database can be arranged according to the subject type

364 Commission of the European Communities, DG Internal Market and Services Working Paper 'First evaluation of Directive 96/9/EC on the legal protection of databases', Brussels, 12 December 2005, p. 3.
365 *Feist Publications, Inc., v. Rural Telephone Service Co., 499 U.S. 340*.
366 Ibid. para 357.
367 Ibid. para 359.
368 Greenbaum 5.
369 *Feist Publications, Inc, v Rural Telephone Service Co, 499 US 340* [363].

(proteins, DNA & RNA data, systems, structures); material type (for example, saliva, tissue, different kind of cell lines); diagnosis (when investigating on a particular disease); according to the source of data (human biological data, mouse, other animals, plants); if a data is curated or not curated and similar. In diseases biobanks, even the donors are selected according to the specific criterion of the research that is going to be performed. The cells, related data or data extracted from the cells, can also be arranged according to a particular question or research object. The ENCODE,[370] for example, organises the genetic data[371] according to organisms it comes from (human and other animals); biosample type (tissue, primary cell, immortalised cell lines, etc.); by organs (brain, skin or body, muscle organ, etc.). The performed analysis are also categorised to Chip-sequences, DNase-sequences, polyA, mRNA, RNA-sequences, and different.

It would be hard to prove that organized genetic information can have at least some level of creativity and originality. The correct outcome would be that such systematisation is mechanical or typical, according to the qualifications of the samples. Different biobanks organize their data according to similar parameters, which makes such databases even less original. Therefore, as rightly indicated by Greenbaum, in many scientific fields, including biogenetic, the databases are considered merely compilations of facts and thus will not qualify for US copyright protection.[372]

Comparing current European and American database related legislation, it seems that they have departed one from another rather significantly. And even if the protection of non-original databases arose in the United States, later it was rejected and now is granted only in Europe. Some authors argue, that such a discrepancy between database protections in the US and Europe has a negative effect in database creation in the US.[373] However, numbers show that despite this lack of protection, the American database industry did not stop thriving and from 1991 to 1997 the number of databases increased 35% from 7637 to 10338.[374] Despite any legislative database protection the growth and amount of databases in the US it much higher than in the EU. Between 2002 and 2004, in Europe, the percentage of created databases decreased from 33% to 24% while in the US the share increased from 62% to 72%. The ratio

370 The ENCODE (Encyclopedia of DNA Elements) Consortium is an international collaboration of research groups funded by the National Human Genome Research Institute (NHGRI). The purpose of ENCODE is to build a comprehensive list of functional elements in the human genome, including elements that act at the protein and RNA levels, and regulatory elements that control cells and circumstances in which a gene is active. Stanford University, 'ENCODE' <https://www.encodeproject.org/> accessed 8 May 2018.

371 Stanford University, 'ENCODE Experiment Matrix' <https://www.encodeproject.org/matrix/?type=Experiment&status=released> accessed 8 May 2018.

372 Dov Greenbaum, 'Are We Legislating Away Our Scientific Future? The Database Debate' [2003] Duke Law & Technology Review 5.

373 See Dov Greenbaum, 'Are We Legislating Away Our Scientific Future? The Database Debate' [2003] Duke Law & Technology Review, where the author mentions the proposition of US legislator to act H.R. 354 law, that would have given strong intellectual property protection to databases.

374 Ibid. 12.

of European-US database production, which was nearly 1:2 in 1996, has become 1:3 in 2004.[375] Some authors state, that according to their analysis European database production returned to predictive levels almost immediately after the Database directive was implemented.[376]

Stronger legal protection of the databases in Europe seems to not influence database creation, as in the US, where no specific laws exist, databases are created with equal if not a bigger incentive. On the other hand, the lack of legal protection in the US has not lead to open access to genomic databases, because protections are found through the trade secret model, licensing and technological self-help and the legal prohibition of circumvention technologies.[377] The *sui generis* right is given to promote the development of databases and the main rationale for this right was the incentive to invest in the making of databases. However, the numbers show that these databases are created despite an incentive and that they would be created anyway, even if there were no protection available.[378] Moreover, in biobanks, the incentive to create a database cannot be stimulated by the *sui generis* protection. The stimulus of creating and expanding the biobanks' databases is to positively influence the broader and wider scientific research and not to restrict the access to such information by applying database rights. Derclaye also raises an important question if the protection of creation and delivery of data in the biobanks balances between the fair reward for presenting the data, a remuneration which is given in order to encourage the data presentation, and the public's interest in obtaining the data at the lowest possible costs.[379] Biobanks act as a research infrastructure with the goal to improve the health of the human population. Therefore, the use of database rights would not reflect the main purpose of the biobanks.

4. Negative aspects of database protection in biobanks

Same as copyrights does not require any formal registration to be valid, neither the databases protection require any formalities. So from the date of completion of the making of the database, the fifteen years period of protection automatically applies (Database directive Article 10(1)). Even if the exception for scientific use would be implemented, such reforms, although useful, would be inherently limited. For most scientists, having the right to

375 Commission of the European Communities, DG Internal Market and Services Working Paper 'First evaluation of Directive 96/9/EC on the legal protection of databases', Brussels, 12 December 2005, 22.

376 Stephen M Maurer, P Bernt Hugenholtz and Harlan J Onsrud, 'Europe's Database Experiment' (2001) 294 Science 790.

377 Julia Gladstone, 'Exploring the Key Informational, Ethical and Legal Concerns to the Development of Population Genomic Databases for Pharmacogenomic Research' (2005) 2 Issues in Informing Science & Information Technology 399.; Arnoud Engelfriet, 'Database Protection in the USA' <http://www.iusmentis.com/databases/us/> accessed 8 May 2018.

378 Gladstone.

379 Estelle Derclaye, 'Databases "Sui Generis" Right: Should We Adopt the Spin-off Theory' (2004) 26 European Intellectual Property Review 410.

download data does not mean much if the extracted information cannot later be reutilised and republished. Authors argue, that creating a useful scientific and educational exemption is impossible under the current European directive.[380] Database right is different from copyright. Copyright law constitutes a balanced regime of public and private interests – it does not protect ideas or data. However, database right protects data that is not original but combined merely in one single database. Reuse of data or facts is permitted by copyright law, but not by database right. A second scientist could not make any use of the information or data, that is in the protected database and is not permitted by its owner or any legal exception. The safeguarding of such information would require using additional funds, to duplicate the creation of knowledge already in existence, and it contradicts the norms of science, which favour building on previous discoveries and the sharing of research results.[381]

Scientists could not combine data legitimately accessed from one commercials database with data extracted from other databases to make a sophisticated new database for addressing hard problems without obtaining additional license or permissions.[382] Such prohibition not solely discourages competition but more importantly, hold back the innovation.

The first risk is that use of database rights by the biobanks might unreasonably increase the costs of information. In the field of genetics, most information and data are sole-source information, available only from one database or biobank (for example disease related biobanks store information about particular sickness, population biobanks have information about specific race). There is little if any competitions between collecting and storing such data. In the absence of competition, the price of accessing the database becomes artificially high and scientists, wishing to access such information much pay unreasonable fees. Also, differently from copyright, no first-sale (copyright) doctrine applies to databases. So a scientist, obtaining the information through the license, or after paying to access protected databases could not routinely lessen overall transaction costs by lending, borrowing, or transferring the data they extracted to others working on a common problem.[383]

Furthermore, the data would not enter the public domain for at least fifteen years, and possibly never, if the database creator would continue to invest in maintenance and updates of a dynamic database.[384] The main idea of the science is to be build from the already existing science. Genetic researchers are not creating the information from scratch. They use the data

380 Maurer, Hugenholtz and Onsrud 790.
381 ibid 807.
382 Reichman and Uhlir 808.
383 JH Reichman and Paul F Uhlir, 'Database Protection at the Crossroads: Recent Development and Their Impact on Science and Technology' (1999) 14 Berkeley Technology Law Journal 809.
384 Article 10(3) of the Database directive reads: „Any substantial change, evaluated qualitatively or quantitatively, to the contents of a database, including any substantial change resulting from the accumulation of successive additions, deletions or alterations, which would result in the database being considered to be a substantial new investment, evaluated qualitatively or quantitatively, shall qualify the database resulting from that investment for its own term of protection."

that already exist. The existing legal prohibition can be crucial for the further research and innovation. The ban to use the current data freely for the 15 years period is a very long time that can burden research fundamentally. The Database directive does not limit the rights of the database owner. As an outcome, raw data, scientific facts and similar, can obtain the most forceful scope of protection available from any intellectual property regime (except maybe classical patent paradigm itself).[385]

Genetic science operates a lot on databases. The near-complete digitisation of data collections started a few decades ago, allows to find almost every aspect of the natural world, human activities, captured in an electronic database.[386] As we noted in the previous chapter of the thesis, biological data are growing at incredible speed, allowing more and more information to be stored and found in electronic databases. If researchers are reduced the possibility to access such data, or if such data is available only under a particular fee – such costs would either be passed on to the government or taxpayer thought the increased grant request or they would simply reduce the resources available to researchers and education.[387] Database right can easily disrupt the system of cheap access to raw data for purposes of a basic research, it would then lead to even higher prices for the acquisition of data used in applied research, and finally, it would suppress the ability to add value to research and allow industries to improve, transform, or develop follow-on databases and related information products.[388] The science and technology should advance on already existing data, and not duplicate the previous factual compilations or discoveries, which might happen under the database protection regime.

The initiatives to legislate on the field for protecting unoriginal databases were raised at the national levels, like in the US, and also international level. Discussions at WIPO[389] and the research it ordered, proves that not only Europe was initiating such debate. However, none of the territories, except EU, legislated in this field. It can be quite a substantial proof that database protection, forbidding the use of unoriginal, raw, naturally-occurring, data and information does little if any good. Even if in the Commission's First evaluation of Database directive it was evaluated as giving a positive influence to the creation of databases in Europe, the arguments and questions were also raised if directive does not restrict access to data. I find

385 JH Reichman and Pamela Samuelson, 'Intellectual Property Rights in Data?' (1997) 50 Vanderbilt Law Review 94.

386 Reichman and Uhlir 813.

387 ibid 816.

388 Reichman and Uhlir 820;Paul F. Uhlir, 'From Spacecraft to Statecraft: The Role of Earth Observation Systems in the Verification and Enforcement of International Environmental Agreements' (1995) 2 GIS Law 1.

389 WIPO has prepared or commissioned number of studies on the topic of protection of non-original databases. These analyses and studies can be found at <http://www.wipo.int/copyright/en/activities/non_original_db_studies.html> accessed 8 May 2018; also see ICSU/CODATA Group on Data and Information 'Position Paper on Access to Databases' (1997) <http://www.codata.info/resources/databases/data_access/wipo.pdf> accessed 8 May 2018.

little social arguments to support the use of database protection in the field of biobanks. Unfortunately, as far as there are no legal exceptions or courts' practices staying otherwise, the database protection applies to the biobanks' resources.

There are several other technological or legal measures, that can protect the non-original database. Such legal instruments as technological protection measures,[390] trade secrets or unfair or "parasitic" competition, enrichment without cause, undue appropriation, etc. are available and can offer reasonable protection to owners of non-original databases.[391] Moreover, some authors suggest that if there is a need for greater database protection than currently exists, it could be achieved through changes to the legislation on unfair competition or undue appropriation. Already existing legal rights can protect the database owners against piracy on the part of their competitors without affecting users' access to the information, a particularly sensitive subject in such fields as education or science.[392]

The scientific community finds database rights disruptive. International Council for Science (ICSU) issued a set of principles regarding database protection in the field of science. In these principles the advantages of open access to data, the necessity to ensure cooperation rather than the competitiveness of data, encouragement of data sharing and affordability of data for the research even with a tight budget, are mentioned.[393] The paper of ISCU opposes the idea of a database right, on the ground that it may have potentially adverse effects on the conduct of science. Moreover, both the collection of raw sequenced data and the annotations or proposals for the functions of the genes in the databases often represent substantial pieces of research in themselves. One of the most important sources of new data for biobanks is direct submissions of sequences or records/databases from scientists.[394] Each of the scientists could claim a contribution in collection, verification or presentation of data. So to whom then the database rights should belong?

Private bodies can take legal advantages from such broad protection. Public bodies usually are providing genetic information freely available and free of charge. It may be used by private companies in a profit-making manner, later claiming different IP rights. Celera Genomics corporation[395] benefited from the publication by the Human Genome Project of all

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390 Regulated in Europe by the Directive 2001/29/EC of the European Parliament and of the Council of 22 May 2001 on the harmonisation of certain aspects of copyright and related rights in the information society, OJ L 167, 22.6.2001, p. 10–19.

391 Andrés López, 'The Impact of Protection of Non-Original Databases on the Countries of Latin America and the Caribbean' (2002) 12.

392 ibid 11; Maurer, Hugenholtz and Onsrud 790.

393 ICSU/CODATA Ad Hoc Group on Data and Information, 'Access to Databases. A Set of Principles for Science in the Internet Era', Paris (2000), available at <http://www.icsu.org/publications/icsu-position-statements/access-to-databases/389_DD_FILE_ACCESS_TO_DATABASES_Jun_00_.pdf > accessed 8 May 2018.

394 Jasper A Bovenberg, *Property Rights in Blood, Genes and Data: Naturally Yours?* (Brill | Nijhoff 2006) 79.

395 Currently it was not possible to find information about the company. From the found information, the conclusion that company has been merged or aquired by Quest Diagnostics Incorporated is made.

newly sequenced DNA fragments on its website. Under the Bermuda Agreement, the public consortium is obliged to publish newly sequenced genes onto a publicly accessible website within 24 hours. Celera was not bound by such constraints but took advantage of them.[396] The company was willing to commercialise the human genome. It was claiming the copyright and patent protection over its databases.[397]

Scientists and researchers are the primary users of the information stored in the biobanks. The legal protection of genetic sequence database can have a strong influence to the genetic research, and not necessarily a positive one. Database protection doubtingly encourages the creation of genetic information databases what was the main object of the Database Directive. As already described, genetic information databases are created not because of the incentive to have legal protection. Their purpose is to be helpful and useful for the researchers and scientists, and that they would be used and acknowledged.

[396] Deborah Josefson, 'Biotechnology company claims to have 97% of human genes on its database', West J Med. 2000 Apr; 172(4): 228. Available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1070823/> accessed 8 May 2018.

[397] M Scott McBride, 'Bioinformatics and Intellectual Property Protection' (2002) 17 Berkeley Technology Law Journal 1338.

CHAPTER IV

THE ROLE OF GENE PATENTING IN BIOBANKS

The intellectual property law and its subject matters are changing rapidly every day. The rise of new objects – programming codes, software, biological discoveries – influenced new legislative acts and new rules, providing intellectual property rights to such newcomers. The traditional doctrines of intellectual property laws have been extended to new subject matters such as genes, proteins and other unicellular and multicellular living organisms, which previously remained outside the grab of intellectual property law.[398] For quite a time, new court precedents and of legislative acts, allowed patent offices to issue patents claiming sequenced genes. This patenting process has already started, and a multi-billion dollar industry has been built on the premise that quite fundamental genetic patents are available.[399]

Gene concepts emphasising particulate materiality, information content, or encoded algorithmic programs, coupled with DNA sequencing and recombinant DNA technologies, facilitated a view, that one could "invent" DNA-based innovations just as one could write software to run on a computer.[400] Newly-sequenced genes, as long as they had been isolated from a human body and purified, could now be claimed as inventions allowable for patent protection. Sadly, the biotechnology industry is substantially based on gene and gene-based inventions, therefore the number of such patent applications increase. The products of that industry are made possible by technologies that allow genes to be located within the genome, sequenced DNA by DNA, isolated out of their original genomic loci and spliced into brand new place, and expressed more or less than usual.[401] In the field of biotechnology, the industry relies strongly on the availability of patent protection to gain the economic value of genes. The judicial, executive or legislative bodies are not going to upset the premise of genes patenting, even if some have their doubts about whether it was ever correct either as a matter of law or as a matter of desirable innovation policy.[402]

Differently from the legislator, presumably greatly influenced by lobbyist, the scientific community, different political groups and non-governmental organisations do not support the

398 Kshitij Kumar Singh (ed), *Biotechnology and Intellectual Property Rights. Legal and Social Implications* (Springer India 2015) 1.
399 Boyle (2003a) 110.
400 Torrance AW, 'Gene Concepts, Gene Talk, and Gene Patents' (2010) 11 Minnesota Journal of Law, Science & Technology 160.
401 Torrance AW (2010) 181.
402 Boyle (2003a) 110.

idea of gene patenting. Already before the issue of the Directive 98/44/EC on the legal protection of biotechnological inventions (the Biotechnology directive),[403] the EU Commission's Group of Advisers wrote: "Genes and partial gene sequences whose functions are unknown should be made expressly unpatentable to end the international debate on the matter. In due course the Community should try to arrange an international agreement on the patentability tests for inventions resulting from genetic research programmes".[404] Biobanks' representatives have also expressed concern about researchers obtaining and enforcing patents using their data. A representative from Coriell Institute for Medical Research state, that they want data from the Personalized Medicine Collaborative project "to be accessible for discovery, to push the envelope on new knowledge. [It] should be used in a manner to gain new knowledge rather than for patents on DNA."[405] Opposition in gene patenting claims that obtaining a patent on a genetic sequence, single nucleotide polymorphism (SNP), or haplotype, for example, might limit the ability of other researchers to use that data for further research.[406]

Professor James Boyle[407] very comprehensibly classifies the arguments against gene patenting into several categories: 1) religious beliefs (genes are created by nature and not by a human being); 2) moral reasons[408] (it is immoral to own a gene, it must be freely available to everyone); 3) environmentalistic critics (owing a gene can lead to manipulations, commodifications of the nature, naturally occurring facts. Humans should not tinker environment); 4) argument that it is a common heritage of a man kind (therefore, cannot be owned by a single person); 5) that a gene belongs to its source (a donor) (and ownership cannot be claimed by anyone else); 6) legislative arguments (it is not a patentable subject matter according to the law); 7) that it goes against the innovation (the thing the intellectual property rights and patents should promote in the first place).

It would be out of the scope of this research to make an in-depth analysis of all the possible arguments against the patenting of gene sequences. Furthermore, as rightly stated by prof. James Boyle, simply talking about the different reasons of why genetic patents should not have been granted, can do very little. The biotechnology industry has strong incentives to maintain the patentability of gene inventions. Patent protection for genes and their products is

403 Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions 1998. OJ L 213, 30.7.1998, p. 13–21.

404 EU Commission, 'Opinions of the Group of Advisers on the Ethical Implications of Biotechnology of the European Commission EU Commission, 'Opinions of the Group of Advisers on the Ethical Implications of Biotechnology of the European Commission [Working Document]' (1993) [Working Document]' (1993) 35.

405 Brenda M Simon and others, 'How to Get a Fair Share: IP Policies for Publicly Supported Biobanks' (2008) 452 Stanford Journal of Law, Science & Policy 69.

406 Simon BM and others 67.

407 Boyle (2003a), 97-107.

408 On this topic see also the World Health Organization, 'Genetics, Genomics and the Patenting of DNA : Review of Potential Implications for Health in Developing Countries' (2005) 30–32.

a keystone asset of pharmaceutical and biotechnology companies, as well as a valuable source of revenue for universities and government research institutes.[409]

I. Patentable subject matter

In the previous chapter I have already stated, that biobanks are moving from sample centred towards data-centred perspective. Therefore information about a gene: nucleotide or protein sequences, protein crystal structures, gene-expression measurements, protein and genetic interactions and other original data coming from sample research are more and more important for the further studies.

Although many thousands of patents and patent applications have employed the words "gene" or "genes" within their claims, seldom do patent applicants trouble themselves with defining these specific terms in specifications. Professor Andrew W. Torrance, looked at fifteen US federal court opinions that discuss gene definitions, and in only two (Amgen, Incorporated v. Chugai Pharmaceutical Company[410] and Carnegie Mellon University v. Hoffman-La Roche Incorporated[411]) finds a provided definition of a gene.[412] In the Amgen decision, the definition is given "A gene is a chemical compound, albeit a complex one", and the Carnegie Mellon University definition is - "A gene may be defined as a region of DNA that contains information that a cell uses to make a particular protein." Torrance notes that both these definition are either too general or scientifically inaccurate (e.g., because it ignores introns), vague, and uninformative. The technical definition of a gene can be found in the scientific dictionaries, and there a gene is described as "a distinct sequence of nucleotides forming part of a chromosome, the order of which determines the order of monomers in a polypeptide or nucleic acid molecule which a cell (or virus) may synthesize."[413]

When talking about gene patenting, it is essential to distinguish between the human genome – the total human complement of DNA present in each of our cells – which cannot be patented, and particular sections of DNA, called genes, which can be patented.[414] In both the United States and Europe, patents can be granted based upon particular human DNA sequences but not upon the sequence of the entire human genome.

A stem cell is a cell that can develop into many different cell types in the body during early life and growth. Additionally, in many tissues they serve as a kind of internal repair system, dividing essentially without limit to replace other cells.[415] An adult stem cell is a

409 Torrance AW (2010) 182.
410 *927 F 2d 1200 - Amgen Inc v Chugai Pharmaceutical Co Ltd [1206]*.
411 *Carnegie Mellon University v Hoffman-La Roche Inc, Nos 07-1266, -1267 (Fed Cir Sept 8, 2008)* [8].
412 Torrance AW (2010) 180.
413 English Oxford Dictionaries, available online at https://en.oxforddictionaries.com/ accessed 2018 May 8.
414 Gitter (2001) 1630.
415 National Institutes of Health, 'STEM CELL INFORMATION' <https://stemcells.nih.gov/info/basics/1.htm> accessed 8 May 2018.

similar cell that is found in a differentiated (specialised) tissue in the adult.[416] Scientists discovered ways to obtain embryonic stem cells from early mouse embryos in 1981. In 1998 by studying the biology of mouse stem cells the scientists discovered a method to take stem cells from human embryos and grow the cells in the laboratory.[417] Stem cell of the various types having a possible future therapeutic application are stored in the biobanks and can be used for the future research purposes.[418] One of the main organelles of the cell is the nucleus. It contains genes, collections of DNA, that determine different aspects of human anatomy and physiology. The DNA which is designed from chromosomes and contains the blueprint specific for each type of cell which allows the cell to replicate.[419]

The arguments are raised, that excluding DNA from patentability as a chemical compound or "composition of matter" may be incompatible with TRIPS agreement.[420] Even if there is nothing in the Agreement obligating the grant of patents over substances existing in nature (even if isolated), the TRIPS require Member countries to make patents available for any inventions, whether products or processes, in all fields of technology without discrimination, subject to the normal tests of novelty, inventiveness and industrial applicability. It is also required that patents be available and patent rights enjoyable without discrimination as to the place of invention and whether products are imported or locally produced (Article 27(1)).[421] This may also be one of the aspects leading to acceptance of patent applications claiming gene-related inventions.

A study performed by the European Commission in 2002 found 2,029 patent applications applied or patents granted for stem cells and 512 patents applied for or granted for embryonic stem cells world-wide.[422] Today's search discloses 5,532 results found in the Worldwide database for "human stem cell" and more than 10,000 results if only the text phrase "stem cell" is used. More than 10,000 results are given if the phrase "gene sequence" or "protein structure" are searched; 3,843 results for a "ribonucleic acid" (or RNA); 3,329 for "nucleotide polymorphism". Of cause, the data shows the patents and the patent applications that are filed, therefore not all these numbers will indeed become the granted patents. Also, the search is looking for information in the title or the abstract of the patent application, so not all the

416 EU Commission, 'Opinions of the Group of Advisers on the Ethical Implications of Biotechnology of the European Commission [Working Document]' (1993) 9.

417 National Institutes of Health, 'STEM CELL INFORMATION' <https://stemcells.nih.gov/info/basics/1.htm> accessed 8 May 2018.

418 Silvana Bardelli, 'Stem Cell Biobanks' (2010) 3 Journal of Cardiovascular Translational Research 128.

419 Dr Chris, 'Human Cell Diagram, Parts, Pictures, Structure and Functions' <https://www.healthhype.com/human-cell-diagram-parts-pictures-structure-and-functions.html> accessed 8 May 2018.

420 WHO Human Genetics Programme, 'Genetics, Genomics and the Patenting of DNA: Review of Potential Implications for Health in Developing Countries' 45.

421 World Trade Organization, 'Overview: The TRIPS Agreement' <https://www.wto.org/english/tratop_e/trips_e/intel2_e.htm> accessed 8 May 2018.

422 European Commission, 'Study on the Patenting of Inventions Related to Human Stem Cell Research', 23.

patent applications containing these phrases must necessarily be related with the patenting of indicated materials (as it can be only a part of the description in the abstract). However, it does not diminish the substantial numbers revealed.

It would be out of the scope of this dissertation to analyse in depth the patent applications or patents related to stem cells. However, there are some titles, I wish to mention. One is US application No. 2009269845 (A1) with a title Pluripotent cells. Its abstract discloses "*The present invention is directed to pluripotent cells that can be readily expanded in culture on tissue culture substrate that is not pre-treated with a protein or an extracellular matrix, and do not require a feeder cell line. The present invention also provides methods to derive the pluripotent cell line from human embryonic stem cells".* This application is extended to several national jurisdictions.[423] Another Korean patent No. KR101653992 (B1), claims an invention related to a stem cell having a multi-layered thin film structure, its production method, and its use in a cell therapy product. According to the present invention, it is possible to provide the stem cell having the multi-layered thin film and showing improved stability and regulated multi-functionality. The stem cell having the multi-layered thin film can be applied as a treatment agent for treating various diseases. US patent No. US6200806 (B1) is claiming cultured primate embryonic stem cells and purified preparation of primate embryonic stem cells. The cells of the preparation are human embryonic stem cells, that have normal karyotypes, and continue to proliferate in an undifferentiated state after continuous culture. A method for isolating a primate embryonic stem cell line is also patented.

Gene patents can claim in the application the protection for the all gene or part of it. Such patents can also cover many kinds of inventions involving the components of genes or genetic technologies. For example, associations between a DNA variant and a disease, condition, or function can be within the scope of patent protection. The DNA sequence that produces a particular protein, controls a gene or can be used to study genetic variations or RNA sequences that shift genes, control other functions as well as cell lines, methods of treatment, and diagnostics can be patented.[424]

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[423] Family list can be found at <https://worldwide.espacenet.com/publicationDetails/inpadocPatentFamily?CC=US&NR=2009269845A1&KC=A1&FT=D&ND=4&date=20091029&DB=EPODOC&locale=en_EP> accessed 2018 May 8.

[424] Robert Cook-Deegan, 'Gene Patents' in Mary Crowley (ed), *From Birth to Death and Bench to Clinic: The Hastings Center Bioethics Briefing Book for Journalists, Policymakers, and Campaigns* (Garrison, NY: The Hastings Center 2008) 69.

II. Patenting of a gene. US and European practices.

1. US case law

Common law and continental law differences are influential when trying to answer gene patenting questions. The US courts, having a strong precedent forming powers, are drawing lines between patentable and not patentable subject matters. In Europe, courts are bound by the legislative acts and in general, cannot overrule them but merely interpret and apply. Hence, the disputes on the validity of the gene patents in different jurisdictions have been solved differently.

The landmark decision in the US was reached in case Diamond v. Chakrabarty. After this decision, the United States Patent and Trademark Office (USPTO) began regularly to issue patents claiming sequenced genes.[425] Chakrabarty (Plaintiff) developed a new species of the bacterium capable of metabolising hydrocarbons in a manner unknown in naturally occurring organisms using recombinant DNA processes. The microorganisms exhibited grand promise to treat the oil spills. Chakrabarty applied for an invention patent, but it was denied by the Patent Office on the basis that the microorganisms were products of nature and therefore unpatentable. However, the Supreme Court ruled that claimed micro-organism qualifies as patentable subject matter, as such micro-organisms qualify not as unknown natural phenomenon, but as a "non-naturally occurring manufacture or composition of matter – a product of human ingenuity having a distinctive name, character use". The decision ruled that the patentee has produced a new bacterium with markedly different characteristics from any substances found in nature, and the bacterium is having the potential for significant utility. The discovery was not treated as nature's handiwork, but as a product of an inventor, therefore the subject matter was patentable.[426]

Another leading case was Parke-Davis & Co. v. H.K. Mulford & Co., where a court held that highly purified human adrenaline was patentable, because even though adrenaline is a natural product, in its natural state it only occurs in small quantities intermixed with the rest of the cellular milieu.[427] The court noted that by purifying the adrenaline, the inventor had for all practical purposes created a chemical product that did not exist in nature, and can be patentable for significant therapeutic benefits. This principle has been extended to isolated

425 Torrance AW (2010) 160.
426 *Diamond v Chakrabarty, 447 US 303 (1980)*. Page 447, 130-131.
427 *Parke-Davis & Co v HK Mulford & Co, 189 F95 (1911)*.

polynucleotides, proteins and other biomolecules, and is one of the precedent cases for many future gene patents issued.[428]

US courts repeatedly have stated that "federal law permits the patenting of organisms that represent the product of "human ingenuity," but not naturally occurring organisms. Human cell lines are patentable because "[l]ong-term adaptation and growth of human tissues and cells in culture is difficult - often considered an art ... ," and the probability of success is low. It is this inventive effort that patent law rewards, not the discovery of naturally occurring raw materials."[429]

Nevertheless, at least in the United States, this practice of patenting human genes is changing. The notable decisions on patents of BRCA1 and BRCA2 give another direction of what can or cannot be a patentable subject matter in the genetic field. The patents on the mentioned genes were granted in the United States and Europe, and later in both jurisdictions, they have been invalidated.

The facts of the Myriad case are the following. Myriad Genetics, Inc. (Myriad), obtained several patents after discovering the precise location and sequence of the BRCA1 and BRCA2 genes, mutations of which can dramatically increase the risk of breast and ovarian cancer. Mutations in BRCA1 and BRCA2 genes accounted for an estimated 5–10% of breast cancer cases, as well as significantly elevated risk for ovarian and other cancers.[430] Myriad develop medical tests useful for detecting mutations in these genes in a particular patient to assess the patient's cancer risk. If valid, Myriad's patents would give it the exclusive right to isolate an individual's BRCA1 and BRCA2 genes, and would give Myriad the exclusive right to synthetically create BRCA cDNA.[431]

Along with the Association for Molecular Pathology and the University of Pennsylvania, also joined by other parties: researchers at Columbia, NYU, Emory, and Yale universities, several patient advocacy groups and several individual patients, filed the appeal against the decision of the US PTO to grant patents for BRCA1 and BRCA2 genes' sequences. The grounds of the appeal were that it is unpatentable products of nature and that the diagnostic method claims are mere thought processes that do not yield any real-world transformations, and that the drug screening claims were just describing the basic processes of doing science.

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428 CM Holman, 'Bilski: Assessing the Impact of a Newly Invigorated Patent-Eligibility Doctrine on the Pharmaceutical Industry and the Future of Personalized Medicine' (2010) 10 Curr Top Med Chem, 1939 <http://www.ncbi.nlm.nih.gov/pubmed/20615185>.

429 *Moore v Regents of the University of California, 51 Cal 3D 120 (1990)*. 143, emphasis added.

430 Robert Cook-Deegan, 'Gene Patents' in Mary Crowley (ed), *From Birth to Death and Bench to Clinic: The Hastings Center Bioethics Briefing Book for Journalists, Policymakers, and Campaigns* (Garrison, NY: The Hastings Center 2008) 70.

431 From the syllabus of the case *Ass'N For Molecular Pathology v. Myriad, 133 S.Ct. 2107 (2013)*.

The case reached the Supreme Court of the United States. The court handed down Association for Medical Pathology v. Myriad Genetics case,[432] stating that simply isolated genes and genetic sequences, like DNA or gDNA, fall within the "natural product" doctrine and therefore are not treated as "inventions" under the patent law. US patent law's "products of nature" doctrine excludes from patentability naturally occurring materials. The Supreme Court has earlier acknowledged that "anything under the sun that is made by man" falls within patentable subject matter, meaning that things under the sun not made by man do not fall within patentable subject matter. Indeed, the Court had formulated that items such as "a new mineral discovered in the earth or a new plant found in the wild" would constitute unpatentable products of nature.[433]

In the Myriad case, quoting previous decisions,[434] the court stated that patent law provision of the Section 101 of the Patent Act, "contains an important implicit exception[:] Laws of nature, natural phenomena, and abstract ideas are not patentable. Rather, they are the basic tools of scientific and technological work that lie beyond the domain of patent protection."[435] The court affirmed that Myriad did not create or alter any genetic information encoded in the BRCA1 and BRCA2 genes, neither it created or altered the genetic structure of DNA.[436]

The US decision, however, did not give a clear answer to question what genetic substances can be patentable. As rightly stated by some authors,[437] the Myriad judgement teaches that simply isolated genes and genetic sequences are natural products, but it does not explicitly explain what a natural product is. When in the decision the court ruled, that cDNA can be patented as it is a man-made product,[438] the evidence that cDNA also, in fact, exist naturally, even in humans, was not taken into account.[439] The argument that a cDNA does not exist in nature and can be patent object is often viewed as a legal twist and is not approved by the most geneticists.[440] Indeed, patenting on genes and genomic sequences is intrinsically

[432] *Ass'N For Molecular Pathology v. Myriad, 133 S.Ct. 2107 (2013).*

[433] Dan L Burk, 'Anticipating Patentable Subject Matter' (2013) 65 Stanford Law Review 109.

[434] Refering to a case *Mayo v Prometheus, 132 S Ct 1289 (2012)*.

[435] *Ass'N For Molecular Pathology v. Myriad, 133 S.Ct. 2107 (2013)* [2116].

[436] *Ass'N For Molecular Pathology v Myriad, 133 SCt 2107 (2013)* [2117].

[437] See Lai (2015); and Joshua D Sarnoff, 'The Current State of Patent Eligibility of Medical and Biotechnological Inventions in the United States' [2012] Edward Elgar Press 109.

[438] In the decision court stated: "[T]he lab technician unquestionably creates something new when cDNA is made. cDNA retains the naturally occurring exons of DNA, but it is distinct from the DNA from which it was derived. As a result, cDNA is not a "product of nature" and is patent eligible under § 101, except insofar as very short series of DNA may have no intervening introns to remove when creating cDNA. In that situation, a short strand of cDNA may be indistinguishable from natural DNA.", *Ass'N For Molecular Pathology v. Myriad*, 133 S.Ct. 2107, 2119 (2013)

[439] See David Baltimore, 'Viral RNA-Dependent DNA Polymerase: RNA-Dependent DNA Polymerase in Virions of RNA Tumour Viruses' (1970) 226 NATURE 1209.; Howard M Temin and Satoshi Mizutani, 'Viral RNA-Dependent DNA Polymerase: RNA-Dependent DNA Polymerase in Virions of Rous Sarcoma Virus' (1970) 226 Nature 1211.

[440] The ESHG Working Party on Patenting and Licensing, 'Patenting and Licensing in Genetic Testing: Recommendations of the European Society of Human Genetics' [2007] European Journal Of Human

different from the patenting of methods, or technologies. There is no possibility to invent around a DNA, RNA or cDNA.

The insufficiency of the Supreme Court's decision to provide a clear test of what a natural product is, created even more insecurities when applying the judgement to newer technologies. For example, does the judgement exlains how the doctrine could help to assess DNA or DNA-like sequences made *ab initio*? Does it make a difference if the sequences are virtually the same as something known to exist in nature even if it is made synthetically to make the same naturally existing proteins?[441]

The US PTO in it's 2014 Guidance for Determining Subject Matter Eligibility of Claims Reciting or Involving Laws of Nature, Natural Phenomena, & Natural Products (Guidance)[442] advices to test the patent application looking "whether any element, or combination of elements, in the [patent] claim, is sufficient to ensure that the claim amounts to significantly more than the ["product of nature"] exception." If the claim does not include any additional features that could add significantly more to the exception, it is not eligible for protection and should be rejected under 35 U.S.C. 101[443]. However, if "the claim includes a nature-based product that has markedly different characteristics [from what exists in nature], the claim does not recite a ''product of nature'' exception and is eligible [for protection]"[444].

But how to know if a product has those "markedly different characteristics"? The patent application is evaluated based on what is recited in the claim on a case-by-case basis. The US patent office gives non-limiting examples of the types of characteristics considered by the courts when determining whether there is a marked difference. It can be expressions of biological or pharmacological functions or activities; chemical and physical properties; phenotype, including functional and structural characteristics; structure and form, whether chemical, genetic or physical[445].

US PTO thus seems to take a mixed structural-functional approach – the differences from naturally occurring elements can be found either in the structure of a material or its function. At the end of the day, the term "marked" is subjective and not clear cut. The PTO stated that not all differences are "marked" differences, giving the example that simply isolating nucleic acid is not "marked." The guidelines tells nothing more than what in Myriad case told the court. If an isolated nucleic acid is modified by a researcher, is this then "markedly different"?

Genetics 2.

441 Lai 1065.

442 United States Patent and Trademark Office, 'Federal Register, Rules and Regulations. 2014 Interim Guidance on Patent Subject Matter Eligibility' (2014).

443 Ibid. p 74626.

444 Ibid. p 74623.

445 Lai 1065.

Does this depend on the type and kind of modification? Or the function of the modification performs or if it is a new property that is introduced?[446]

Jessica C Lai, concludes, that neither the decision nor guidelines give the answer if genetic materials from prokaryotes, which have no introns and thus no "cDNA", genomic biomarkers, which are genetic sequences used for identification of species or diseases, RNA molecules can be patentable. The US Supreme Court failed to address the question whether the RNA analogues of DNA for polypeptide production, noncoding RNA (ncRNA), transfer RNA (tRNA), ribosomal RNA (rRNA), micro RNA (miRNA), and small interfering RNAs (siRNA) can have patent protection. No reference to polypeptide sequences was also made.[447]

Without a clear separation between patentable and not patentable subject matter in human genetics, patents are being granted by the US PTO. Patent scholars will peacefully discuss the claim that current PTO utility guidelines, or the PTO's practices in reviewing patents on gene sequences, might be too liberal and provoking the issuance of patents too far "upstream" in the research cycle[448].

2. Regulation in Europe

The necessary requirements for patenting biotechnological inventions in Europe are comparable to those in the United States. Such requirements in Europe are set in the EPC[449] and Biotechnology Directive.[450] According to Article 52(2) of the EPC, the categories of unpatentable subject matter in Europe are similar to those in the United States. These categories include: (a) discoveries, scientific theories, and mathematical methods, (b) aesthetic creations, (c) schemes, rules and methods for performing mental acts, playing games or doing business, and programs for computers, and (d) presentations of information. European opponents of patents on life forms, especially Green Party members and environmentalists, have contended that living organisms, including human DNA sequences, are not patentable inventions but they arguments have failed in Europe under both the EPC and the Biotechnology Directive.[451]

The Biotechnology Directive regulates the patentability questions of biological materials or processes. It acknowledges that, with respect to biotechnological inventions, European

446 Lai 1066.
447 Ibid. 1065.
448 James Boyle, 'Enclosing the Genome: What the Squabbles over Genetic Patents Could Teach Us' (2003a) 50 Advances in Genetics 97.
449 The European Patent Convention.
450 Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions, *OJ L 213, 30.7.1998, p. 13–21.*
451 Gitter (2001) 1645.

legal framework includes principles such as determining whether the claim is a discovery or an invention, especially when in comes to element of human origin, and whether patent protection should be allowed. Mere discovery seems to be ineligible for patent protection, especially if it is an element of the human body, and in broader sense, because it does not fulfil the requirements of patentability (novelty, the inventive step and industrial applicability).[452] The Directive had the purpose to harmonise the patentability of biotechnological inventions among the Member States and to ensure that all EU Member States *do* protect gene-related technologies. The Biotechnology Directive was intended to be propatent.[453] It can be read from the preamble of the Directive, where it is written that only adequate legal protection can make profitable genetic engineering, where the research and development requires a considerable amount of high-risk investment,[454] and that differences in the legal protection of biotechnological inventions offered by the laws and practices of the Member States can create barriers to trade.[455]

Also, differently from the interpretations given in the above mentioned US case law, in Europe naturally occurring inventions can be patentable if they fulfil patentability requirements. The preambular paragraph 20 of the Directive states that:

> „an invention based on an element isolated from the human body or otherwise produced by means of a technical process, which is susceptible of industrial application, is not excluded from patentability, even where the structure of that element is identical to that of a natural element, given that the rights conferred by the patent do not extend to the human body and its elements in their natural environment.“

The Biotechnology Directive further explicitly discusses why isolated genetic sequences are patentable subject matter, stating that:

> “such an element isolated from the human body or otherwise produced is not excluded from patentability since it is, for example, the result of technical processes used to identify, purify and classify it and to reproduce it outside the human body, techniques which human beings alone are capable of putting into practice and which nature is incapable of accomplishing by itself.”[456]

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452 Nicholas C Whitley, ‘An Examination of the United States and European Union Patent Systems With Respect To Genetic Material’ 35 Arizona Journal of International & Comparative Law 476.

453 Jessica C Lai, ‘Myriad Genetics and the BRCA Patents in Europe: The Implications of the US Supreme Court Decision’ (2015) 5 UC Irvine L. Rev., p. 1053.

454 Biotechnology Directive preambular paragraph 2.

455 Biotechnology Directive preambular paragraph 5.

456 Biotechnology Directive preambular paragraph 21.

The national law of the EU Member states also follows the same path. Article 1(2) of the German patent act[457] establishes that:

> "Patents are also granted for inventions, as defined in paragraph 1 (in all fields of technology, provided they are new, involve an inventive step and are capable of industrial application (*author's note*)), that have as their object a product consisting of a biological material or is containing or is produced with the biological material or is processed with such material. The biological material is regarded such material that by means of a technical process is isolated or produced from its natural environment. It can be the subject of an invention even if it previously occurred in nature."[458]

UK patent act[459] also rules, that:

"An invention shall not be considered unpatentable solely on the ground that it concerns — (a) a product consisting of or containing biological material; or (b) a process by which biological material is produced, processed or used.

Biological material which is isolated from its natural environment or produced by means of a technical process may be the subject of an invention even if it previously occurred in nature."

Similarly is regulated in Spain. The Spanish law on patents[460] in Article 4(1) foresees that:

"Patents can be issued from all fields of technology when inventions are new, involve an inventive step and are capable of industrial application.

Patentable inventions may relate to a product composed of biological material or containing biological material, or a method by which it is produced, processed or uses the biological material."[461]

The Article continues in the second and third part, adding that:

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457 Patentgesetz in der Fassung der Bekanntmachung vom 16. Dezember 1980 (BGBl. 1981 I S. 1), das zuletzt durch Artikel 4 des Gesetzes vom 8. Oktober 2017 (BGBl. I S. 3546) geändert worden ist 2017 1.

458 Original text: „Erster Abschnitt Das Patent § 1 (1) Patente werden für Erfindungen auf allen Gebieten der Technik erteilt, sofern sie neu sind, auf einer erfinderischen Tätigkeit beruhen und gewerblich anwendbar sind. (2) Patente werden für Erfindungen im Sinne von Absatz 1 auch dann erteilt, wenn sie ein Erzeugnis, das aus biologischem Material besteht oder dieses enthält, oder wenn sie ein Verfahren, mit dem biologisches Material hergestellt oder bearbeitet wird oder bei dem es verwendet wird, zum Gegenstand haben. Biologisches Material, das mit Hilfe eines technischen Verfahrens aus seiner natürlichen Umgebung isoliert oder hergestellt wird, kann auch dann Gegenstand einer Erfindung sein, wenn es in der Natur schon vorhanden war."

459 United Kingdom Patents Act 1977.

460 Ley 24/2015, de 24 de julio, de Patentes 2015.

461 Original text „1. Son patentables, en todos los campos de la tecnología, las invenciones que sean nuevas, impliquen actividad inventiva y sean susceptibles de aplicación industrial. Las invenciones a que se refiere el párrafo anterior podrán tener por objeto un producto compuesto de materia biológica o que contenga materia biológica, o un procedimiento mediante el cual se produzca, transforme o utilice materia biológica."

"2. Biological material isolated from its natural environment or produced by a technical process may fall under the definition of an invention, even if it previously existed in nature.

3. For the purposes of this Act, the term "biological material" means ***any material containing genetic information itself or being reproduced in a biological system and "microbiological process" means any process using microbiological material including a presentation on the or resulting microbiological matter*** *(emphases added)*".[462]

The examples of given national legislation follow the path of Biotechnology Directive, that biological or genetic inventions can be patented. It does not change anything, if a genetic invention already exists in nature, for example, human DNA sequence; it still can be patented and have a legal protection when the industrial applicability is demonstrated.

But, the Spanish legal act differs from other national laws, by giving an exception to patent a mere sequence of deoxyribonucleic acid (DNA) without indication of any function (Article 5(6)).[463] The exception is favourable and can be used either by the patent examiner or by the opposing party, to reject the patent application. However, it still depends a lot on every case. If the patent applicant can demonstrate sufficiently clear, that the DNA sequence is performing some function, a patent still could be granted.

Not only Biotechnology Directive and national legal acts but also the European Patent Convention with its Implementing Regulations and Guidelines allow genetic sequences as patentable subject matter, as long as the industrial applicability is explicitly clear from the patent application but not necessarily in the claims themselves.[464] This path is followed in the decisions of the Boards of Appeal of the European Patent Office.

In 1990, the EPO Technical Board of Appeal in case T 19/90[465] (Onco-Mouse) for the first time approved a European patent for a transgenic mammal. US scientists created this animal to be genetically predisposed to develop breast cancer, intending it to serve as a more effective model for studying how genes contribute to various forms of cancer, as well as for testing drugs for breast cancer. The present patent application concerns, inter alia, genetically manipulated non-human mammals. Board concluded that the present application could not be refused on the ground that Article 53(b) EPC excludes the patenting of animals as such. The

[462] Original text „2. La materia biológica aislada de su entorno natural o producida por medio de un procedimiento técnico podrá ser objeto de una invención, aun cuando ya exista anteriormente en estado natural. 3. A los efectos de la presente Ley, se entenderá por «materia biológica» la materia que contenga información genética autorreproducible o reproducible en un sistema biológico y por «procedimiento microbiológico» cualquier procedimiento que utilice una materia microbiológica, que incluya una intervención sobre la misma o que produzca una materia microbiológica."

[463] Original text „Una mera secuencia de ácido desoxirribonucleico (ADN) sin indicación de función biológica alguna no podrán ser objeto de patente."

[464] More about this matter in Lai (2015).

[465] *T 0019/90 (Onco-Mouse) (1990), ECLI:EP:BA:1990:T001990199010003.*

proper issue to be considered was, therefore, whether or not the subject-matter of the application is an "animal variety". EPO affirmed that the EPC does not exclude the patenting of animals as a per se category, and the patent was allowed.[466]

Then, in 2002 the decision on human DNA patent case was reached under the EPC. Titled as a Relaxin case,[467] the judgement was related to the invention of a DNA sequence encoding a human protein, produced by pregnant women, that had useful applications during the childbirth process.[468] The patent covered the DNA sequence (i.e. the gene obtained from a human ovary) which codes for hormone relaxin, which relaxes the uterus during childbirth. An opposition against this patent was filed in January 1992 by members of the Green Party in the European Parliament on a number of grounds, including the immorality exclusion. The Opposition Division rejected the opponents' arguments that the subject matter of the patent represented a mere discovery and therefore was not patentable.

The Opposition Division's decision was later confirmed by the Technical Board of Appeal.[469] The Board assessed the validity of the arguments that patent should not be issues according to Articles 53(a) EPC as relating to subject-matter which was contrary to "ordre public" and morality and under Article 52(2)(a) EPC for not being concerned with an invention but with a discovery. However, the Board ruled that according to he implementing Rule 23(e)(2), an element isolated from the human body or otherwise produced by means of a technical process including the sequence or partial sequence of a gene may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.[470] Therefore, the invention in the case was not considered as an exception to patentability under Article 53(a) EPC and the appeal was dismissed. In the view of the EPO, DNA is not life but rather a chemical substance which carries genetic information to produce medically useful proteins.

These decisions were followed by already mentioned cases in patenting BRCA1 and BRCA2 genes. As said, these patents were granted but later declared invalid in the United States and also in Europe. However, the EPO declared patents partly void on entirely different grounds than the US court. The EPO Opposition Division and later the Board of Appeal took a strict and structural understanding of the "the same invention". In the decisions, the reasoning followed that a priority could be claimed only if the skilled person can derive the

466 Ibid. at section 4.9.2.
467 *Hormone Relaxin, 1995 OJ EPO 388 (Opp Div)*.
468 DM Gitter, 'International Conflicts over Patenting Human DNA Sequences in the United States and the European Union: An Argument for Compulsory Licensing and a Fair-Use Exemption.' (2001) 76 New York University law review 1623.
469 *T 0272/95 (Relaxin/HOWARD FLOREY INSTITUTE) of 23-10-2002 ECLI:EP:BA:2002:T027295200210 23*.
470 Ibid. para 7.

claimed subject-matter directly and unambiguously, using common general knowledge, from the previous patent application as a whole. The errors in the priority document meant that there was no priority as the prior art document did not disclose "the same invention."[471] For these reasons Myriad Genetics could not claim priority from US patent application (filed on September 2, 1994) that disclosed the BRCA1 sequence, and so could not claim the BRCA1 sequence as a whole. The patent claims were limited to probes (short strands of the BRCA1 sequence) to isolate the gene, cloning vectors, and host cells.[472]

There were three cases in the EPO Boards of Appeal against three different patent applications related with the inventions coming from BRCA gene (all application are being claimed by the same patentee – the University of Utah Research Foundation). The first case, T 1213/05 of 27 September 2007, deals with 17q-Linked breast and ovarian cancer susceptibility gene, the second case T 0080/05[473] of 19 November 2008 analyses the patenting the method for diagnosing a predisposition for breast and ovarian cancer, and the third case T 0666/05[474] of 13 November 2008 copes with mutations in the 17q-linked breast and ovarian cancer susceptibility gene. These decisions narrowed the scope of the patent, but more importantly, they answered the question about the patentability of a human gene. In the above-mentioned decisions, the Board explain the possibility of patenting human genes.

Let's look at the EPO Board of Appeal opinion on the patentability of a gene. As I have already presented, the US courts applied the "product of nature" doctrine to invalidate the Myriad patents. In Europe, the interpretation of the EPO Boards of Appeal was, however, different. In the first reached decision (case T 1213/05) the Board ruled that:

> "It has been submitted by the Opponents that the sequences of the probes according to claim 1 occur in nature and are therefore a discovery rather than an invention. <...> Article 52(2)(a) EPC is to be interpreted in accordance with the implementing Rule 23e(2) EPC which states: "(2) An element isolated from the human body or otherwise produced by means of a technical process including the sequence or partial sequence of a gene may constitute a patentable invention, even if the structure of that element is identical to that of a natural element". <...> These probes are thus isolated elements of the human body as defined in Rule 23e(2) EPC and thus patentable subject-matter."[475]

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471 *T 1213/05 (Breast and ovarian cancer/UNIVERSITY OF UTAH) of 27-9-2007 ECLI:EP:BA:2007:T121305.20070927*. Paras 22–34.

472 Lai (2015) 1058.

473 *T 0080/05 (Method of diagnosis/UNIVERSITY OF UTAH) of 19-11-2008 ECLI:EP:BA:2008:T008005200811119*.

474 *T 0666/05 (Mutation/UNIVERSITY OF UTAH) of 13-11-2008 ECLI:EP:BA:2008:T066605200811113*.

475 *T 1213/05 (Breast and ovarian cancer/UNIVERSITY OF UTAH) of 27-9-2007 ECLI:EP:BA:2007:T121305200709 27.*Paras 43-45.

This finding was once again confirmed in the Boards of Appeal cases T 0080/05 and T 0666/05. Board ruled that "an element isolated from the human body or otherwise produced by means of a technical process may constitute a patentable invention. This finding applies to claims relating to products, here genes, and is a fortiori applicable to the method claims here at issue".[476]

In the decisions, T 0080/05 and T 0666/05, the Board also rejected the argument that a method for diagnosing a predisposition for breast and ovarian cancer in a human subject should not be regarded as a patentable invention according to Article 53(c) EPC. This Article foresees that "the methods for the treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body shall not be regarded as inventions which are susceptible of industrial application". However, the Board found that the mentioned article "excludes diagnostic methods practised *on* the human or animal body only if the method steps of technical nature belonging to the preceding steps which are constitutive for making a diagnosis as an intellectual exercise are performed *on a living human* or animal body."[477] In the BRCA1 patents, all the method steps were of the technical nature, which were performed on a tissue sample of a human subject and not on a live human, therefore it did not come under the exception of Article 53(c) EPC and could have been patented.[478]

This decision is significant to biobanks, that were performing research on the human (or animal) samples. The ruling opens the door to patent different diagnostics and research methods performed on biological samples. A person can be restricted access to the technology that is used for investigating a sample, DNA segment, cell line, or similar. Broad patent claims, because they would use methods that reveal mutations in patented genes (diagnostic method claims), might be infringed by someone using the whole-genome analysis.[479]

The Board also rejected the opponents' arguments for the negative socio-economic consequences of the patenting of the claimed subject-matter in BRCA gene according to Article 53(a) EPC. The opponents stated that in the present case, genetic patenting has consequences on ethical issues. Patenting of the claimed subject-matter would not only result in increased costs for patients but would also influence the way in which diagnosis and research would be organised in Europe, which would be apparently to the detriment of

476 Decision of the Case T 0080/05 para 59, emphasis added; also see the decision of the Case T 0666/05 para 74-76.

477 Decision of the Case T 0080/05 para 62, emphasis added; also see the decision of the Case T 0666/05 para 77-79.

478 Decision of the Case T 0080/05 para 63.

479 Robert Cook-Deegan and Subhashini Chandrasekharan, 'Patents and Genome-Wide DNA Sequence Analysis: Is It Safe to Go into the Human Genome?' (2014) 42 J Law Med Ethics, 2.

patients and doctors. Opponents argued that the fact that a particular group of patients, i.e. patients suspected to carry a predisposition to breast cancer, would be faced with severe disadvantages and would become dependent on the patent proprietor, which was contrary to human dignity.[480]

The Board rejected this argument. According to the Boards' opinion, the arguments indicated by the opponents are simply related to the exploitation of a patent and not the exploitation of the invention. As "Article 53(a) EPC refers to the "exploitation of the invention", not about the "exploitation of the patent". <...> An objection, which goes to the exploitation of the patent and not to the exploitation of the invention, does not fall within Article 53(a) EPC".[481]

Also, the Board neglected to evaluate socio-economic factors of the case and stated: "that the EPO has not been vested with the task of taking into account the economic effects of the grant of patents in specific areas and restricting the field of patentable subject-matter accordingly". In the Board's opinion the possible consequences of exploitation of the patent identified by opponent are "the result of the exclusionary nature of the rights granted by a patent, that is the right to stop competitors from using the invention". Board found the objection raised being a simple consequence of the inevitable outcome of the exploitation of the patent when the monopoly rights are granted to a patent holder. Logically to the Board, "such an objection applies to the exploitation of any patent, as the nature of the consequences of the exploitation of a patent (which derive from the exclusionary nature of private property rights), are the same for all patents"[482] – to limit the competitors and have monopoly rights.

The decision rejects the possibility, that patent monopoly rights, even if having negative consequences to the society as such, could be a burden to grant a patent. The Board does not wish to be a policy-makers and leaves such questions to be solved at a legislative level. Differently, from the powers granted to the US courts, in Europe, the judicial body is restricting itself to the pure application and interpretation of the existing laws, what is also visible from the current decision.

The EU court did not find Myriad patent being a naturally existing element, a discovery, unlike the courts in the United States. The judicial definition of what is patentable in genetics is therefore different in the United States and Europe. Genetic patent applications nevertheless are submitted to US PTO and patents are granted, but in this regard, the European law seems to be less strict and to allow a broader scope of patentable subject matters. It is possible that

480 Decision of the Case T 0666/05 para 81; Decision of the Case T 1213/05 para 52.
481 Decision of the Case T 1213/05 para 53.
482 Ibid.

the biotech industry will see Europe as a friendlier environment within which to undertake biotech research and – more to the point – to commercialise biotech inventions.[483]

III. Can biobanks patent genes?

The patent owner can be either institution or inventor, who have invented a new patentable object. The dependency of the biological samples stored in the biobanks seems to influence highly the ownership of the invention or discovery. In order to solve the puzzle of who is the owner of intellectual property rights of the genetic invention, it is convenient to clarify the question of the ownership of the genetic materials first. The supposition is that it can be either the source subject (the donor or research participant), the researcher, the authority or company (the biobank), or all of them. Depending, of who owns a sample, the same subject has the ownership of intellectual property rights.

1. The participant's right to samples

Biobanks collect, store and provide the samples and data for the researchers. They are guardians of the information and also takes responsibility for ethical and moral issues and ensures proper use of the samples and data. The question still sometimes occur, if a patient, a person whose samples were taken can claim any rights to the specimen? And whether a researcher may obtain intellectual property rights through observation, isolation and manipulation of the human genetic material, without recognising and admitting contribution of research subjects and patients?

The approach of personal rights reflects the classical assumption of the continental system of law and the common law that the human being is not good which can be subject to private property rights.[484] The prohibition to use human body for a commercial gain is a global concept.[485] European countries, identically to the US, have made illegal any financial uses of human bodies or its parts. A variety of proprietary claims are being made on the human genetic material. Intellectual property claims are also being made concerning the human gene as patenting of isolated and purified human gene is allowed. Due to the commodification of human genome in different ways, patients and research subjects are claiming personal

483 'Myriad Genetics and the BRCA Patents in Europe: The Implications of the US Supreme Court Decision' (2015) 5 UC Irvine L. Rev. 1067.

484 Martín Uranga A and others, 'Outstanding Legal and Ethical Issues on Biobanks. An Overview on the Regulations of Member States of the EuroBioBank Project' (2005) 22 Rev Derecho Genoma Hum 18.

485 Some exceptions, however, exist. One of the few countries that have legalised the sale of organs is Iran. More on that in Rupert WL Major, 'Paying Kidney Donors: Time to Follow Iran?' (2008) 11 McGill Journal of Medicine : MJM 67.

proprietary claims on their genetic material used in research.[486] However, the current trends in property and intellectual property laws are approaching to a point where the donor has no rights over the findings coming from their sample. As far as the sample is removed and separated from the human body, it does not belong to a person but medical or research institution – in our case to a biobank. The regulation of property rights regarding the human samples is similar in the US and Europe. In both legal systems, the donor cannot claim any property rights to his or her sample.

One of the latest cases that dealt with the property rights of human biological samples was the Washington University v Catalona[487] decision (Catalona decision). United States Court of Appeals confirmed that patients do not own their biological samples given to a biobank. The court ruled that donating biological materials to Washington University (the research institution) is equal to the inter vivos gifts. Such donation is a voluntary transfer of property by the owner to another, without any consideration or compensation as an incentive or motive for the transaction.[488] Therefore, the University performing a research is the owner (or more widely used word the "guardian") of the biological samples. After the contribution of tissue, the patients hold no ownership interest, the court ruled that: "<...> research participants did not retain the right to revoke and physically repossess the donated biological materials. Nor did the research participants retain the right to direct or authorise the use, transfer, or destination of the biological materials after their donation."[489]

The Catalona decision was the outcome of the previous decisions in the United States, that dealt with the property rights question of the human biological samples. The landmark decision, which answered this question, was the Supreme Court's of California case Moore v. Regents of the University of California.[490] In the case, the court essentially followed the logic that when cells are removed from a person's body, the disposition of those cells is limited. A person cannot sell the cells, and after the cells are used for research, they must be disposed of according to health department guidelines.[491]

In the case, John Moore underwent the treatment for hairy-cell leukaemia at the Medical Center of the University of California at Los Angeles (UCLA Medical Center). Moore first visited UCLA Medical Center on October 5, 1976, shortly after he learned that he had hairy-cell leukaemia. After hospitalising Moore and "withdrawing extensive amounts of blood, bone

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486 Jasper A Bovenberg, *Property Rights in Blood, Genes and Data: Naturally Yours?* (Brill | Nijhoff 2006) 4.
487 *Washington University v. Catalona, 490 F. 3d 667*. (2007).
488 Ibid. para. 18.
489 Ibid. para. 22.
490 *Moore v. Regents of the University of California, 51 Cal. 3D 120 (1990)*.
491 Robin Feldman, 'Whose Body Is It Anyway? Human Cells and the Strange Effects of Property and Intellectual Property Law' [2011] Stanford Law Review 1382.

marrow aspirate, and other bodily substances," his physician Mr. Golde confirmed that diagnosis.[492] Mr. Golde and other involved persons (defendants in the case) found that "certain blood products and blood components were of great value in a number of commercial and scientific efforts" and that access to Moore's blood contained these substances and that they would provide "competitive, commercial, and scientific advantages."[493] Mr. Golde established a cell line from Moore's T-lymphocytes, and the Regents applied for a patent on the cell line. The patent was issued on March 20, 1984 (U.S. Patent No. 4,438,032). With the Regents' assistance, Golde negotiated agreements for the commercial development of the cell line and products to be derived from it. Under an agreement with Genetics Institute, Golde "became a paid consultant" and "acquired the rights to 75,000 shares of common stock". Genetics Institute also agreed to pay Golde and the Regents at least $330,000 over three years.[494]

In the case, Moore attempted to characterize the invasion of his rights as a conversion – a tort that protects against interference with possessory and ownership interests in personal property. He claimed that he continued to own his cells following their removal from his body, at least for the purpose of directing their use, and that he never consented to their use in potentially lucrative medical research.[495] Moore claimed a proprietary interest in each of the products that any of the defendants might ever create from his cells or the patented cell line.

The court found out that "what Moore is asking is to impose a tort duty on scientists to investigate the consensual pedigree of each human cell sample used in research. To impose such a duty, which would affect medical research of importance to all of society, implicates policy concerns far removed from the traditional, two-party ownership disputes in which the law of conversion arose."[496]The court followed explaining that "Moore clearly did not expect to retain possession of his cells following their removal, to sue for their conversion he must have retained an ownership interest in them. <…> The subject matters of the Regents' patent – the patented cell line and the products derived from it – cannot be Moore's property."[497]

The court continued explaining that "since the laws governing such things as human tissues, transplantable organs, blood, fetuses, pituitary glands, corneal tissue, and dead bodies deal with human biological materials as objects sui generis, regulating their disposition to achieve policy goals rather than abandoning them to the general law of personal property."[498]

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492 Moore v Regents of the University of California, 51 Cal 3D 120 (1990) [125].
493 Ibid para. 126.
494 Ibid.
495 Ibid at 134.
496 Ibid at 135.
497 Ibid at 137.
498 Ibid at 138.

The court explained, that the specialized statutes are regulating the use of human biological samples. Therefore, these specific laws must be applied and not an ordinary property laws when deciding on the disposition of human biological materials.

Court also noted, that in the patent text the protection for production of lymphokines is granted and not for the cells of one particular individual. "Lymphokines <...> have the same molecular structure in every human being and the same, important functions in every human being's immune system."[499] - explains the judge. Lymphokines are not unique to Moore. The patented cell line was both factually and legally distinct from the cells taken from Moore's body. Therefore, Moore could not claim any rights coming form the patent.[500]

In deciding whether to create new tort duties, as asked by Moore, the court considered the impact that such expanded liability would have on activities important to society. It highlighted the vital policy consideration – scientists engagement in socially useful activities, new products' developments and performing research. The decision highlighted the need to ensure that research is not hampered by any property rights on the samples and the possibility to analyse the samples and make scientific discoveries is not restricted. Court ruled that, "since inventions containing human tissues and cells may be patented and licensed for commercial use, companies are unlikely to invest heavily in developing, manufacturing, or marketing a product when uncertainty about clear title of the samples exists."[501]

This decision shows the importance to reach an appropriate balance of the policy considerations ensuring scientists engagement in socially useful activities and performing research. The court recognized that "uncertainty about how courts will resolve disputes between specimen sources and specimen users could be detrimental to both academic researchers and the infant biotechnology industry, particularly when the rights are asserted long after the specimen was obtained."[502] Therefore, the court concluded that Moore has no property rights over his samples and also, no rights to claim any financial or moral benefits from the patent granted to the University. The fiduciary-duty and informed-consent theories were found sufficient to protect patients directly, and, according to the court, no additional protection was needed. Especially such protection that could "punish innocent parties or create disincentives to the conduct of socially beneficial research."[503]

499 Ibid at 139.
500 Ibid at 141.
501 Ibid at 144.
502 Ibid at 145.
503 Ibid.

The same conclusion, regarding the property rights of the sample, has been reached in another US case Greenberg v. Miami Children's Hospital (Canavan Disease Case).[504] In this case, in order to develop tests to determine carriers of the disease, Greenberg (the plaintiff) approached Dr. Matalon (the defendant), a research physician, to discover the gene sequence of Canavan disease. He convinced Canavan families worldwide to donate tissue, blood and financial support to Matalon's project. Later, Matalon filed a patent application for the genetic sequence he identified, but he had never informed Greenberg nor the Canavan families about his intentions to seek patent protection.[505]

Greenberg alleges his arguments that in his belief, any carrier and prenatal testing developed in connection with the research for which the samples and funding were given, would be affordable and accessible to everyone and would remain in the public domain. His wish was that the research would promote the discovery of more effective treatments and, to effectuate a cure for Canavan disease.[506] The court, however, dismissed the conversion claim by denying any property interest for the body tissue and genetic information was treated as voluntarily given. The body tissue and genetic samples were donations to research without any contemporaneous expectations of return.[507]

The discussion in the above mentioned US cases are based on the principle of non-commercialization and the prohibition of the use of the human body for profit.[508] The state is protecting that human body or its parts, including blood, would never become the goods of commerce. Decisions also express serious concerns about interfering with advancements in medical science, if property rights would be granted to the individuals. Therefore, the mentioned rulings highlight that a person who provided the samples to a medical institution has no property rights, including no intellectual property rights arising from research that used such sample. Although researchers can achieve claiming intellectual property rights related to those cells, the person who contributed the cells can achieve no such rights under his or her association with the cells.[509] The rights of the donor are restricted only in the concepts of the

504 *Greenberg v Miami Children's Hospital, 2003 WL 21246347 (SD Fla May 29, 2003); 264 F Supp 2d 1064 (SD Fla 2003)*.

505 Singh 204.

506 Greenberg v. Miami Children's Hospital, 2003 WL 21246347 (S.D. Fla. May 29, 2003); 264 F. Supp. 2d 1064 (S.D. Fla. 2003).

507 Singh 205.

508 Important international documents reaffirm that the human body and its parts, including blood, should not give rise to financial gain; particularly the United Nations Educational, Scientific and Cultural Organization (UNESCO) Universal Declaration on the Human Genome and Human Rights. Nov 11, 1997; UNESCO International Declaration on Human Genetic Data (2003); and UNESCO Universal Declaration on Bioethics and Human Rights. Paris, France (2005). For example, Article 4 of the *Universal Declaration on the Human Genome and Human Rights* states that "the human genome in its natural state shall not give rise to financial gains."

509 Robin Feldman, 'Whose Body Is It Anyway? Human Cells and the Strange Effects of Property and Intellectual Property Law' [2011] Stanford Law Review Robin Feldman, 'Whose Body Is It Anyway? Human Cells and the Strange Effects of Property and Intellectual Property Law' [2011] Stanford Law

fiduciary duty that a doctor owes to a patient and are commonly centred on the doctor's obligation to obtain informed consent. The analysis of cases above concludes that humans do not have any particular rights to their cells or to the information contained in their cells, outside of their relationship with health care providers[510].

In Europe, the Convention on Human Rights and Biomedicine (Oviedo Convention)[511] regulates the questions of use of human biological materials. The Convention is the first legally-binding international instrument intended to preserve human dignity, rights and freedoms, within a series of basic principles and main prohibitions against the misuse of biological and medical approaches. It is signed and ratified by a majority of European countries, such as Spain, Italy, France and others[512]. Article 21 of the Convention declares that: "The human body and its parts shall not, as such, give rise to financial gain". Article 22 continues, that "when in the course of intervention any part of a human body is removed, it may be stored and used for a purpose other than that for which it was removed, only if this is done in conformity with appropriate information and consent procedures". Article 22 requires performing information and consent procedures when using human body part.

The interpretation of those articles can be double – first explanation can be that the individual has no right of property over his or her body or parts; another interpretation can be that the individual does have a right of property, but does not have a right to exploit his or her body for financial gain[513].

Macilotti raises the hypothesis of "occupation" doctrine, according to which tissue removed from the human body would, once separated, be comparable to the legal concept of *res nullius*, or goods that are the property of no one. Macilotti explains, that "according to this theory, it is presumed that tissue is abandoned at the time of its removal with the consequence that whoever possesses it becomes their owner. In this case <...> other subjects (e.g. the surgeon, the hospital, the biobank, etc.) could be considered the owner, and, as a consequence, the individual is not able to transfer property rights over tissue through the expression of their informed consent"[514].

The lack of European Union regulations regarding the collection and use of human biological samples for the research purposes is a burden to answer more clearly the sample's

Review 1379.

510 Singh 213.

511 Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine 1997. Entered into force on 1 December 1999. European Treaty Series No. 164, Oviedo, 4.IV.1997

512 However, the instrument was not signed by Germany and the United Kingdom.

513 Carlo Petrini, 'Is My Blood Mine? Some Comments on the Convention on Human Rights and Biomedicine' (2013) 11 Blood Transfusion 321.

514 M. Macilotti, *Informed Consent and Research Biobanks: A Challenge in Three Dimensions,* in Matteo Pascuzzi, Giovanni; Izzo, Umberto; Macilotti, *Comparative Issues in the Governance of Research Biobanks* (Springer-Verlag Berlin Heidelberg 2013), 151.

belongingness question. The Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells[515] explicitly excludes researches using human tissues and cells, such as when used for purposes other than an application to the human body, e.g. *in vitro* research or animal models, from its scope of regulation. However, as an analogy, Article 12 of the above mentioned directive can be indicated. Article 12 prohibits paid donations of tissues and cells. According to the article, "Donors may receive compensation, which is strictly limited to making good the expenses and inconveniences related to the donation." Again, seeking to prevent any possibilities of human trafficking or selling parts of human bodies, the legal instrument implicitly prohibits any economic gain from a donation.

The legislation, stating that donors do not retain property rights of their samples, have also been applied in the national laws. For example Article 45 of the Spanish Law 14/2007 on Biomedical Research[516] guarantees that all the processes of donation, use, assignment, storage of the biological samples, must be devoid of any profitable purpose. The article continues that all the personal genetic information cannot be used for commercial purposes. The Spanish legislation determines the subject's loss of ownership and that the institution storing the sample has the rights on the sample, subject to the purpose or purposes of the donation.[517]

Estonian Human Genes Research Act implicitly states that right of ownership of a tissue sample belongs to a biobank and that tissue samples and uncoded information in the ownership of the biobank and written consent of gene donors are not transferable. Upon termination of activity of the chief processor, the right of ownership of tissue samples and data, as well as written consents of gene donors, is transferred to the Republic of Estonia.[518] Finnish biobank law also states that a "biobank owns the samples in its possession, unless otherwise stipulated in an agreement on the transfer of samples."[519]

In the material transfer agreement form, the UK Biobank also include the rule, that "the UK Biobank is the owner of the property in the samples and that with the material transfer agreement the UK Biobank grants the applicant a limited, revocable, worldwide, royalty-free, non-exclusive licence (but not any ownership rights) to use the samples for the permitted purpose only."[520]

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515 Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells. OJ L 102, 7.4.2004, p. 48–58.

516 Ley 14/2007, de 3 de julio, de Investigación biomédica 2007 (BOE nú m) 28826.

517 Martín Uranga and others 51.

518 Human Genes Research Act 2000 (Riigi Teataja I) 1. RT I 2000, 104, 685, Article 15.

519 Finland Biobank Law 688/2012 2012. Article 7.

520 UK Biobank, 'Annex II: Material Transfer Agreement for Data And/or Samples' <http://www.ukbiobank.ac.uk/wp-content/uploads/2012/09/Material-Transfer-Agreement.pdf> accessed 8 May 2018.

There are other perspectives, however. The biobank laws if Island does not grant ownership rights to a biobank. A biobank is not deemed to be the owner of health information materials but has right of disposal over them. A biobank may thus not pass the health information materials to another party.[521] However, the act is mute about the question if the ownership of the samples remains to the donor.

The interpretation of regional EU instrument, as well as the national laws of the European states, can lead to the same readings of law as the one expressed in the US court's decisions. Individuals have no right of property to his or her body or body parts, or even if they do, they have no right to exploit the body or its parts for a financial gain. Moreover, the concerns are being made that conferring property rights to individuals in their body cells may endanger the basic concept of human dignity. It could encourage the commercialisation of human body and could also erode the reverence of human life that gives ground to legal doctrines, particularly, those that forbid ownership of human beings in the form of slavery. Treating human cells as property could give rise to a situation where those in financial need will be coerced into selling human tissues, for example, because of the circumstances of their poverty, raising serious concerns regarding health.[522]

The conclusion is that when IPR arise from the use of individual's cells, he or she is not able to claim any economic rights according to the valid laws in Europe or precedents in the United States. Hardly imaginable that sample donor (or a specifically defined group) could be included in the list of inventors, or applicants when the patent application is filed. As donors have not performed any experimentation or made any inventive steps, they are not competent to claim patent rights. Very likely, donors to not understand the technical features and the technical problem solved by the invention. Research participants do not contribute directly to the disclosure of the invention, even if their body cell has been used as a material for a study. The donor of the sample does not take part in the inventive step, and consequently, he or she would not have the right to be a part of the patent resulting from the sample.[523]

Nevertheless, the perspectives of the ownership of a sample should not be confused with the doctrine of the informed concept. These are two different concepts and have different rules and requirements when and how they are applied. While the donors have the right to know about the use of their samples (informed consent doctrine), they do not possess property rights to their sample, including claiming ownership of any intellectual property rights nor the right to gain any financial benefits from the donation (ownership concept). As the informed consent doctrine is based on the individual data protection laws and the protection of personal data

521 Iceland Biobanks and Health Databanks Act No. 110/2000, as amended by Act No. 27/2008, No. 48/2009 and No. 45/2014. Article 10.
522 Singh 212.
523 Martín Uranga and others 63.

and private information, the prohibition to receive any financial benefits from the donation is based on the reasoning that human body should never be a direct object of commerce. This principle known as *res extracomercium* is based on the concept that the human being is an aim on itself and not a mean, and this has been translated into the law of most countries prohibiting payments in exchange of tissue donations.[524] These two perspectives – informed consent and ownership concept – even if related to the same biological sample, are totally different and the lack of consent would not be a cause to invalidate the patent. Even if it is advisable to inform the research participants about patenting possibilities, the consent form is required for the scientific research use, but not as a patenting requirement. That is to say; no patent office is requesting the informed consent forms when the patent application forms are filed or application examined. Neither the European nor the national laws wanted to do of the consent a requirement to patentability, but a simple instrument to impose explicitly the practice of the free and informed consent. The revenues from intellectual property rights and economic advantage are following indirectly from the use of the sample.[525] Such advantages as economic gain, the economic benefits that can arise from the intellectual property rights are not considering the prohibited use of the human body for the economic gain, as it is not the sample *directly* that gives economic revenues, instead, the research outcomes from such use.

2. Biobank's and researcher's intellectual rights

Biobanks usually are responsible for storing the information and providing it to outside researchers. Academics proposes three phases in the establishment of a biobank: the creation phase – when the biobank is established; the collection phase – when the samples and data are collected and stored; the access phase – when the tissues and data are provided to the research community.[526] Most important part, of course, is the last part – the access phase. This is the phase where most intellectual property rights are created, and so, most patent applications are submitted.

Here is also quite important to remember different types of biobanks: public (including universities' biobanks) and private, and the different goals such biobanks have in performing their functions. Biobanks can supply its resources to academic researchers, where commercial interests are not primary focus; to academic and industrial cooperative researchers, where commercially usable results are important; or to industrial researchers, where primary focus is

524 Amelia Martín Uranga and others, 'Outstanding Legal and Ethical Issues on Biobanks. An Overview of the Regulations of the Member States of the EuroBioBank Project' (2005) 22 Rev Derecho Genoma Hum. 53.

525 Christian Lenk and others, *Human Tissue Research: A European Perspective on the Ethical and Legal Challenges* (Oxford University Press 2011) 124.

526 Saminda Pathmasiri and others, 'Intellectual Property Rights in Publicly Funded Biobanks : Much Ado about Nothing ?' (2011) 29 Nature Publishing Group 319.

on commercially quick marketable results.[527] So public biobanks, working under the provisions and regulations of the state are less likely to engage in patenting of research results, differently from the private biobanks that has mainly financial objectives. Some authors argue, that under particular circumstances public biobanks can still claim some rights in IPR arising from research, as they have invested a great deal of time and energy to collect, treat and store the data and samples that gave rise to the IPRs in question.[528] Certain biobanks indeed can consider taking part in downstream IPRs as one source of income, but only if invention occurred directly in biobank's premises or was invented by biobank's personnel. The public biobanks are not restricted from gaining certain level of financial return by applying for patent rights. However, as mentioned in the first Chapter of this thesis, for their services biobanks usually already charge some fees. So even if generally, custodianship, ownership or stewardship of the samples as data remains with the biobank,[529] when the samples or information is purchased by the third party, very unlikely the biobank could claim any intellectual property rights from new discoveries. Understandably, if the sample (a drop of blood or saliva) as such have no intellectual property rights, and a researcher (not bound by employment relationships) orders such samples for his particular project paying appropriate fees, the biobank should not assert any ownership for the discoveries that an individual researcher makes.

First of all, if there is no legal bond between the biobank and the research institution or researcher, there hardly is any laws that would allow a biobank to claim any ownership for the invention.[530] Of cause, it is possible to reach a contractual obligation, that a biobank is also one of the patent applicants. However, such contracts would limit the use of the biobanks, as very unlikely a commercial entity would be willing to enter into such agreement. It would also create a stronger competition between the biobanks, opposite to the beneficial cooperation, that is expected from biorepositories. If such rules apply, biobanks would be in a global contest, of who can offer better policies for the researchers.

This research found no biobank that would claim ownership in its general rules or material transfer agreements to the patent belonging to another entity, even if the information that generated patentable invention was provided by a biobank. In its material transfer agreement form, the UK Biobank states that it will have no rights or licence to the Intellectual Property Rights in relation to any inventions or findings developed by the applicant as a result

527 From the informational slides Medical University Graz, 'Biobank of Medical University Graz' <http://www.meduni07.edis.at/files/sargsyan_mug_biobank.pdf> accessed 8 May 2018.

528 Saminda Pathmasiri and others 320.

529 Ariane Mallette and Anne Marie Tassé, 'P3G Model Framework for Biobank Access Policy: Core Elements' 1.

530 Differently would be if the inventor and the biobank would be bond by employment relationship. Then, in many jurisdictions, the biobank would be the applicant and holder of the patent.

of using the materials.[531] Public biobanks, to my knowledge, usually are not willing to be involved in patenting. As the very purpose of a biobank is the dissemination of knowledge and information, and not to monopolise the research outcomes.

UK biobank implicitly states that "is not expected in itself to lead to patentable inventions that return significant income either to researchers or UK Biobank, but it is expected to become a valuable shared resource for research".[532] However, if so would happen, the UK Biobank also secures that any income received from access fees or intellectual property will be reinvested in the resource.[533]

On the other hand, biobanks do not restrict patenting of the research outcomes by other institutions and informs about a chance that research conducted using the biobank's resource (which might be conducted by researchers in the public or commercial sector, as well as the academic and charity sector) can subsequently support the development of an invention that returns profit. Commercial companies and other research endeavours that stand to make a profit are allowed access to UK Biobank if their proposal falls within the UK Biobank purpose and complies with the usual scientific and ethics requirements.[534]

It would not be a bad policy consideration for a biobank to restrict patenting in any soft or obligatory means. If state legislation allows patenting of genetic materials or gene sequences, biobanks cannot go against such legislation in its internal rules and regulations. It can be only a benevolent action of a biobank to give the information freely to researchers and not to occupy and monopolise it by any legal ways.

Even if biobanks hardly can claim any rights arising from the research they provided samples to, the biobanks entirely other require returning remaining samples, which have not been utilised. The da Vinci European BioBank[535] requests the recipient of the samples to destroy any surplus biological sample not used in the research or to send it back to the biobank.[536] UK biobank asks to destroy or return forthwith any remaining samples.[537] This return can be justified by the lack of tissues and the need to use them as broadly as possible. So it is different from the position that biobanks can claim intellectual rights from legally independent institutions – such statement seem not to have a firm ground.

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531 Rule 3.7 of the UK Biobank's Material Transfer Agreement for data and/or samples form.

532 UK Biobank Ethics and Governance Framework 2007 1. Part III.C.2. 'Intellectual Property'.

533 Ibid.

534 Ibid.

535 Based in Italy, the da Vinci European BioBank collects, stores, processes and distributes biospecimens and the associated data.

536 From the da Vinci European BioBank Sample Request Form rule, more information at <https://www.davincieuropeanbiobank.org/> and <http://www.scienzedellavita.it/?q=servizi&language=en> accessed 8 May 2018.

537 Rule 13.1.3. of of the UK Biobank's Material Transfer Agreement for data and/or samples form of 20th August 2012.

However, the situation changes, if the biobank itself or its employees perform research and invents something new. Biobanks are not only the holders and guardians of samples and data. They also conduct primary research or collection sites.[538] Especially private biobanks, or biobanks created next to universities, where researchers work within the premises of the biobank, can easily claim ownership of their inventions. Oppositely from the public biobanks, generation of income is one of the primary purposes of private biobanks or private genetic studies. Private biobanks do not refrain from patenting and do not wish to share their information freely. 23andMe, Inc.[539] is a private company that collects data and samples from people and uses this data in a variety of genetic studies with company's internal research teams or with one of many company's collaborators at research universities or pharmaceutical companies. The company has several patent applications and patents worldwide, one patent[540] is for the invention that provides human polymorphisms that are associated with Parkinson's disease. The invention also discloses the compositions and methods for use in diagnostics, prognostics, prevention, treatment and study of Parkinson's disease.

Examples of other biobanks conducting research themselves include disease-focused biobanks such as the Multiple Myeloma Research Foundation[541] and ongoing cohort studies such as the Framingham Heart Study.[542] The Institute of Human Genetics of the Technical University Munich today performs at least four distinct studies: a study on mitochondrial disorders, research on next-generation sequencing, research on functional genomics of mitochondrial, SNP genotyping project.[543] IPRs are also developed as a result of research projects that access the materials contained in biobanks.[544]

Patenting by universities' biobanks can be quite a common reality. Supported by the Bayh-Dole Act, the universities have become productive sources of gene patents, and have gained vast sums from licensing these patents to the biotechnology industry.[545] The biotechnology industry itself and its market value today is secured more by granted genetic patents rather than actual commercial products. This reality has also contributed to the flood of gene patent applications. In Europe, public research organisations are also encouraged to take a pro-active role in the innovation process by managing IPR arising from research

538 Table one information from Susan M Wolf and others, *Managing Incidental Findings and Research Results in Genomic Research Involving Biobanks & Archived Datasets*, vol 14 (Genet Med 2012).

539 23andMe, 'Research' <https://www.23andme.com/en-int/research/> accessed 8 May 2018.

540 'US8187811(B2) "POLYMORPHISMS ASSOCIATED WITH PARKINSON'S DISEASE"'.

541 Multiple Myeloma Research Foundation, 'Posts' <https://themmrf.org/research-partners/mmrf-data-bank/> accessed 8 May 2018.

542 Susan M Wolf and others, p. 6; also the Framingham Heart Study <https://www.framinghamheartstudy.org/> accessed 2018 May 8.

543 'Helmholtz Zentrum München Institute of Human Genetics' <https://www.helmholtz-muenchen.de/ihg/research/groups/index.html> accessed 8 May 2018.

544 Pathmasiri and others 320.

545 Andrew W Torrance, 'Gene Concepts, Gene Talk, and Gene Patents' (2010) 11 Minnesota Journal of Law, Science & Technology 161.

results.[546] For quite a while, European universities are applying for patents and successfully licensing the invented technologies.[547]

If patented by university's biobank, patent rights most likely would belong to the university. Most universities consider all data and specimens collected by an investigator with a formal connection with that university to be owned by the university. Such ownership rights are often written in the institutional technology transfer offices and patent policies.[548]

In the already mentioned case Washington University v Catalona, the Univerity worker Dr. Catalona, moved to another university and sought to take with him cancer research tissues from his former employer's Washington University's biorepository. In the case the court stated that biological samples, donated to the University belong to the university and not to the university's worker, Dr. Catalona.[549] In the court's decision is indicated that:

> "Dr. Catalona's privileges to and treatment of biological samples while at Washington University comports with the terms of Washington University's Intellectual Property Policy, which provides all intellectual property (including ... tangible research property) shall be *owned by the University* if significant University resources were used or if it is created pursuant to a research project funded through corporate, federal or other external sponsors administered by the University." (emphasis original).

Other factors, such as material transfer agreements and research agreements acknowledged the university's sole ownership of the biological samples, concluding that the university's employee could not claim any IP rights coming from the research of collected samples. The university also provided the majority of the funding for the maintenance and operation of the repository, and the remainder of the funding came from public and private grants to the university, that only confirmed the university's ownership of IPR.[550]

There is a wide divergence of statutory legal regimes governing ownership of inventions across Europe. However, when we talk about the service inventions, the invention was made as a function covered under the employment agreement, countries assign the service inventions to the employer. Several countries include the right to fair compensation to the employee inventor.[551] Most of the European countries' regulations are imposing a legal obligation on the inventors, bound by the employment relationships, to disclose inventions to

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546 European Commission, 'Working Paper "Management of Intellectual Property in Publicly-Funded Research Organisations: Towards European Guidelines"' (2004).

547 European Commission's Expert Group on Knowledge Transfer Metrics, 'Metrics for Knowledge Transfer from Public Research Organisations in Europe' (2009).

548 Elena L Grigorenko and Susan Bouregy, 'Biobanking on a Small Scale: Practical Considerations of Establishing a Single-Researcher Biobank' [2009] Stanford Journal of Law, Science & Policy, p. 42.

549 *Washington University v Catalona, 490 F 3d 667 [23]*.

550 Id. para. 3.

551 European Commission, 'Working Paper "Management of Intellectual Property in Publicly-Funded Research Organisations: Towards European Guidelines"' (2004), 15.

the public research organisation in order to secure the possibility of protection and development. In practice, this is merely preventing the inventors from filing a patent application on their own or to exploiting inventions to their own personal benefit without first offering the public research organisation to exploit them for the benefit of the public.[552]

The ownership of the inventions found in the biobanks, therefore, depends on the relationship between an inventor and a biobank. If an inventor is a researcher or a worker in the biobank, the IPR arising from the research will belong to a biobank. However, if a researcher is working autonomous, or is from another institution, merely providing the samples or relevant data, will give no rights for biobanks to claim any ownership to a newly created IPR.

IV. The influence of gene patenting to innovation

1. Hamper of future research

Internationally, gene patents are granted, and this trend seems to stay for the upcoming years. There are two different views: some authors that argue that patents do restrict innovation and that: "...there is no empirical evidence that [patents] serve to increase innovation...",[553] while others argue that "...the weight of the evidence supports the claim of a positive causal relationship between the strength of patent rights and innovation"[554] and that "reward [must be given to] inventors who provide access to molecules that were previously giving no benefit."[555] I believe that that patent protection cannot be unlimited and that when we talk about gene patenting very clear lines must be drawn between the patentable claims and discoveries, and information that must be free to use for anyone.

The negative consequences of gene patenting have been pointed out by academia or non-governmental organizations. Can be highlighted such drawbacks as: 1) changing the overall concept of a genetic research, 2) too broad patent protection, 3) the possibility to patent essential genetic information, 4) the impossibility to go around the patented gene, 5) the problem of patent thicket, and 6) as the final outcome, the restriction of access to the better health care.

552 Ibid.
553 Boldrin M and Levine DK, 'The Case Against Patents' (2013) 27 Journal of Economic Perspectives 1.
554 Stephen Haber, 'Patents and the Wealth of Nations' (2016) 23 George Mason Law Review 814.
555 Dan L Burk, 'Anticipating Patentable Subject Matter' (2013) 65 Stanford Law Review 109.

1.1. Changing the overall concept of genetic research

The patenting of a gene is essential not only to a patent system but to the science and society as well. Professor Torrance notes that inaccurately simplified and predictable gene concept accepted by the patent system might even influence gene concepts in science. The "patent gene concept", as named by the Torrance, might influence biologists to describe, and even think about, genes in a manner consistent with patent availability.[556] The possibilities of patenting genetic findings and gaining financial benefits from it are taken into account by biologists, especially those involved in medical research. Torrance explains, that "although there may be other rewards for pursuing biology, such as Mertonian norms of free enquiry and free exchange of ideas, prestige, intellectual challenge, and a sense of importance to society, the possibility of winning the patent-lottery by patenting a lucrative gene may be a significant incentive not to undermine the patentability of genes, even at the expense of debate within the biology community."[557]

Gene patenting might change the overall perception of the scientific community about the need to perform genetic research, need to share the findings with colleagues and the promotion of the developments in the genetic testing and the gene used in general. Not only the commercial entities, that depend on patenting but also scientists may thus possess an incentive to patent and protect their inventions. Instead of promoting debate about competing researchers and findings, universities might follow the lead of patenting the inventions and commercialising them for profit. In short, the "patent gene concept" may also influence how biologists portray and conceive of genes, encouraging them, for example, to emphasise the certainty of knowledge about the gene over the uncertainty.[558] The run might start between the scientists and research institutions, who will have more patents on the genes, and the sharing of information might be broadly discouraged.

1.2. Broad patent monopoly

The principal objective of IP law and, in particular, the patent law, is to offer protection to the inventor against free riding and to encourage the development and disclosure of knowledge and innovation with a goal to promote scientific, in our case especially medical, and social progress in the interest of society at large.[559] The monopoly rights granted to one person should always be balanced with the society's needs and should not impair the most

556 Torrance AW (2010) 187.
557 Ibid.
558 Ibid.
559 Geertrui van Overwalle and Esther van Zimmeren, 'Functions and Limits of Patent Law', in Claes E, Devroe W, Keirsbilck B, *Facing the Limits of the Law* (Springer Science & Business Media 2009) 421.

critical human rights, such as the right to health care.[560] The patent law should not only grant a right providing patent protection to the private inventor as an incentive to innovate, but should also guarantee fundamental rights, adopt measures necessary to protect public health and safeguard the freedom to do research more widely. The TRIPS agreement clearly states its main objectives, that is "the protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations" (Article 7). However, in gene patenting case, the balance of rights between the inventors and the users seems to be distorted. Does current patenting rules in genetics fulfil the primary objectives of patent law?

Public and nonprofit sector researchers generally favour DNA sequence patents only when the utility and non-obviousness standards are satisfied. The problem of gene patenting is that excessively modest interpretation of these criteria hampers the biological research and international scientific collaboration. Not really strict and clear patenting requirements permits patent holders with only a vague notion of a sequence's function to claim broad intellectual rights protection. And the international biotech firms, having the interest to generate their patent portfolios, assert that broad patent protection is necessary to stimulate costly biotech research and development.[561]

The European Society of Human Genetics (ESHG) in its recommendations pointed out, that patents on disease-related genes typically not only include claims on the nucleic acid sequence, but also on the protein and on the antibodies that can subsequently be generated, and on the animal models, even if they (still) have to be developed.[562]

The question has been already raised whether patents on gene sequences (DNA sequences) should be allowed according to the classical model of patent claim, whereby a first inventor can claim an invention which covers possible future uses of that sequence, or whether the patent should be restricted so that only the specific use disclosed in the patent application can be claimed ("purpose-bound protection").

The Report from the Commission to the Council and the European Parliament on the development and implications of patent law in the field of biotechnology and genetic

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560 The Preamble of WHO Constitution (1946) enshrines "…the highest attainable standard of health as a fundamental right of every human being."

561 DM Gitter, 'International Conflicts over Patenting Human DNA Sequences in the United States and the European Union: An Argument for Compulsory Licensing and a Fair-Use Exemption.' (2001) 76 New York University law review 1679.

562 The ESHG Working Party on Patenting and Licensing, 'Patenting and Licensing in Genetic Testing: Recommendations of the European Society of Human Genetics' [2007] European Journal Of Human Genetics 4.

engineering[563] (Second Report), did not take any position on this question. In the Second Report the Commission concluded, that "as a specific field of technology becomes mature, the application of the normal patent criteria of novelty, inventive step and industrial applicability means that future patents are necessarily limited in scope because the invention claimed has to be distinguished from the vast array of what is already known in the field. <…> It may be questionable whether attempting to further refine the scope of protection of gene sequence patents in the light of divergences between national legislations will have any significant effect on actors in the field.

Against this background, the Commission does not at present intend to take a position on the validity of transposition according to the choice between classical and limited scope of protection for gene sequences."[564]

The representatives of public organizations express doubts if patenting of genes is the best way to go. In 1999, the director of the National Institutes of Health Harold Varmus, and Francis Collins, director of the Human Genome Project, wrote a letter to the US PTO Commissioner expressing the concerns about "PTO's apparent willingness" to grant patent claims based on "theoretical" functions of the gene. The letter argued that while databases may help researchers develop hypotheses about a gene's function, these databases do not provide quality proof of such function, much less give researchers new ideas for pharmaceutical products.[565] Two prominent leaders of research organisations urged the German science ministry's secretary of state for research, to interpret the EPC and the Biotechnology Directive so as to preclude patents that cover all possible applications of a particular gene sequence. The leaders insisted that patents should be restricted only to the identified functions of a gene, otherwise the patent owner on a gene sequence could block the commercialisation of any newly discovered function of this sequence.[566]

The European Parliament in the resolution on patents for biotechnological inventions[567] (the Resolution) also raises concerns that over-generous granting of patents can stifle innovation. In the Resolution the European Parliament calls on the European Patent Office and the Member States to grant patents on human DNA only in connection with an established and exact application and for the scope of the patent to be limited to only this application so that other users can use the same DNA sequence for other applications (proposal for a "purpose-bound protection")(Article 5 of the Resolution). The European Parliament also

563 Report from the Commission to the Council and the European Parliament - Development and implications of patent law in the field of biotechnology and genetic engineering (COM(2005) 312 final). Text adopted on 14 July 2005.

564 Ibid. section 2.1.

565 Gitter (2001) 1669.

566 Gitter (2001) 1670.

567 European Parliament Resolution on Patents for Biotechnological Inventions (2005). Texts adopted on 26 October 2005, No. P6_TA(2005)0407.

highlighted that germ cells are not patentable as part of the human body and they are certainly not an invention (Article 9 of the Resolution).[568]

The proposal shows the initiative to limit the broad interpretation and prevent broad monopoly rights to the genetic inventions. Sadly, the direct interpretation of the Directive does not show intentions for such limitations. The combined effect of the Biotechnology Directive and EPO law and case law is to allow for product claims covering sequences or partial sequences of a gene when produced by a technical process and so long as an industrial application is provided.[569] The intention of the Biotechnology Directive was apparently not to have only use or application claims.

1.3. Patenting essential genetic information

In genetic research, the high obstacle for the innovation and research is the patenting of the upstream genetic information. Such basic genetic research tools as gene fragments expressed sequence tags (ESTs), single nucleotide polymers (SNPs), today can be protected by patent law or other IP rights. It is argued that patenting of such upstream discoveries would potentially block downstream research, which in turn blocks the development and access of new treatments.[570] Current patenting and commercialisation process in the field of human genetics have made it more difficult for academic researchers to access and build upon scientific discoveries, and to openly disseminate their research results. These research tools have no immediate therapeutic or diagnostic value but have a great value in conducting research.[571]

More and more authors[572] argue, that granted patents now restrict access to technology, hamper future research and that patent law grants excessive monopoly rights to the patent holder. In some cases, patent law can have the paradoxical effect of blocking further research and development, and access to health care service. Michael A. Heller and Rebecca S. Eisenberg write about the unintended consequence of biomedical privatisation: "a proliferation of intellectual property rights upstream may be stifling life-saving innovations

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568 In the Resolution the European Parliaments mentions patent EP1257168 (title of invention: 'Method of cryopreserving selected sperm cells') as constituting an infringement of the Biotechnology Directive and asks the Commission to file a notice of opposition to patent EP1257168 without delay. This patent was revoked by the Boards of Appeal of the European Patent Office case T 1199/08 on 03 May 2012.

569 Jessica C Lai, 'Myriad Genetics and the BRCA Patents in Europe: The Implications of the US Supreme Court Decision' (2015) 5 UC Irvine L. Rev. 1053.

570 ibid.

571 Kshitij Kumar Singh, *Biotechnology and Intellectual Property Rights. Legal and Social Implications*, vol 1 (Springer India 2015) 143.

572 See for example Michele Boldrin and David K Levine, 'The Case Against Patents' (2013) 27 Journal of Economic Perspectives 3; James Boyle, 'Enclosing the Genome: What the Squabbles over Genetic Patents Could Teach Us' (2003a) 50 Advances in Genetics 97; Heller MA and Eisenberg RS, 'Can Patents Deter Innovation? The Anticommons in Biomedical Research.' (1998) 280 Science (New York, N.Y.).

further downstream in the course of research and product development.[573] It is because "[e]ach upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation."[574] Nuffield Council took the view that "the exercise of a monopoly over what are now essentially discoveries of genetic information accessible by routine methods is, in principle, highly undesirable."[575] It opined that "in general, the granting of patents which assert rights over DNA sequences as research tools should be discouraged and the best way to discourage the award of such patents is by a stringent application of the criteria for patenting, particularly that of utility."[576]

1.4. Impossibility to invent around the patented gene

One of the greatest fears is that gene patents could inhibit scientific progress, as researchers might be unwilling to perform new tests on already patented genes. Making genes in the laboratory is essential for many kinds of research, and restrictions on the use of patented genes would be challenging to work around. Differently from other fields, such as electronics or mechanics, patents in the genetic sector are usually impossible to go around, to invent similar "technology". There is a finite number of genes, and therefore a limited number of tools, including platform technologies, for researchers to employ in gene-based research.[577] A gene is defined as a stretch of deoxyribonucleic acid (DNA), which itself is a sequence comprised of four nucleotide bases - adenine (A), cytosine (C), guanine (G), and thymine (T). Sequencing the genome refers to the process of determining the exact order of these nucleotide bases in the entire set of hereditary information for a given organism.[578] Adenine always binds to thymine, while cytosine and guanine always bind to one another. This relationship is called complementary base pairing. These complementary bases are bonded together via hydrogen bonds, which can be easily broken apart when the DNA needs to unzip and duplicate itself.[579] Gene nucleotide bases cannot be connected anyhow, otherwise, even if connected, it will not transfer information to the cell and will not perform any function, it will not encode the genetic instructions used in the development and functioning of living organisms. Moreover, the lack of substitutes for certain biomedical discoveries (such as

573 Heller and Eisenberg 698.
574 Ibid. 699.
575 Nuffield Council of Bioethics, 'The Ethics of Patenting DNA' (2002). Para. 5.41.
576 Ibid.
577 WHO Human Genetics Programme, 'Genetics, Genomics and the Patenting of DNA: Review of Potential Implications for Health in Developing Countries' 40.
578 Heidi L Williams, 'Intellectual Property Rights and Innovation: Evidence from the Human Genome' [2010] NBER working paper series 3.
579 Genetics Generation, 'Nucleotides and Bases' <http://knowgenetics.org/nucleotides-and-bases/> accessed 8 May 2018.

patented genes or receptors) may increase the leverage of some patent holders, thereby aggravating holdout problems[580]. ESHG separates the patenting of novel technical tools for genetic testing (eg. PCR or chip technologies), as they can promote investment and still allow for invention around them, and DNA (RNA, cDNA) sequences, that is not possible invent around.[581]

The empirical research was done by Heidi L. Williams[582] provided evidence that even very short forms of intellectual property – lasting only one year – can have persistent effects on subsequent innovation[583]. The empirical research used data on the sequencing of the human genome by the public Human Genome Project and the private firm Celera. Genes originally sequenced by Celera were protected with IPR for about two years, but was released into the public domain once re-sequenced by the public initiatives. Across a range of empirical specifications, the evidence was found that Celera's IP led to reductions of 20 to 30 percent in subsequent scientific research and product development. If Celera genes had counterfactually had the same rate of subsequent innovation as non-Celera genes, there would have been 1,400 additional publications between 2001 and 2009, and 40 additional diagnostic tests as of 2009[584]. Furthermore, this study also find out that there was a clear possibility that Celera's scientists might have targeted their sequencing efforts based on a gene's *ex-ante* known location on the genome and to have IP on certain chromosomes that were estimated to be more "gene-rich" than others, and so, more important for other researches[585].

However, later study, performed by the same academic, already questions these estimates. Empirical research published in 2015 and 2017 by Heidi L. Williams and Sampat[586] claims that the impact of gene patenting to the follow-on research is less significant than estimated before. Comparing scientific publications and the number of gene patent applications and granted patents, using quasi-experimental approach, the authors conclude finding little evidence that patent grants have had any effect on follow-on innovation outcome[587]. On the other hand, the study also concluded that no credible empirical evidence exists supporting the claim that stronger patent rights – either longer patent terms or broader patent rights –

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580 Michael A Heller and Rebecca S Eisenberg, 'Can Patents Deter Innovation? The Anticommons in Biomedical Research.' (1998) 280 Science (New York, N.Y.) 700.

581 The ESHG Working Party on Patenting and Licensing, 'Patenting and Licensing in Genetic Testing: Recommendations of the European Society of Human Genetics' [2007] European Journal Of Human Genetics 1.

582 Heidi L Williams, 'Intellectual Property Rights and Innovation: Evidence from the Human Genome' [2010] NBER working paper series 1.

583 Ibid. 12.

584 Ibid. 10.

585 Ibid. 9.

586 Sampat Bhaven and Heidi Williams, 'How Do Patents Affect Follow-on Innovation? Evidence from the Human Genome' (2015) XXXIII NBER Working Paper 81; Heidi L Williams, 'How Do Patents Affect Research Investments?' [2017] National Bureau of Economic Research.

587 Heidi L Williams (2017) 26.

encourage research investments into developing new technologies.[588] As a result, the question if patents have a positive effect on the innovation seems to be unanswered.

1.5. Problem of patent thicket

The commercial products of genetic research often require the use of several gene fragments, each of which may be patented by a different person or entity. So if licensing arrangements need to be obtained in order to develop a new product, it could prove prohibitively expensive to provide such product to the market. For example, Dr. William Haseltine from Human Genome Sciences,[589] has remarked that researchers who create inventions involving the CCR5 receptor gene could obtain separate patents which complement the Human Genome Sciences' patent, resulting in a scenario where drug developers would have to pay several entities in order to produce one drug.[590]

The phenomenon of patent thickets resulting in royalty stacking can restrict future innovation, as researcher faces a problem of acquiring too many licenses from different patent holders. Related license fees may ultimately hinder potential licensees from developing and commercialising new products. The proliferation of patents and subsequent collection of royalties may thus well suppress innovation.[591]

Moreover, according to EPC article 67, a European patent application shall, from the date of its publication, provisionally confer upon the applicant the same protection and rights as is given by the granted European patent. So even if the patent is not granted yet, the applicant may claim the same rights as the patent holder and may restrict the use of technology to any other party. There are always long delays between the filing and issuance of biotechnology patents. During this period of pendency, there is substantial uncertainty as to the scope of patent rights that will ultimately issue. So, according to the law, patent applicant can have quite an extended protection period and claim monopoly rights of still patent-pending technology.

Moreover, although in the US the situation is different, and patent law does not recognise enforceable rights for the pending patent applications, firms and universities typically enter into license agreements before the issuance of patents, and firms raise capital on the basis of the inchoate rights preserved by patent filings. In effect, each potential patent creates a spectre of rights that may be larger than the actual rights, if any, eventually conferred by the patent office. Worked into the calculations of both risk-taking investors and risk-averse product

588 Heidi L Williams (2017) 28.
589 Human Genome Sciences is a biopharmaceutical company that was founded in 1992.
590 Gitter (2001) 1669.
591 Overwalle and Zimmeren 425.

developers, these overlapping patent filings may compound the obstacles to developing new products.[592]

One issue is that patent holders could block access to essential research material, but some critics have also raised the fears that patents could impede innovation by creating an "anticommons" effect, in which scientists avoid approaching research that would require lengthy and expensive negotiations with multiple patent holders.[593] Granting too many rights in previous discoveries, that are necessary for performing future research and develop new technologies, can become an obstacle for social or scientific improvements. Transactions costs of having the patent license in many cases may exceed the potential future gain, which is unknown when the negotiations are started. The existence of patents on research tools could slow or even block many subsequent research efforts as innovators might face a problem of paying licensing fees to a large number of enterprises having relevant patents before even commencing their own projects. Also, not to reject the possibility, that license can be even denied (and no permission for use given).[594]

The example case, showing the reduction of use of the patented technology can be the hemochromatosis testing. Hemochromatosis is a genetic disease that results in an overload of iron in the body and can lead to arthritis, diabetes, liver cirrhosis, liver cancer, and heart failure. It is a genetic disease. The testing and treatment of this disease have decreased by 30% in the United States after the patents for the mutation in genes, that have been linked to the disease, have been granted. US patents (no. 5,712,098; 5,753,438; and 5,705,343) covering the hemochromatosis genetic test for C282Y and H63D were first issued to Mercator Genetics in early 1998. The patents granted the right to perform testing for these two mutations. In 1998, an exclusive licence to perform diagnostic genetic testing was given by the patent holder to Smith Kline Beecham Clinical Laboratories. The Laboratories from their side contacted numerous research centers in the United States and offered a sub-licenses agreements in exchange for very high up-front royalties: the company asked academic laboratories to pay a fee of $25,000 for a sublicense, and 5 to 10 times higher fees were required from commercial laboratories, plus per-test royalties fees of as much as $20 per test were asked.[595] 119 laboratories were surveyed and 30% of those already offering diagnostic genetic testing for hemochromatosis stopped performing their tests after the patents and exclusive licenses were granted. Fewer institutions were carrying out genetic tests, which

[592] Michael A Heller and Rebecca S Eisenberg, 'Can Patents Deter Innovation? The Anticommons in Biomedical Research.' (1998) 280 Science (New York, N.Y.) 699.

[593] Ibid. 698.

[594] WHO Human Genetics Programme 'Genetics, Genomics and the Patenting of DNA: Review of Potential Implications for Health in Developing Countries' 39.

[595] Jon F Merz and others, 'Diagnostic Testing Fails the Test: The Pitfalls of Patents Are Illustrated by the Case of Hemochromatosis' (2002) 415 Nature 577, 3.

means fewer data are available to researchers seeking to better understand the disease, and fears have been expressed that high costs and royalties from the patent holders are likely to flow down to patients, who will pay more to access genetic tests.[596]

2. Hamper of human right to health care

A specific human right to health care has been widely accepted at the national level, with more than seventy states incorporating provisions guaranteeing a right to health care into their constitutions or statutes.[597] The World Health Organization has published a document, where the concerns are expressed that "patents can adversely affect access [to genetics and genomics] in at least two ways: by hindering access to the products of innovation in genomics in the short term; and, indirectly, hindering genomics innovation, particularly in areas relevant to developing countries, by creating barriers to research."[598] In the document the fears that gene patenting can lead to an increase of prices in genetic testing were also indicated.[599] WHO point, that the genetic researchers can give very important information in treating diseases. Molecular genetic testing can be used for many purposes: accurate diagnosis; predictive testing for conditions without any current form of treatment such as Huntington's disease to allow individuals to make personal decisions for family planning; predictive testing leading to preventive treatment for such disorders as familial adenomatous polyposis; predisposition testing for conditions like familial breast cancer; carrier testing for recessive disorders like thalassaemia and Tay-Sachs disease; and, prenatal and neonatal testing.[600] Currently, in some developed countries, recombinant DNA technology is firmly established in clinical genetics, where it is being used widely for genetic counselling, prenatal diagnosis, and, to a limited degree, for population screening. Investigations carried out in the recent years provides increasing evidence that a varying proportion of many different populations have genetically determined resistance to critical infectious diseases, including malaria, tuberculosis and HIV/ AIDS.[601] Genomics offers significant opportunities for the development of new vaccines, diagnostics and therapeutic agents.[602] WHO expresses fears, that least developed countries, where the investment in resources for innovation and technology are much lower than in developed countries, can be restricted from using genetic testing because of issued patents.

[596] WHO Human Genetics Programme, 'Genetics, Genomics and the Patenting of DNA: Review of Potential Implications for Health in Developing Countries' 38; Merz and others.

[597] Pier Deroo, '"Public Non-Commercial Use" compulsory Licensing for Pharmaceutical Drugs in Government Health Care Programs' (2011) 32 Michigan Journal of International Law, 364.

[598] WHO Human Genetics Programme, 'Genetics, Genomics and the Patenting of DNA: Review of Potential Implications for Health in Developing Countries' 37.

[599] Ibid. 38.

[600] World Health Organization. Advisory Committee on Health Research., 'Genomics and World Health: Report of the Advisory Committee on Health Research. Geneva : World Health Organization.' (2002) 47.

[601] Ibid. 84.

[602] Ibid. 93.

The role of patents in encouraging domestic innovation and the monopolisation of particular fields by large companies might be unbalanced with the need to protect health-related interests and promote health priorities.

In the EPO Boards of Appeal case T 1213/05,[603] the opponents stressed that the Myriad Genetics invention concerning breast and ovarian cancer and had a significant impact on public health, thus in these special circumstances the Board should apply Article 53(a) EPC to the exploitation of the patent.[604] The argument was not accepted by the Boards. However, IP legislation does allow patenting exceptions in cases where the public interests can be harmed. For example, the TRIPS Article 8 permits member countries to "adopt measures necessary to protect public health and nutrition, and to promote the public interest in sectors of vital importance to their socio-economic and technological development" as well as "measures ...to prevent the abuse of intellectual property rights by right holders."

A starting point from this perspective is to acknowledge that every WTO Member is free to design its domestic IP policies to suit local needs. Only the minimum standards of TRIPS must be ensured. The TRIPS objective is that IP protection and enforcement contributes to both technological innovation and dissemination of technology, serves the interests of users and producers of technology, and overall facilitates social and economic welfare.[605] In the context of public health, all WTO Members agreed in the Doha Declaration on TRIPS and Public Health that TRIPS "can and should be interpreted and implemented in a manner supportive of WTO Members' right to protect public health and, in particular, to promote access to medicines for all."[606] The Doha Declaration then lists an interpretation of all TRIPS provisions in light of the balancing objectives in Article 7 and public interest principles in Article 8 in order to ensure that TRIPS supports, rather than counters, public health policies.[607]

So countries are allowed to legislate exceptions or restrictions to patentability if they are needed to protect public health. Such restrictions can also be foreseen in the biobank's rules. For example, UK Biobank in its material transfer agreement states that UK Biobank will have no rights or licence to the Intellectual Property Rights in relation to any inventions or findings

603 *T 1213/05 (Breast and ovarian cancer/UNIVERSITY OF UTAH) of 27-9-2007 ECLI:EP:BA:2007:T12130520070927 [53].*

604 The Board accepted the argument that public health care is a sensitive area, however the it saw no basis in the EPC to distinguish in this respect between inventions concerning different technical fields. The decision explained that EPO has not been vested with the task of taking into account the economic effects of the grant of patents in specific areas and restricting the field of patentable subject-matter accordingly. So this argument raised by the opponents was rejected.

605 Agreement on Trade-Related Aspects of Intellectual Property Rights 1994.Article 7 foresees that under the customary principles of treaty interpretation in international law, the object and purpose of a treaty form one of the core elements driving the treaty interpretation exercise.

606 Doha Declaration on TRIPS and Public Health 2001 para 4.

607 Henning Grosse Ruse-Khan and Roberto Romandini, 'Patentability of Pharmaceutical Inventions under TRIPS. Domestic Court Practice as a Test for International Policy Space' (2016) 2 Max Planck Institute for Innovation and Competition Research Paper 30.

developed by the users of its resources, however the exception would apply where applicant generated inventions are, or are in the process of being, used unreasonably to restrict health-related research and/or access to healthcare anywhere in the world. If, at its reasonable discretion, UK Biobank considers that an unreasonable restriction to health-related research or healthcare system exists or is likely to exist then it shall promptly notify the user and automatically, on receipt of such notification, the user shall be deemed to grant a perpetual, irrevocable, worldwide, fully paid-up, royalty-free, fully sub-licensable licence to UK Biobank to use such invention in order to remove or mitigate the before mentioned negative causes.[608]

Academics also stress the possible negative consequences of gene patenting in health care. Heller and Eisenberg highlights, that privatization of ideas must be more carefully deployed if it is to serve the public goals of the biomedical research. The direct paradoxical consequence of patenting upstream discoveries in biomedicine can be the increase of prices and a decrease of useful products in the health sector. Authors note that policy-makers should seek to ensure coherent boundaries of upstream patents and to minimise restrictive licensing practices that can harm downstream product development.[609] Allowing patents on genetic diagnostics may create a possibility that the test would not be available to a patient for purposes of diagnosing the health problem, hindering patient care.

Prof. D. Shabalala identifies multiple concerns regarding technology access. Where access to technologies is required to change the nature of a production process, some of the most challenging problems to overcome are refusals to license, the high cost of licensing, and patent owners maintaining a monopoly on the knowledge so as to prevent competition. He writes that the maintaining of monopoly is particularly undesirable as it precludes, countries or firms to produce competing products, achieving more efficiently in the dissemination of the knowledge and creation of products. Claiming monopoly restricts the knowledge about the technology to be used to adapt it to local market conditions.[610] The exclusive licensing, giving the same monopoly rights to a licensee, is no less troubling than patenting of genes itself. A legacy of exclusively licensed gene patents casts a shadow of patent infringement liability over the future of multi-allele testing and full-genome analysis.[611]

608 UK Biobank's Material Transfer Agreement for data and/or samples form part 3.7 and 3.8 .
609 Heller and Eisenberg 701.
610 Shabalala Dalindyebo, 'Climate Change, Technology Transfer and Intellectual Property: Options for Action at the UNFCCC' [2014] Dissertation to obtain the degree of Doctor at Maastricht University 12.
611 Julia Carbone and others, 'DNA Patents and Diagnostics: Not a Pretty Picture' (2010) 28 Nat Biotechnol., 785.

Isis Innovation Limited patent US6258540 (B1)[612] (also granted patents EP0994963 (B2), JP4245666 (B2), CA2282793 (C)) claims the detection method performed on a maternal serum or plasma sample from a pregnant female, which method comprises detecting the presence of a nucleic acid of foetal origin in the sample. The invention enables non-invasive prenatal diagnosis including for example sex determination, blood typing and other genotyping, and detection of pre-eclampsia in the mother. The patent relates to a non-invasive test of a pregnant woman's blood to detect fetal DNA in order to screen for genetic abnormalities such as Down Syndrome. Doctors say such tests have dramatically reduced the need for invasive tests such as amniocentesis, which carry a small risk of miscarriage.[613] In the case of diagnostic gene patents, doctors must either obtain a license to provide such a test or send a sample to be tested at the corporation that holds the patent. Any of the ways increase the diagnosis fee distinctly. Due to the high licensing fee, the doctor may even choose to perform an inferior procedure, perhaps resulting in inaccurate results or even failure to screen for the specific disease.[614]

Not always the legislative instruments regulate the balance of rights between the rights holder and the user. There is no guarantee that the legal instruments endorse the equality and balances rights of the different social groups (in our case the rights of the inventor to claim ownership to its invention and the human right to health). Indeed, given the complexity of the work to turn the prosperity of raw genomic data into practical solutions, it would be excellent to permit as many researchers as possible to participate in this challenge. Promoting widespread access to gene sequences and other upstream discoveries that are inevitable research tools, could prompt a larger number of researchers and institutions to undertake the complex tasks to develop end-products needed to the society. Patent standards are currently being stretched to accommodate arguably sub-patentable items such as gene sequences. While these useful discoveries may deserve some protection, they in most cases may not deserve the absolute protection provided by patents that exclude access.[615] However, there are solutions that can minimize the negative consequences caused by gene patenting to research and right to access to health. The open biobanks can play a significant role in ensuring the right access to genetic knowledge.

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612 The patent was later appealed in US courts. US Court of Appeals in Case *ARIOSA DIAGNOSTICS, INC v. SEQUENOM, INC.*, No. 14-1139 (Fed. Cir. 2015) ruled that the claims of this patent should not be allowed as being too broad and indefinite. The claims are directed to methods for detecting paternally-inherited fetal DNA in maternal blood samples, and performing prenatal diagnosis of such DNA, and such claims do not involve patent-eligible subject matter. Appellants and amici have argued that a broad range of claims of this sort can cause risks for diagnostic claims in general. It was also said that a crisis of patent law and medical innovation might be in jeopardy.

613 Andrew Chung, 'Supreme Court Refuses to Review Prenatal Test Patent Dispute' [2016] *Reuters*.

614 Singh 164.

615 WHO Human Genetics Programme 'Genetics, Genomics and the Patenting of DNA: Review of Potential Implications for Health in Developing Countries' 49.

CHAPTER V

PERSONAL DATA AS INTELLECTUAL ASSET IN BIOBANKS

I. Privacy issue in biobanking

Biobanks store extensive scope of personal information. It is not only the human samples, but also related data – information about the participants, their lifestyle, their family members, and similar. Therefore, there are many discussions about the adequate protection of personal data in the biobank. Evolving privacy regulations, such as new data protection requirements in Europe, and legal frameworks have already had a significant impact on research. Health data are considered especially sensitive, and as a result, severe restrictions are imposed on researchers and investigators[616]. Sensitive data are regulated more strictly, than other personal data. Data protection rules are applied to protect individuals from misuse or abuse of their sensitive information.

On the other hand, too rigid regulation of sensitive data can harm the research. Inflexible regulations can end up creating strict and unspecific rules that may detrimentally impact and restrict the use of limited information for biobank researchers. The right balance must be sustained between the privacy as a personal right and the research freedom and a right to health.

In the extraordinary development of biological sciences and medicine, the right to privacy was accepted and understood as a right to self-determination in choices regarding individual life and medical treatments (so as the use of contraceptives, abortion, and end-of-life decisions)[617]. The person, or patient, now is free to choose his/her treatment, decide if he/she wants medical assistance, etc. The doctor has no rights to decide what medical care a person must receive. The same self-determination rule applies to participation in biobank's activity. Today's legislative framework allows a person to

616 Deborah Mascalzoni, Angelo Paradiso and Matts Hansson, 'Rare Disease Research: Breaking the Privacy Barrier' (2014) 3 Applied and Translational Genomics 24.

617 Matteo Pascuzzi, Giovanni; Izzo, Umberto; Macilotti, *Comparative Issues in the Governance of Research Biobanks* (Springer-Verlag Berlin Heidelberg 2013) 105.

decide the scope of participation in the biobank, the information he wants to give, the ability to withdraw from participation and many more safeguards.

Personal data can also be treated as part of intellectual property. Even if personal data is not acknowledged as intellectual right the same as patents or copyrights, transactional intellectual property lawyers are treating confidential information as a type of intellectual property. England and Wales Court of Appeal (Civil Division) in the judgment of the case *Stephen John Coogan v News Group Newspapers Limited and Glenn Michael Mulcaire*[618] concluded that "while the prevailing current view is that confidential information is not strictly property, it is not inappropriate to include it as an aspect of intellectual property". "Something less than the whole potential universe of personal information might need to be defined for considering intellectual property protection for personal information in an experimental model", notes Professor Dorothy J. Glancy.[619] Causes, why it may be proper to treat personal information as intellectual assets are, I) the recognition to acknowledge the control and reinforce of the respect for the person whose personal information is handled, or mishandled, II) since personal information has high value (especially to data collectors, data miners, and personal data retailers) unjust enrichment concerns imply that it may be unethical for such personal data handlers to profit from an assets that would not exist without the person who is the subject of the personal information.[620]

Biobanks must ensure that data protecting regulations and rules are applied and the interests of participants protected. It is essential that the personal information and individual rights of the participants be respected. Developing a database containing genetic profiles poses a significant problem – privacy. Patients may not want to share their genetic profiles for fear that they may be discriminated against by insurance companies, employers, and others. Roger Brownsword presents three important personal data protection criterion that biobank must follow. A biobank must ensure: (i) that participation and the use of participants' samples and data are based on free and informed consent; (ii) that the privacy, confidentiality, and fair data processing rights of participants are respected; and (iii) that the proprietary rights of participants are respected.[621] Data protection rules are one of the reasons why participants can have more trust in biobanks and a reason why they decide to participate in biobanks' activities. Naturally, if a person

618 *Coogan v News Group Newspapers Ltd & Anor [2012] EWCA Civ 48, Cases No: A3/2010/2862 and A3/2011/0688,* paragraph 39.

619 Dorothy J Glancy, 'Personal Information as Intellectual Property' [2005] Berkeley Technology Law Journal 2.

620 Glancy 1-3.

621 Pascuzzi, Giovanni; Izzo, Umberto; Macilotti 42.

is safe knowing that at any time he/she can withdraw from participation, that his/her personal information will not be revealed to any third party, it is more likely that under such conditions a person will give his/her samples and data for research use.

However, as there is no one-size-fits-all solution for patenting biological inventions, there are no such solutions when we talk about data protection in biobanks. Individual interest is not a general concept having the same extension and weight whatever the issue and context. We have to envisage a way of considering and weighing all the interests at stake: individual interests versus group interests, versus public interests, interests of scientific research, and so on. Unlike in the traditional research setting, tissue stored in a biobank is not only collected for a specific research project but for undetermined future research projects as well. As already presented in this thesis, the broader the samples and information can be used, the better results can be expected from the research.

Participant's opinion to withdrawal from research, or to give broad consent, can be easily influenced by many subjective factors: media news, stories from untrusted sources, or worsts, untrue information. Social networks such as Facebook, Tweeter, Instagram can give unreliable information that is accepted by masses of users as a real fact. Participant's withdrawal from the research can be based on the information read on the internet, somebodies lousy opinion or comment about the existing biobank. Therefore when talking about data protection in this field, an objective criterion is needed for participant's acceptable withdrawal from research. However, today's legislation seems to be very strict regarding protection of personal data. Moreover, biobank participants not only can withdraw from participation but also request not to use their samples in any research, even the one, that is already ongoing.

Data protection rules might also cause limitations in sharing the data or samples between biobanks. NIH privacy protections are a required part of the NIH policy. Data are stored in a two-tiered system based on data sensitivity and privacy concerns. Only if individuals give specific informed consent for open access will de-identified data about them be placed on a publicly available website. In addition to protecting privacy by restricting access, researchers may agree to or be required to abide by certain privacy protections, such as ensuring destruction of the data or sample after research.[622] If biobanks are restricted to share the data and information between different researches, it

[622] Heather L Harrell and Mark A Rothstein, 'Biobanking Privacy Laws in the United States' (2016) 44 Journal of Law, Medicine and Ethics 108.

will negatively influence the research in general, as different investigations cannot be continued, but rather will need to be taken from the beginning.

Data protection rules might differ in one country and another. In the United States the data protection rules are regulated by federal statutes and regulations, state statutes and common law. In Europe common European law applies. Such policies might also differ in the biobank's institutional rules and contractual agreements of researchers and biobanks. When observed in the context of international biobanking, it regularly becomes difficult to conclude with any certainty whether international sharing of specimens and health information is lawful. In this chapter, I will look at the data protection regulations applied to biobanks and will question if the regulations as applicable today are adequate to ensure that biobanks can continue performing research and improving the health care situation of the population.

1. Special protection of the personal data

A person has personal rights to his private information. According to the today's legislation, nobody's data can be used without person's consent. Property rights have significance for those involved in biobanking (including researchers, managers, and participants) as they assign rights, duties, and responsibilities that are legally enforceable and form the way that a biobank is constructed and managed.[623] Participants have certain rights, and freedoms concerning their health or genetic information and researchers must respect such rights. There are legal and equitable causes of action that protect individuals from adverse consequences of disclosure of information, such as privacy protection rules, the rights granted by the data protection legislation.

Even if there is no global standard for privacy protection regarding the use of personal genome and omics data, some international instruments shall be mentioned. The European Convention of Human Rights proclaims the defence of privacy as a fundamental human right: 'Everyone has the right to respect for his private and family life, his home and his correspondence' (Article 8(1)). The Convention has been ratified by all 47 Members of the Council of Europe, and its provisions have been incorporated into the laws of many European nations, thereby becoming enforceable.

[623] ibid 79.

More recent and more detailed the Charter of Fundamental Rights of the European Union (Charter of Rights)[624] has the same provision. Article 7 of the Charter of Rights proclaims that 'Everyone has the right to respect for his or her private and family life, home and communications'. Article 8(1) of the Charter of Rights continue ensuring the protection of personal data. Everyone has the right to the protection of personal data concerning him or her. Such data must be processed fairly for specified purposes and on the basis of the consent of the person concerned or some other legitimate basis laid down by law. Everyone has the right of access to data which has been collected concerning him or her, and the right to have it rectified (Article 8(2)). Compliance with these rules shall be subject to control by an independent authority (Article 8(3)).

Privacy protection principles are also established in the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (Oviedo Convention)[625]. The Article 2 of the Oviedo Convention states that, the interests and welfare of the human being shall prevail over the sole interest of society or science. Article 5 reads: "An intervention in the health field may only be carried out after the person concerned has given free and informed consent to it. This person shall beforehand be given appropriate information as to the purpose and nature of the intervention as well as on its consequences and risks. The person concerned may freely withdraw consent at any time (*emphasis added*)."

These provisions embody a well-known rule of biomedical ethics, according to which medical treatment may only be carried out after a patient has been informed of the purpose, nature, risks and consequences of the intervention, and has freely consented to it. This principle has its origins in the Nuremberg Code of 1947, which was developed during the trial of Nazi physicians who researched concentration camp prisoners.[626] In the Convention, the informed consent is required for the first time as a general principle for any biomedical intervention in the international binding instrument.[627] Article 12 of Oviedo Convention, complementing Article 11, states that predictive genetic testing "may be performed only for health purposes or for scientific research linked to health purposes, and subject to appropriate genetic counselling". Another legal instrument, the

624 Charter of Fundamental Rights of the European Union, 2010 O.J. C 83/02, (Charter of Rights).

625 A 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 1994 (European Journal of Health Law) 381.

626 Roberto Andorno, 'The Oviedo Convention: A European Legal Framework at the Intersection of Human Rights and Health Law' (2005) 2 Journal of International Biotechnology Law 138.

627 Ibid. 133.

Recommendation Rec(2006) 4 of the Committee of Ministers to member states on research on biological materials of human origin,[628] has a goal that the Member States will protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity, right to private life and other rights and fundamental freedoms with regard to any research governed by the recommendation.

1.1. EU data protection laws

From these first legal instruments, protecting person's private life evolved more direct rules related to the protection of personal data. In Europe, the recognition of data protection as a fundamental right in itself, independent from the right to respect for private life, has been accepted.[629] Today, the most significant legal instrument regulating the protection of personal data is Regulation 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation or GDPR).[630] The General Data Protection Regulation repealed the before valid legal act – Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data – and on 24 of May 2016 entered into force. The GDPR is applied in all EU Member States as from 25 May 2018.

The General Data Protection Regulation sets up new requirements and rules for companies that are processing personal data. One of the greatest changes to the regulatory panorama of data privacy appears to be the extension of the jurisdiction of the GDPR. Now rules apply to all companies processing the personal data of data subjects residing in the Union, regardless of the company's location.[631] Which means that company's based outside the EU (for example in the US) would still need to confirm with GDPR requirements if such companies process the personal data of EU citizens. The territorial

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628 Council of Europe Committee of Ministers, 'Recommendation Rec(2006)4 of the Committee of Ministers to Member States on Research on Biological Materials of Human Origin and Its Explanatory Memorandum' (2006).

629 See the Article 16 of the Consolidated Version of the Treaty on European Union, 2010 O.J. C 83/01. and Article 8 of the Charter of Rights.

630 Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC 1.(General Data Protection Regulation or GDPR) (Text with EEA relevance), OJ L 119, 4.5.2016, p. 1–88.

631 Article 3(1) of the General Data Protection Regulation.

applicability of the previous Data protection directive[632] was ambiguous and referred to data process 'in context of an establishment', and applied to the outside companies only according to the public international law rules.[633]

The GDPR establishes fundamental principle relating to the processing of personal data (like lawfulness, fairness, transparency, data minimisation, accuracy, storage limitation, integrity and confidentiality, accountability of the data controller.[634] It also sets the requirements for consent regime,[635] rules of processing sensitive data (such as biomedical data),[636] responsibilities of the data controller,[637] transfer of data to the third countries.[638] It is a legal instrument covering all aspects of personal data, its collection, use, transfer and individual rights regarding his or her data. National laws in every Member State must conform with the GDPR. But only the Member States are bound by this legislative act, but also individual organisations that process personal data. So, EU instrument is comprehensive in its scope and applicability. In can be said, that after entering into force, the GDPR is the central and most important instrument for all Member States in the field of personal data protection. From this perspective, the EU law differs from US legislation, where the data protection is regulated in a number of different federal and state laws.

1.2. US data protection laws

American biobanking laws and practices are dispersed, disjointed, and mostly obscure. A privacy protection standard on the use of personal health data in the United States is called the Health Insurance Portability and Accountability Act of 1996 (HIPAA).[639] HIPAA protects the confidentiality of a patient's medical information by limiting its collection, use, and disclosure. HIPAA was passed in 1996.

632 Directive No. 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data.(no longer in force).

633 Article 4(1)(a) of the Directive No. 95/46/EC, stated that each Member State shall apply the national provisions it adopts pursuant to this Directive to the processing of personal data where the processing is carried out in the context of the activities of an establishment of the controller on the territory of the Member State; part (b) of the same Article stated that the controller is not established on the Member State's territory, but in a place where its national law applies by virtue of international public law.

634 Article 5 of GDPR.

635 Articles 7-8 of GDPR.

636 Article 9 of GDPR.

637 Article 24 of GDPR.

638 Chapter V of GDPR.

639 The Health Insurance Portability and Accountability Act of 1996 (HIPAA).Pub.L. 104–191, 110 Stat. 1936, enacted August 21, 1996.

In compliance with the Administrative Simplification provisions of the Act, another legal instrument was published by the US Secretary. The Standards for Privacy of Individually Identifiable Health Information, more commonly referred to as the Privacy Rule, were finalised on August 14, 2002. The Privacy Rule has provisions on the use of healthcare data for research, reviewing of clinical databases to identify candidates for recruitment to research, authorisation by a patient of research use of data, de-identification of data, and other research-related issues.

The third legal act regulating human subjects protection is the Common Rule. The Common Rule was published in 1991 and today is codified in separate regulations by 15 Federal departments and agencies, including NIH.[640] For all participating departments and agencies, the Common Rule outlines the necessary provisions for informed consent. Human subject research carried or supported by each federal department or agency is governed by the regulations of that department or agency. The head of the department retains final judgment as to whether a particular activity it conducts or supports is covered by the Common Rule.[641]

In 2017 the Common Rule was updated. Newly updated Common Rule is titled as a Final rule. U.S. Department of Health and Human Services (HHS) notes that the Final rule seeks to strengthen "protections for people who volunteer to participate in research" while balancing administrative burden, particularly for low-risk research.[642] The final text of the Final rule allows performing research involving non-identified biospecimens without consent to be obtained to conduct such research. Also, the Final rule does not expand the policy to cover clinical trials that are not federally funded.

Other legal acts regulating the protection of personal data is the Food and Drug Administration (FDA) regulations. They generally mirror the Common and Final rules, thereby vesting decision-making in the hands of the local Institutional Review Board. The FDA regulations are applicable when researching investigational drugs or medical devices with human subjects.[643] Subject means a human who participates in an investigation,

[640] US Federal Policy for the Protection of Human Subjects ('Common Rule') 1981.Full list can be found at U.S. Department of Health and Human Services (HHS) internet page https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html accessed 2018 May 8.

[641] Ibid.

[642] Thomas Sullivan, 'Final Common Rule – Sixteen Agencies Update Regulations on Individuals Who Participate in Human Research' *Policy & Med.* (2018). Available at http://www.policymed.com/2017/01/sixteen-agencies-update-regulations-on-individuals-who-participate-in-research.html accessed 2018 May 8.

[643] 21 C.F.R. § 50.1; 21 U.S.C. § 355, available at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50> accessed

either as an individual on whom or on whose specimen an investigational device is used or as a control.[644]

Apart from the federal acts, the research in the medical field (including biobanks) is broadly regulated by different States' statutory or regulatory law. There are several ways in which state laws may address privacy concerns related to biobank research. States may give individuals a degree of control over their genetic data via informed consent requirements, property rights, notice requirements, or rights of access. Also, states may limit how long genetic information or samples can be retained by biobanks or researchers and may have licensure requirements for those working with genetic information.[645] For example, Nevada law requires destruction of genetic information obtained for research once the study is completed or the individual withdraws from the study.[646] Mississippi law provides that patient-specific health information may be disclosed only following the provisions of the HIPAA Privacy Rule.[647]

The regulation of personal data is quite complex in the US. The activities of the biobanks cannot conflict with the data protection rules; otherwise, the actions of the biobank become illegal, and biobank can be permanently closed. The existing international instruments that establish basic principles, guidelines and requirements regarding protection of individual's data, must also be followed. It is how biobanks become bound by a variety of legal norms that can overlap, differ or be ambiguous. Nevertheless, biobank must follow all the legal provisions and assure the conformity with the rules. A variety of legislature put biobanks in a rigorous position to know all the requirements and apply them rightly. Biobank's personnel must be aware of the current legislative acts and use them in everyday work. It becomes a big burden to the biobank's smooth operation and so, cause the negative consequences of the research in general.

However, as we have seen before, biobanks stores not only the personal information about samples donors (their health records, personal information, information about their habits and lifestyle), but also biological samples, that is a sample of blood, saliva, or other

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2018 May 8.

644 The Secretary's Advisory Committee on Human Research Protections (SACHRP), 'FAQ's, Terms and Recommendations on Informed Consent and Research Use of Biospecimens' (2011). And also 21 C.F.R. § 812.3.

645 Heather L Harrell and Mark A Rothstein, 'Biobanking Privacy Laws in the United States' (2016) 44 Journal of Law, Medicine and Ethics 118.

646 Nevada Revised Statute 2011. § 629.161 "Retention of genetic information of person without consent unlawful; exceptions; destruction of genetic information".

647 Mississippi Code 2013. § 41-119-13 "Confidentiality of health care information and data in network".

human biological material. This calls into question the following analysis, is human biological materials, ripped of the description about a donor, remains a personal data?

2. Biological samples as personal data

There is no consensus on the issue of whether human biological materials should be treated as personal data. Biobanks collect, contain, store and analyse different types of biological samples. Apart from specimens, biobanks collect the accompanying data regarding those samples. The question is if data protection rules apply to the biobanks and if the information held by biobanks is protected as a personal data. Some scholars, commentators and agencies enforcing data protection laws have taken the view that personal data should not be seen to include biological materials for the purposes of data protection laws, while others believe in an opposite.

There are contradicting opinions that samples are not personal data. The Article 29 Data Protection Working Party in its' "Opinion on the concept of personal data"[648] did separate the sample – as a tangible object, from the information that can be retrieved from the sample. The Article 29 Working Party is specifically tasked with providing authoritative interpretations of European data protection law. According to the Article 29 Working Party, the biometrical data can have a dual character: "can be considered both as the *content* of the information about a particular individual as well as an element to establish a *link* between one piece of information and the individual. This dual character also appears in the case of DNA data, providing information about the human body and allowing unambiguous and unique identification of a person." Reading this part, it is quite clear, that the Article 29 Working Party expresses an opinion that DNA is data and the data protection regulations apply to DNA. However, the document continues explaining that: "Human tissue samples (like a blood sample) are themselves sources out of which biometric data are extracted, but they are not biometric data themselves (as for instance a pattern for fingerprints is biometric data, but the finger itself is not). Therefore the extraction of information from the samples is a collection of personal data, to which the rules of the Directive[649] apply. The collection, storage and use of tissue samples themselves may be subject to separate sets of rules". Similarly, the official position of the

[648] Article 29 Data Protection Working Party, 'Opinion 4 / 2007 on the Concept of Personal Data' (2007).
[649] Explanation: the mentioned the Article 29 Working Party's Opinion was prepared when the old Data protection directive 95/46/EC was in force.

UK's Information Commissioner was reported: a sample is not treated as personal data, "because it is physical material".[650]

It seems that the Article 29 Working Party, being the authorized body to interpret EU data protection rules, does separate the information, when it is already extracted from the sample, and the sample, as such: a drop of blood, or other human tissue. Sadly, this statement is not clearly explained in the document and so further interpretations might be misleading. It is not elaborated in the Opinion exactly why samples cannot be understood to be included under the "data" definition.

But there are contradicting opinions, that talk about samples being data. D. Hallinan and P. De Hert discuss why samples are data, and not only physical materials.[651] "Samples do contain data – DNA is data" - they state. DNA is understood as information both popularly and in the genomics. Authors present the sample as an "information carrier". In the biobanks' activities, the biological sample is sequenced to produce genomic information. The sequenced genomic data is used by researchers to produce information; researches are based on the finding from the sequenced genes. This information can be used for general findings about a specific disease, that means the information is used not for a specific individual, but rather to disclose a general biology of human beings. Such information might also be referred to as knowledge. D. Hallinan and P. De Hert make a good point that genetic samples are only collected, so that the information they contain may be processed and analysed. Samples are collected and exchanged between biobanks according to the information they are presumed to contain. Biobanks have all the tools and human resource (such as sequencing machines, special software, cloud-based tools to keep and transfer the information, the qualified academic personnel) to convert the sample into digital information and process that information. BBMRI also agrees that to the extent biobanks collect, store and process human biological material, in combination with other forms of personal data, including sensitive data, such as genetic and health data, GDPR applies to the biobank's activities.[652]

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650 Beyleveld, Deryck *et al.*, "The UK's Implementation of Directive 95/46/EC" in, Deryck Beyleveld and others, *Implementation of the Data Protection Directive and Medical Research Across Europe (Data Protection and Medical Research in Europe)* (2004) 428.

651 Article 'Many Have It Wrong – Samples Do Contain Personal Data: The Data Protection Regulation as a Superior Framework to Protect Donor Interests in Biobanking and Genomic Research' in Brent Daniel Mittelstadt and Luciano Floridi (eds), *The Ethics of Biomedical Big Data* (Law, Gover, Springer International Publishing Switzerland 2016) 119–137.

652 BBMRI Common Service ELSI, 'The EU General Data Protection Regulation. Answers to Frequently Asked Questions 1.0'.

It would be rather a reasonable statement, that samples collected by biobanks are donor's personal data. Furthermore, if, as will be presented later, donor's are free to withdraw their samples from a biobank, it is quite clear that they withhold personal rights of the samples and can decide on their following use, even when the material is separated from the body. Previously, a programming coding was accepted as a language by a court.[653] If a programming code is a speech, how can a blood sample not be a source of information?

Looking to the new GDPR, the reflections that sample is data can be found. GDPR implicitly defines:

> „*Genetic data should be defined as personal data relating to the inherited or acquired genetic characteristics of a natural person which result from the analysis of a biological sample from the natural person in question, in particular chromosomal, deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) analysis, or from the analysis of another element enabling equivalent information to be obtained."*[654]

Recital 35 of GDPR informs that: "Personal data concerning health should include all data pertaining to the health status of a data subject which reveal information relating to the past, current or future physical or mental health status of the data subject. This includes information derived from the testing or examination of a body part or bodily substance, including from genetic data and biological samples; and any information on, for example, a disease, disability, disease risk, medical history, clinical treatment or the physiological or biomedical state of the data subject independent of its source, for example from a physician or other health professional, a hospital, a medical device or an in vitro diagnostic test."[655]

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653 In the United States before 1974, software and its source code was not copyrightable and did not have any IPR protection. However, in 1974, the US Commission on New Technological Uses of Copyrighted Works (CONTU) decided that "computer programs, to the extent that they embody an author's original creation, are a proper subject matter of copyright". The rule was later enforced by the 1976 Copyright Act in Section 102(b), to make as obvious as possible that the scope of the copyright protection extends to computer programmes. In 1999, in the US case Bernstein v. the United States it was further ruled that source code could be considered a constitutionally protected right of free speech. Proponents of free speech argued that source code must be protected as a form of communication because it conveys information to programmers, is written in a language, and can be used to share humour and other artistic pursuits.

654 Recital 34 of the GDPR (emphasis added).

655 Recital 35 of the GDPR.

The Regulation does not give a definite answer if biological sample as such should be treated as genetic data, or only the information extracted from such sample falls under the scope of GDPR. However, if considering that samples are not data, it would very much limit the regulatory sphere of the EU legal act. If GDPR would apply only to processed DNA information, it would mean that GDPR is not applicable to tangible human samples and that such samples can be collected without person's consent or without obeying other legal requirements (for example ensuring a right to withdrawal). Broadly speaking, if GDPR would not apply to human samples, biobank's could collect them freely. Only when a need to sequence the genes from such samples would arise, biobank's would be required to conform with GDPR. Naturally, such interpretation would contradict with the primary goals of the GDPR and would go against data protection policies.

Every sample has information in itself. There is no sample without information. There is no blood drop that would not contain DNA. To give some parallels, we can compare the biological sample with any other tangible document containing protected personal data. If the information is kept, as an example, in a USB stick, that USB stick has protection, or if a paper document contains personal information, such document also falls under the data protection regulations. Therefore, it seems to be entirely inaccurate to conclude that samples are not protected by GDPR.

Biobanks also seem to support the position that samples must be treated as personal data. In the 'Answers to Frequently Asked Questions 1.0' prepared by the BBMRI Common Service ELSI[656] is stated that General Data Protection Regulation does affect biobanking. Furthermore, the sample can reveal the identity of the sample donor and so, should fall under the definition of Article 4(1) of the GDPR, which describes personal data as *"any information relating to an identified or identifiable natural person ('data subject'); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such <...> one or more factors specific to the physical, physiological, genetic, mental, <...> identity of that natural person"* (emphasis added).

Looking at the US legislature, samples also seem to fall under the definition of personal data. The US Common Rule applies "*to all research involving human subjects conducted, supported or otherwise subject to regulation by any federal department or agency which takes appropriate administrative action to make the policy applicable to*

[656] BBMRI Common Service ELSI, 'The EU General Data Protection Regulation. Answers to Frequently Asked Questions 1.0' 1.

such research".[657] The biobank research, if conducted through American academic and health care institutions conducting human subjects research, must comply with the Common Rule regardless of its funding source. Plus, to be subject to the Common Rule, a biobank, database, or researcher must be involved in "human subjects research."[658] Parallel FDA regulations are applicable to research on specimens, not only data. Therefore, biobanks are subject to FDA regulations if they are engaged in research with their specimens, or researchers are using biobank specimens in their studies if the research studies an investigational drug or medical device.[659]

Furthermore, genetic information, medical data and other biometric data are treated as sensitive data. Under data protection regulations, sensitive data has even stronger protection. There are more stringent requirements for the consent of the data subject concerning processing sensitive data. The jurisprudence of the European Court of Human Rights (ECtHR) in some of the cases — such as *Z v Finland* and *MS v Sweden* — suggest normative importance of data subjects' consent regarding sensitive data, particularly, medical information.[660] If a sample can be used to disclose the specific sensitive information about the individual, how can it not fall under the scope of data protection rules? Not to forget, that sensitive data can be processed only if some specific requirements are met.

2.1. Sensitive data and research exception in EU

The GDPR establishes a general principle that sensitive personal data should not be processed.[661] Special categories of personal data which merit higher protection should be processed for health-related purposes only where necessary to achieve those purposes for the benefit of natural persons and society as a whole. Member States should be allowed to maintain or introduce further conditions, including limitations, with regard to the processing of genetic data, biometric data or data concerning health.[662] Biometric data falls under the definition of sensitive personal data. Regulation defines biometric data "as personal data resulting from specific technical processing relating to the physical,

657 45 C.F.R. § 46.101 (a).

658 Office for Human Research Protections, 'Coded Private Information or Specimens Use in Research, Guidance' (2008). Available at <http://www.hhs.gov/ohrp/policy/cdebiol.html> accessed 2018 May 8.

659 ibid.

660 Worku Gedefa Urgessa, 'The Feasibility of Applying EU Data Protection Law to Biological Materials: Challenging "Data" as Exclusively Informational' (2016) 7 JIPITEC 107.

661 Recital 51 of the GDPR.

662 Recital 53 of the GDPR.

physiological or behavioural characteristics of a natural person, which allow or confirm the unique identification of that natural person, such as facial images or dactyloscopic data."[663] Information and samples stored and collected for research purposes in biobanks would be regarded as person's genetic data and biometric data, and so, the strict rules of the GDPR applies.

Recitals 53[664] and 54[665] of GDPR allows sensitive data to be processed for health-related purposes and, under special circumstances, even without the consent of the data subject. Article 9 of the GDPR[666] only allows processing personal sensitive data for the following needs: for the healthcare practice and the management of health systems,[667] public health[668] and research[669] sectors where the processing is authorised under specific conditions. Focusing on the research exception, Article 9(2)(j) foresees that legal processing of sensitive personal data for scientific research purposes can be performed when is necessary, for the benefit of natural persons and society as a whole, and based on Union or Member State law "*which shall be proportionate to the aim pursued, respect the essence of the right to data protection and provide for suitable and specific measures to safeguard the fundamental rights and the interests of the data subject."*

The performance of biobanks to carry out researches and to advance the development of the medicine should fall under the research exception. The new GDPR implicitly includes a public interest needs and scientific research goals as justifications to process sensitive personal data. Public health research is treated as a subset of scientific research under the GDPR (see Recital 159), and, therefore, the same research exceptions for biobanks' activities apply.

663 Article 4(14) of the GDPR.

664 Recital 53: „*Special categories of personal data which merit higher protection should be processed for health-related purposes only where necessary to achieve those purposes for the benefit of natural persons and society as a whole, in particular in the context of the management of health or social care services and systems, including processing by the management and central national health authorities of such data for the purpose of quality control, management information and the general national and local supervision of the health or social care system, and ensuring continuity of health or social care and cross-border healthcare or health security, monitoring and alert purposes, or for archiving purposes in the public interest, scientific or historical research purposes or statistical purposes, based on Union or Member State law which has to meet an objective of public interest, as well as for studies conducted in the public interest in the area of public health.<...>",* emphasis added.

665 Recital 54: „*The processing of special categories of personal data may be necessary for reasons of public interest in the areas of public health without the consent of the data subject. Such processing should be subject to suitable and specific measures so as to protect the rights and freedoms of natural persons.<...>",* emphasis added. See more about this exception in the following paragraph of this thesis.

666 Article 9(2) and Recitals 51–54 of the GDPR.

667 Article 9(2)(h) of the GDPR.

668 Article 9(2)(i) of the GDPR.

669 Article 9(2)(j) of the GDPR.

This research exemption under the GDPR is quite broad, and it covers practically all types of research (including commercial researches). Recital 159 explains that "<...> For the purposes of this Regulation, the processing of personal data for scientific research purposes should be interpreted in a broad manner including for example technological development and demonstration, fundamental research, applied research *and privately funded research* <...>" (emphasis added). Research regarding data protection is not limited to government-funded research institutions or research universities, but it also seems to cover commercial investigations. That would mean not only public but also private biobanks could exploit this exception.

Some authors even interpret the research exception as allowing processing of personal data without any requirements of consent. Kart Pormeister writes, that "processing for research purposes will be free from consent requirements entirely since the 'purpose limitation' (meaning that data collected for specified, explicit and legitimate purposes cannot be further processed in a manner that is incompatible with those purposes) does not apply in regard to the research exemption. Furthermore, the 'storage limitation' will not apply to the research exemption either, meaning that data with links to the data subject can be stored for an unspecified time for research purposes."[670]

However, as long as such exception is not implicitly allowed to be used in all biobank's activities, hardly every biobank in Europe can count on it. As such exceptions (until directly and unequivocally stated in the legislative acts) are always evaluated on a case by case basis. Therefore, one research performed in the biobank can be treated as fulfilling all the requirements of the exception, while another can be treated as not being sufficiently relevant to society and so not able to benefit from the exception.

The legal precedents show that the balance between the individual rights and social needs are very fragile and sensitive personal data must always be treated with caution. In the Marper case[671] the European Court of Human Rights (ECtHR) specifically recognized genetic data as 'intrinsically private' and gave some reasons for genetic data's specific sensitivity. The ECtHR noted that even if the interests of the data subjects and the community as a whole in protecting the personal data, including fingerprint and DNA information, may be outweighed by the legitimate interests, such as the prevention of

[670] Kart Pormeister, 'Genetic Data and the Research Exemption: Is the GDPR Going Too Far ?' (2017) 7 Oxford University Press 140.

[671] *S and Marper v United Kingdom [2008] ECHR 1581 nos 30562/04 and 30566/04*.

crime, the use of such information without a consent from the data subject must be weighted carefully[672].

In the case law of the ECtHR found that the blanket and indiscriminate nature of the powers of retention of the fingerprints, cellular samples and DNA profiles of persons suspected but not convicted of offenses, fails to strike a fair balance between the competing public and private interests and that United Kingdom laws has overstepped any acceptable margin of appreciation in this regard. The retention of DNA profiles for the mentioned reason constituted a disproportionate interference with persons' right to respect for private life and was not regarded as necessary in a democratic society.[673] It is settled case-law that the principle of proportionality, which is one of the general principles of European Union law, requires that measures implemented by acts of the European Union are appropriate for attaining the objective pursued and do not go beyond what is necessary to achieve it.[674]

Another significant decision can be found in national precedents in Europe. An Icelandic Supreme Court in case No. 151/2003[675] ruled even though individual provisions of Iceland Act No 139/1998 repeatedly stipulate that health information in the Health Sector Database should be non-personally identifiable, it was far from adequately ensured under the statutory law that this stated objective is achieved. The Court found that such information about one person can be easily linked to his family members. In light of these circumstances, and taking into account the principles of Icelandic law concerning the confidentiality and protection of privacy, Court concluded that an heir has a right to refuse permission to the information of his/her deceased family members to be entered into the Health Sector Database. The Court concluded that the applicant in the case could not exercise this right acting as a substitute for her deceased father, but it was recognised that she might, on the basis of her right to protection of privacy, have an interest in preventing the transfer of health data concerning her father into the database, as information could be inferred from such data relating to the hereditary characteristics of her father which might also apply to herself.

The case law shows that protection of personal data is one of the main issues protected by courts. Therefore, reasons for violating ones privacy must be unquestionable

672 Ibid. para 104.
673 Ibid para 125.
674 Ibid. and also *C-58/08 Vodafone and Others[2010] ECR I-0000*. para. 51.
675 *Ragnhildur Guðmundsdóttir vs The State of Iceland (Icelandic Supreme Court case No 151/2003) (2003)*. An English translation of the decision available at https://epic.org/privacy/genetic/iceland_decision.pdf accessed 2018 May 8.

significant and legitimate. Indeed, one of the requirements that must be fulfilled to allow interference with personal rights, according to ECHR, is the legitimacy[676]. More precisely, existing legal ground approved by domestic legislative or judicial authorities must be implemented. And indeed, the Article 9(2)(j) of GDPR imperatively states that such exception must be in accordance with Article 89(1) and based on Union or Member State law. Article 89(2) of the GDPR allows processing sensitive data solely for archiving purposes in the public interest, scientific or historical research purposes or statistical purposes. For such reasons GDPR implementing legislative acts can also derogate from the right of access by the data subject,[677] the right to rectification,[678] the right to restriction of processing,[679] the right to object to processing of personal data.[680] However, all these exceptions and derogations must be established either in a new EU or national legislative act. As written in GDPR, research exception can be valid only when all its subject, purposes, scopes, and other questions are regulated in a new legal act.

It is very probable that the Member States will use the opportunity to derogate from general prohibitions to use sensitive data in the research field. For example, the UK Department for Digital, Culture Media & Sport has announced that derogation can occur if the "compliance [with GDPR specified obligations in relation to an individual's personal data] would seriously impair these organisations' ability to carry out research, archiving or statistics-gathering activities. <...> Research organisations will not have to comply with an individual's rights to rectify, restrict further processing and, object to processing where this would seriously impede their ability to complete their work, and providing that appropriate organisational safeguards are in place to keep the data secure."[681]

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676 The successful invocation of any of the legitimate purposes attaching to the second paragraphs of Articles 8 to 11 of ECHR is contingent upon compliance with two vital conditions: that the interference, or limitation, is prescribed by, or is in accordance with, law (the "rule of law test"); and that it is necessary in a democratic society in pursuit of one or more of the second paragraph objectives (the "democratic necessity test"). More on that in Steven Greer, 'The Exceptions to Articles 8 to 11 of the European Convention on Human Rights' [1997] Human Right Files 64. Available at http://www.echr.coe.int/LibraryDocs/DG2/HRFILES/DG2-EN-HRFILES-15(1997).pdf accessed 2018 May 8.

677 Article 15 of the GDPR.

678 Article 16 of the GDPR.

679 Article 18 of the GDPR.

680 Article 21 of the GDPR.

681 GOV.UK, 'A New Data Protection Bill: Our Planned Reforms Statement of Intent' 30. Available at: https://www.gov.uk/government/consultations/general-data-protection-regulation-call-for-views accessed 2018 May 8.

It is a negative feature of the research exception, that it is not entirely harmonized in the GDPR and the derogations must be made individually by the Member State or other EU legislative act. This situation is mainly due to an absence of conferred competency to the EU to harmonise legislation in the field of health and scientific research. The EU has only a support competency in these fields remaining principally regulated by national laws.[682] While there was hope for achieving a new level of harmonisation of EU data protection laws, general application rules, such as the right to be forgotten or the right to data portability, could not apply in the field of research, if contradicting EU or Member States laws are established.

The GDPR was introduced to create a coherent and robust framework of data protection. However, as seen through the derogations made possible by Article 89, scientific research is very much a national matter. The absence of harmonisation will lead to a decline in legal certainty and will make it hard for scientists to work internationally due to differing legislation. The possibility that data protection law differs from country to country can act as a blockade to share scientific data related to personal data and can hamper research.[683] First, a broad definition of scientific research in GDPR and second, the possible derogations by the Member States could lead to not so common implementation of GDPR as was foreseen by the legislator. Because derogations can differ from country to country, scientists or scientific organisations, including biobanks, can intentionally choose its place of business in countries where data protection rules are less strict. It can also lead to a form of 'forum shopping'.

The position of research and patient organisations, published on September 2016, encourages Member States to introduce clear laws for research with safeguards and exemptions that support research while respecting people's privacy.[684] In the position the invitation for states to work with national ministries and the research community to ensure that laws and guidelines are practical, proportionate to any risks, and build on current good practice. Another encouragement is to work together to promote

682 Gauthier Chassang, 'The Impact of the EU General Data Protection Regulation on Scientific Research' (2017) 11 E cancer medical science 11.

683 Danny Koevoets, 'The Influence of Article 89 GDPR on the Use of Big Data Analytics for the Purpose of Scientific Research' [2017] Tilburg Institute for Law, Technology, and Society Tilburg Law School 40–43.

684 Marie Timmermann and Beth Thompson, 'Implementing the General Data Protection Regulation [2016/679] to Maintain a Competitive Environment for Research in Europe. Position of Research and Patient Organisations'. Available at: https://www.scienceeurope.org/wp-content/uploads/2016/10/EU-GDPR-implementation-Sep-2016.pdf accessed 2018 May 8. The European biobanks' network – BBMRI-ERIC – is among 56 research institutions that signed the document.

harmonisation and compatibility between national systems where possible, to facilitate cross-border research.

Looking at the research exception of GDPR, it seems that biobanks can have considerable broad discretion in establishing its own rules for processing personal sensitive data for research purposes. Even public biobanks can use the research exception for their good and value. However, such capabilities must be ensured either by the national laws or the court precedents. So far, such legal acts or case law seems not to exist. Therefore, biobanks must be cautioned and not to contradict with the main principles of GDPR. As far as biobanks can positively manoeuvre between the rules of GDPR and take all the advantages of the research exception to achieve their goals and objectives, it should, however, keep the balance between individual rights and research objectives. Otherwise, it may overstep legal red lines. As will be presented in the next chapter, lack of sufficient informed consent or too broad informed consent can lead to a violation of privacy and data protection rules.

2.2. Anonymisation. To follow or refrain?

The use of otherwise protected personal data for research purposes also has additional conditions. Controllers that process personal data for research purposes must implement "appropriate safeguards" as established under Article 89(1) of GDPR. These controllers must put in place "technical and organizational measures" to ensure that they process only the personal data necessary for the research purposes, in accordance with the principle of data minimization.[685] When processing personal data for research purposes, Recital 33 informs that controllers should act "in keeping with recognised ethical standards for scientific research."

Article 89(1) provides that one way for a controller to comply with the mandate for technical and organizational measures is through the deployment of pseudonymisation. The GDPR gives the following definition of pseudonymisation – "the processing of personal data in such a manner that the personal data can no longer be attributed to a specific data subject without the use of additional information, provided that such additional information is kept separately and is subject to technical and organisational measures to ensure that the personal data are not attributed to an identified or identifiable

[685] According to the Article 5(1)(c) of GDPR, 'data minimisation' means data that is adequate, relevant and limited to what is necessary in relation to the purposes for which data is processed.

natural person."[686] Referring to the same action other legal documents or scientific literature are using such terms as deanonymisation, unlinked, de-identified, de-linked, confidential, etc.

Pseudonymisation means that the linkability of a dataset with the original identity of a data subject is reduced to a minimum. Pseudonymisation consists of replacing one attribute (typically a unique quality) in a record by another. However, the natural person is still likely to be identified indirectly; accordingly, pseudonymisation when used alone will not result in an anonymous dataset.[687] As pseudonymised data can be attributed to the data subject, it does not fall outside of the scope of data protection rules. Such data is still protected as somebody's personal information.

Pseudonymisation is different from anonymisation. According to the description of anonymisation, anonymised information should never be related to the data subject. If anonymised, the specimen in biobank cannot be related to the person from whom it was taken. Therefore, such specimens are not considered human subjects research objects and so the data protection rules generally do not apply. Anonymity can and still is a tool helping researchers to perform a more free, more open investigations on the samples. Non-identifiable information can be shared more widely between different biobanks. Norway's Health Research Act allows the use of research on anonymous human biological material and anonymous data without informed consent.[688] When data is anonymised, it means that researchers are not bound by strict informed consent requirements. Therefore, the anonymisation has a high significance.

Article 14 (c) of the International Declaration on Human Genetic Data[689] states that: „Human genetic data, human proteomic data and biological samples collected for the purposes of scientific research should not normally be linked to an identifiable person. Even when such data or biological samples are unlinked to an identifiable person, the necessary precautions should be taken to ensure the security of the data or biological samples." Recommendation Rec(2006)4 of the Committee of Ministers[690] to member states on research on biological materials of human origin supports the anonymisation of biological data. Article 3 of Appendix to the Recommendation states that anonymity is

686 Article 4(5) of GDPR.
687 Article 29 Data Protection Working Party, 'Opinion 05/2014 on Anonymisation Techniques' (2014) 14.
688 ACT 2008-06-20 no. 44: Act on medical and health research (the Health Research Act) 2008., para. 20.
689 UNESCO, 'International Declaration on Human Genetic Data' (2003).
690 Council of Europe Committee of Ministers, 'Recommendation Rec(2006)4 of the Committee of Ministers to Member States on Research on Biological Materials of Human Origin and Its Explanatory Memorandum' (2006).

achieved when a person cannot be identified "with reasonable efforts". Article 8 (1) promotes the anonymisation of biological materials and associated data as far as appropriate to the research activities concerned. Part 2 of the same Article, reads: "any use of biological materials and associated data in an identified, coded, or linked anonymised form should be justified by the researcher."

In the US an exemption No. 4 of the Common Rule is very relevant to biobanks. It reads as follow "Research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy: <...> (4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects"[691] (emphasis added). Recently, the new Final Rule[692] (amending Common Rule), did not adopt the proposal to require that also the research involving non-identified biospecimens be subject to the Common Rule. The Final Rule also does not require that consent be obtained to conduct such incognito researches.[693]

The US Health Insurance Portability and Accountability Act (HIPAA) sets forth a rule exempting data from the HIPAA's regulation if specific identifiers of the person are removed. If 18 criterion are removed, then data is treated as anonymous and data protection rules do not apply.[694] Another document in the US (in the form of Non-binding Recommendations) also expresses the opinion that unidentified biospecimen is not treated as one's personal information. The guidance document "Guidance on Informed Consent

691 45 C.F.R. § 46.101(b)(4). 88.

692 'Federal Policy for the Protection of Human Subjects (the Final Rule)' (2017) 82 Federal Register 7149.

693 U.S. Department of Health & Human Services, 'Final Rule Enhances Protections for Research Participants, Modernizes Oversight System' <http://wayback.archive-it.org/3926/20170127095200/https://www.hhs.gov/about/news/2017/01/18/final-rule-enhances-protections-research-participants-modernizes-oversight-system.html> accessed 8 May 2018.

694 De-identification "means that the identities of data subjects cannot be readily ascertained or otherwise associated with the data by the repository staff or secondary data users []; the 18 identifiers enumerated [in the HIPAA Privacy Rule] are removed; and the submitting institution has no actual knowledge that the remaining information could be used alone or in combination with other information to identify the subject of the data". Ibidem. The 18 identifiers that must be removed pursuant to HIPAA include names; addresses; dates relating to the individual (such as birth date and date of admission to the hospital), except for the year; telephone and fax numbers; email addresses; social security numbers; medical record numbers; health plan beneficiary numbers; account numbers; certificate/license numbers; vehicle identifiers and serial numbers, including license plate numbers; device identifiers and serial numbers; URLs; Internet Protocol (IP) address numbers; biometric identifiers, including finger and voice prints; full face photographic images and any comparable images; and any other unique identifying number, characteristic, or code". 45 C.F.R. para 164.514(b) (2)(i) (2007).

for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable"[695] allows research with tissues that were collected without consent if several conditions are met. The most important condition is that "The specimens are not individually identifiable, i.e., the identity of the subject is not known to and may not readily be ascertained". If the specimen is coded, it will be not be considered individually identifiable. Coded means that neither the researcher nor the sponsor nor any other person associated with the investigation can link the specimen to the subject from whom the sample was collected, either directly or indirectly through coding systems."[696]

In Europe, the rules of anonymisation seem to be stricter than in the US. The GDPR is applicable only to personal data that can be linked to an individual. Recital 26 of the Preamble of the Regulation informs, that "the principles of data protection *should not apply to anonymous information*, namely information which does not relate to an identified or identifiable natural person or to personal data rendered anonymous in such a manner that the data subject is not or no longer identifiable. This Regulation does not, therefore, concern the processing of such anonymous information, including for statistical or research purposes" (emphasis added).

However, the GDPR applies a different standard of reasonability when data is held anonymous. There is no list of identifiers that must be removed so that data is considered entirely unrelated to the data subject. The GDPR foresees that only when data cannot be identified by any means "reasonably likely to be used <...> either by the controller or by another person,"[697] such data is considered anonymous. Therefore, in Europe, when a researcher no longer has the ability to re-identify a data set, such data set may still be regulated under the GDPR if it could be re-identified with a reasonable effort.[698] No definition of what constitutes a "reasonable effort" is given in the Regulation. The term implies that an organisation has taken high standard, market-accepted approaches to reach a goal, but does not signify that organisation performed every available step. And to

695 U.S. Department of Health & Human Services FDA, 'Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens That Are Not Individually Identifiable' 1. Available at <https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071265.pdf> accessed 2018 May 8.

696 HHS Secretary's Advisory Committee on Human Research Protections, 'FAQ's Terms and Recommendations on Informed Consent and Research Use of Biospecimens' <https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2011-october-13-letter-attachment-d/index.html> accessed 8 May 2018.

697 Recital 26 of GDPR.

698 Gabe Maldoff, 'How GDPR Changes the Rules for Research' *International Association of Privacy Professionals* (2016). Available at <https://iapp.org/news/a/how-gdpr-changes-the-rules-for-research/> accessed 2018 May 8.

determine whether any means can possibly be used to identify the natural person, account should be taken of all objective factors, such as the costs of and the amount of time required for identification, taking into consideration the available technology at the time of the processing and technological developments (Recital 26 GDPR). As interprets the BBMRI-ERIC, anonymity is not a static term, but depends on context knowledge and 'all the means reasonably likely to be used' to re-identify the individual behind a data record.[699] Whether information qualifies as anonymous, is always evaluated on a case-by-case basis, requiring a risk assessment. Most important is to consider the objective factors (such as the costs of and the amount of time required for identification, the available technology at the time of the processing and technological developments) when deciding whether this standard is sufficed in practice.

The evaluation if the data processing institution did take all "reasonable effort" in de-identification of data, will most likely be explained by the precedents of the highest European courts on a case by case basis. Unfortunately, till today no case law on this subject in the field of genome research is found.

Article 29 Data Protection Working Party (WP) has given a relevant opinion to the anonymisation questions in Anonymisation Techniques[700] document. In the official documents, WP examines the effectiveness and limits of anonymisation techniques and places them in the context of data protection law. In its Opinion, the WP analyses the effectiveness and limits of existing anonymisation techniques against the EU legal background of data protection and provides recommendations to handle these techniques. An important message is delivered, that a criterion to be applied in order to assess whether the anonymisation process is sufficiently robust, is to assure that identification has become "reasonably" impossible. The documents also raise the issue, that research, tools and computational power evolve and therefore, it is hard to provide an exhaustive enumeration of circumstances when identification is no longer possible.

The document raises privacy concerns about publicly accessible genome data. Genetic data profiles are an example of personal data that can be identified if the sole technique used is the removal of the identity of the donor. The combination of publically available genetic resources (e.g. genealogy registers, obituary, results of search engine queries) and the metadata about DNA donors (time of donation, age, place of residence)

699 BBMRI Common Service ELSI, 'The EU General Data Protection Regulation. Answers to Frequently Asked Questions 1.0' 1.

700 ibid.

could reveal the identity of unique individuals even if that DNA were donated "anonymously". WP is referring to the experiment of US researchers and hackers who managed to expose the identity of 50 individuals whose DNA was donated anonymously for scientific study through consortiums such as the 1000 Genomes Project.[701]

Another study showed that individuals whose genomes were in seemingly anonymous pools of DNA data could be identified by specific genetic markers, known as single nucleotide polymorphisms, or SNPs.[702] This re-identification of a donor was the first time when people have been identified without needing a sample of their DNA as a reference and having only the extracted genetic markers from DNA sequences from a research database plus using freely available internet tools and search engines.

The unprecedented amount of publicly available online and offline information leads to sharp criticism towards the achievement of effective anonymisation. With big data, almost all information will become personal data due to its potential ability to identify natural persons. For researchers working with 'anonymized' data, this can create legal uncertainty about whether they have to adopt data protection principles in their processing.

2.2.1. Deficiencies of anonymisation

The problem with anonymisation is evident – the information still can be in one way or another disclosed. It is sometimes debated that in the strict sense absolute anonymity can never be achieved, because theoretically, genetic samples and data can be re-attributed to the donor.[703] So even if biobanks' can exploit the anonymisation exception and taking all the "reasonable effort" can bypass data protection laws, in practice, the absolute anonymity seems to be hardly reachable and the possibility that one day somebody will disclose the human subject behind the sample remains entirely possible.

However, it is not the only deficiency of anonymisation. Anonymity is not always desirable. Anonymity means that data subject can never be recontacted. Moreover, this causes a few crucial problems – first, a person cannot be contacted regarding the research

[701] J Bohannon, 'Genealogy Databases Enable Naming of Anonymous DNA Donors' (2013) 339 Science 262.

[702] Jennifer Couzin, 'Whole-Genome Data Not Anonymous, Challenging Assumptions' (2008) 321 Science 1278.

[703] L Caenazzo, P Tozzo and R Pegoraro, 'Biobanking Research on Oncological Residual Material: A Framework between the Rights of the Individual and the Interest of Society' (2013) 14 BMC Med Ethics 3.

results, second, the research participant cannot withdraw from research and third no further information can be collected if needed for biobank's studies.

Some guidelines recommend that using or providing identifiable data should be avoided, others that researchers balance the gains for privacy with the implications for the scientific enterprise, including the possibility of the validity of results. Anonymisation can affect other participant interests. The first problem affects the research subjects, people who donate the samples. If the tissue sample is irreversibly anonymised and no information regarding the donor can ever be obtained from it, the privacy of the donor is protected, but the results cannot be returned because it is impossible to link the data with the donor.[704] Therefore, some authors argue, that complete anonymisation of data and biospecimens should be avoided, based on the principle that this would preclude re-contacting donors and data subjects to communicate future medical discoveries that may benefit them.[705] Anonymisation may also prevent or complicate the participant's right to withdrawal the samples. It is also impossible to re-contact of the donor to collect additional information.

The second problem is that when data is anonymised the research participant cannot withdraw from a research. Withdrawal is a general right granted to the participants to reject their samples being used for the following studies or forbid using the samples in the ongoing research (more about withdrawal will be explained in the following chapter). If a participant cannot be reconnected with the sample he donated, it is impossible to remove such samples from a biobank's database.

Moreover, a third problem is more important for the scope of the research as such. Since biobanks require an ongoing contribution from the potential research subjects, additional samples, or at least health information and possible lifestyle data, need to be collected over an indefinite period of time. It becomes apparent, that in this situation complete anonymisation of data is impossible, as this would prevent new data being collected and linked with already collected tissue samples or genome-based information needed for ongoing or future researchers. In particular, anonymisation could bar research efforts to achieve translation of research findings into clinical care and treatments.[706] If a need for a new use of the sample occurs or a need to provide a researcher with some additional information, that will enable more accurate analysis of the research outcome,

704 ibid.

705 Deborah Mascalzoni and others, 'International Charter of Principles for Sharing Bio-Specimens and Data' [2015] European Journal of Human Genetics 722.

706 UNESCO, 'International Declaration on Human Genetic Data' (2003).

the anonymisation of data would prevent from improving research. Presume, that for a researcher investigating the possible reasons for a particular disease, information if research participants are smokers is very relevant. If at a time the information was collected, this question was not included in the participation forms, and the participants are anonymised, a researcher cannot finalise the research, or the findings of the research might be false.

The other side of the coin is that the research participants not necessarily are against recontacting. If recontacting is related with a request to add some additional information or to take a new tissue sample for new research, many donors assumedly will provide such information and samples to assist the research. A study published in 2008 found that in general research participants from different jurisdictions (including from the US) do not favour irreversible anonymisation of samples and data. Several respondents admitted that in the biobanks case such anonymisation would preclude the realisation of the study purpose, which includes adding follow up data related to the health of patients and their family members.[707]

Because of all these reasons, pseudonymisation looks like a better way to process research participants' data and samples in biobanks than total anonymisation. The use of a code, to protect personal data is more favourable mean to process personal data in the biobanks than anonymisation. When data is pseudonymized, the donor can be re-identified by the biobank operators using a specific code.[708]

There seems to be a widespread agreement among researchers that biobank-based research should be carried out on samples and data that are coded (or double-coded), and that the code should be broken only in exceptional cases (this is in line with requirements from UNESCO). The information can be decoded only when there is a specific legitimate need for such action, such as a need for new data when carrying out longitudinal studies, and in the context of meta-analysis (to avoid counting individuals twice).[709] Coding also has significant advantages when the need to use samples for the secondary purpose arise. The scientific usefulness of the samples can be kept for a much longer period, since coded information assists for further clinical data to be added to the database, as tracing the sample back remains possible.[710]

[707] Bernice Elger 'Anonymization and Coding' in Bernice Elger and others (eds), *Ethical Issues in Governing Biobanks: Global Perspectives* (Routledge 2008) 172–183.

[708] ibid.

[709] ibid.

[710] Bartha Maria Knoppers, Madelaine Saginur and Howard Cash, 'Ethical Issues in Secondary Uses of Human Biological Materials from Mass Disasters' (2006) 34 The Journal of Law, Medicine & Ethics

The UK Biobank's internal rules ensure pseudonymisation of samples. All identifying information is held centrally by UK Biobank in a restricted access database that is controlled by senior UK Biobank staff. Only a few people within the UK Biobank have access to the "key" to the code for relinking the participants' identifying information with their data and samples. The UK Biobank admits that is important to retain this link with identifying information to allow follow up of participants' health or to eliminate redundant data (e.g. duplicate cases). The pseudonymisation also helps to verify correctness and completeness of data against original records or to establish correct linkages among databases and to find specific data or samples if participants withdraw.[711]

Lars Oystein Ursin[712] writes that the participants choice to deanonymize their data is strongly affected by the general society's view on the biobanks. Providing the genetic information must firstly be morally approved in society to make legitimate recruitment to biobank research possible. Of cause, it would be easier for researchers if they could use anonymised data without any need to receive consent from the research participants. However, as the anonymisation has drawbacks and pseudonymisation still seems to fall under the data protection rules, biobanks must stick to the requirements of informed consent and should use collected data in conformity with ethical standards and take caution not to violate privacy rules.

In general, biobank's are acutely aware of data protection regulations and so, being afraid to step on some prohibitions, are working actively to collect data properly and have all the authorised permissions from the research participants. Firstly, and most importantly, authorized permission must be received from the data donor. Such permission is titled as the informed concept doctrine and is widely and broadly regulated from international to internal legislative rules.

II. Informed consent doctrine. Opt-in or opt-out?

The personal data protection correlates with informed consent inseparably. If there is informed consent from the data subject that he/she agrees to donate the samples for a particular research purpose, no violation of data protection rights would normally occur. For thousands of years, physicians felt-that deception was an integral part of the practice

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711 UK Biobank Ethics and Governance Framework 2007 1, pt C.2.

712 Lars Oystein Ursin, 'Privacy and Property in the Biobank Context' (2010) 22 HEC Forum 211.

of medicine. Over the last 150 years, the concept of physicians establishing a "standard of care" has gradually been replaced by the idea that the well-informed patient can be the master of his/her body.[713] Thus, the practice of informed consent has emerged in mainly all spheres of medical treatment, including sample donation for research.

Informed consent is essential in biobanks. If not anonymised, all data must contain a legal document stating that its donor had agreed to give the sample for a specific purpose. In the 1950s when Henrietta's cells grew, the notion of informed consent that we have today did not exist. Back in those days, people were routinely participating in research even without their knowledge. A lot has changed, and today biobanks are taking good care to have consent of the research participant for all the studies the cell is going to be or will be used.

The beginning of informed consent was ambiguous and vague. Some research institutions used the techniques to collect samples for research purposes without first receiving patient's consent. Such collection of information and data is called "opt-out" (or presumed consent) mechanism. Opt-out means that person's samples can be collected and used unless the data subject specifically expresses, that he/she does not wish that his/her data is collected for research purposes. This rule mainly applies to residual samples. Residual samples refer to tissue that was taken in the course of clinical care and is leftover (e.g., a diagnostic biopsy or therapeutic removal of tissue).[714] It was one of the main characters of Iceland Act on a Health Sector Database, no 139/1998 (the HSD Act).[715] The consent in the democratic community was employed in Iceland to authorized the collection and use of the Icelandic population's samples and data.[716] This approach assumed every individual's consent to the future use of their samples and materials. Article 8 of the HSD Act established an opt-out mechanism by stating the following: "A patient may request at any time that information on him/her not be entered onto the health-sector database." At the time the Act was introduced, this was undoubtedly one of the most significant innovations in the consent field.[717]

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713 Peter M Murray, 'The History of Informed Consent' (1990) 10 The Iowa Orthopaedic Journal 104.

714 Noor AA Giesbertz, Annelien L Bredenoord and Johannes JM van Delden, 'Inclusion of Residual Tissue in Biobanks: Opt-In or Opt-Out?' (2012) 10 PLoS Biology.

715 Icelandic Act on a Health Sector Database No 139/1998.Icelandic title: *Lög um gagnagrunn á heilbrigðissviði*. Original document available at <https://www.althingi.is/lagas/139a/1998139.html> accessed 2018 May 8.

716 Vilhjálmur Árnason and Garðar Árnason, 'Informed Democratic Consent? The Case of the Icelandic Database' (2004) 8 Trames 164.

717 Ants Nõmper, 'Open Consent – A New Form of Informed Consent' [2005] PhD dissertation, University of Tartu 25.

However, the "opt-out" mechanism was later found inadequate to protect personal rights. The similar opt-out mechanism was used by "Care.data" project in Great Britain.[718] "Care.data" relied on an opt-out for legitimacy. Unfortunately, reviewing project's arrangements because of the widespread concerns related to consent led to the cancellation of the "Care.data" project. The critical issues that were distinguished included the lack of information about "Care.data" that made exercising an opt-out a vague process, the defective mechanisms for opting, and the failure of protection for rights and access to the National Health Service (NHS) for those who opt out.[719]

Article 29 Working Party indicated that opt-out is not acceptable for the processing of sensitive data, including health-related data. The requirement for explicit consent means that consent that is inferred will not typically meet the requirement of informed consent. In this regard, it is worth recalling the Article 29 Working Party opinion on electronic health records stating that „In contrast to the provisions of Article 7 of the Directive, consent in the case of sensitive personal data and therefore in an EHR must be explicit. Opt-out solutions will not meet the requirement of being 'explicit'."[720]

With the increase of requirements to protect personal data, the consent in most jurisdictions must be explicit and informed. The "opt-out" method seems not to comply with GDPR. Recital 32 states that "Consent should be given by a clear affirmative act establishing a freely given, specific, informed and unambiguous indication of the data subject's agreement to the processing of personal data relating to him or her, such as by a written statement, including by electronic means, or an oral statement. <...> *Silence, pre-ticked boxes or inactivity should not, therefore, constitute consent.* Consent should cover all processing activities carried out for the same purpose or purposes. *When the processing has multiple purposes, consent should be given for all of them.* <...>" (emphasis added).

The explicit and informed agreement given by the data subject, and used today in most of the biobanks, is called "opt-in" consent. In "opt-in" system the consent must be expressed and written. Such donation system is established in mostly all other European

718 Thomas Meek, 'Caldicott: Care.data Hangs on Engagement' <https://www.digitalhealth.net/2015/10/caldicott-care-data-hangs-on-engagement/> accessed 8 May 2018.

719 John Mark Michael Rumbold and Barbara Pierscionek, 'The Effect of the General Data Protection Regulation on Medical Research' (2017) 19 Journal of Medical Internet Research.

720 Article 29 Data Protection Working Party, 'Working Document on the Processing of Personal Data Relating to Health in Electronic Health Records' [2007] EHR.

states.[721] The Spanish Law 14/2007 on Biomedical Research[722] also requires the expressed consent. However, the initial act of consent might include consenting to further, related but unspecified uses of the samples. The law allows that specific act of consent to include consenting to the use of data and samples in other research projects, "related to the one initially proposed", by the same team or another one (Article 60.2).

The "opt-in" system can be used when talking about: (1) biobank storage for its use in any biomedical research project; (2) preservation as a collection for the purpose of biomedical research in a specific line of research; and (3) use in a particular research project.[723] If the sample collection has several purposes (use in a project and later storage in a biobank), these can be stated in the same document, ensuring that the participant has a possibility to give an independent consent for every purpose.

"Opt-in" consent seems to be equal to informed consent doctrine. Its requirements: voluntariness, adequate information, right to refuse and withdrawal, were codified in the Declaration of Helsinki.[724] Rule 25 to 32 of the Declaration is dedicated to the informed consent. The primary goals of the Declaration are to established a rule that no individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees. Even if exceptions exist, the main rule rarely can be violated.

In the case law of the European Court of Human Rights, a considerable distinction is made between the choices of justification when processing sensitive data. In M.S. v. Sweden,[725] the Court found that the lack of consent of the data subject to the disclosure of certain sensitive data was a key element in the finding of an infringement of Article 8 (the right to privacy) of the European Convention on Human Rights. Accordingly, the plaintiff's consent would have served to waive the existence of an infringement (§34-35 of the case). Thus, if consent is given according to GDPR requirements established in Article 9(2)(a), there is no interference with the data subject's rights. If a public interest is claimed according to GDPR Articles 9(2)(b)-(j) there is an interference, but it simply has a justification which overrides the individual rights. In human rights law, if the same result can be achieved with less impact on an individual's rights, this option must be chosen. Thus, in relation to the underlying rights at stake, if consent can be obtained – and

721 Pilar Nicolás, 'Spanish Regulation of Biobanks' (2015) 43 Law, Medicine and Ethics 812.
722 Ley 14/2007, de 3 de julio, de Investigación biomédica 2007 (BOE nú m) 28826.
723 Nicolás 810.
724 World Medical Association, 'WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects'. Rule 25-26.
725 *MS v Sweden [1997] ECHR No 20837/92*.

in the biobanking it can – this is the ground under Article 9(2) which should be relied upon.[726]

The international and territorial legal acts have established the necessity of informed concept in the medical research field. Article 5(a) of the 1997 Universal Declaration on the Human Genome and Human Rights establishes that: "Research, treatment or diagnosis affecting an individual's genome shall be undertaken only after rigorous and prior assessment of the potential risks and benefits pertaining thereto and in accordance with any other requirement of national law." Part 5(b) adds: "In all cases, *the prior, free and informed consent of the person concerned shall be obtained*. If the latter is not in a position to consent, consent or authorization shall be obtained in the manner prescribed by law, guided by the person's best interest."

Oviedo Convention's Article 5 states that medical intervention may only be carried out if the subject gives his or her free and informed consent, and is also given the right to withdraw his or her consent. GDPR defines consent as "any freely given, specific, informed and unambiguous indication of the data subject's wishes by which he or she, by a statement or by a clear affirmative action, signifies agreement to the processing of personal data relating to him or her."[727] The new conditions for consent have been strengthened in the GDPR, and companies will no longer be able to use long terms and conditions full of legal language, that donors are unfamiliar. The purpose of data processing will need to be explicitly stated or attached to that consent. The requirements for the consent and easy withdrawal are stated in Article 7 of the GDPR. The first requirement is that consent must be clear, second – distinguishable from other matters and third, provided in an intelligible and easily accessible form, using clear and plain language.

The consent requirement is related not only to the collection and use of the sample but also to other information about a donor. The consent must be collected to use such information as lifestyle, habits, diseases, and also to use the processed data: DNA sequence, description on findings, organisms and fine-scale genetic mapping, single nucleotide polymorphism (SNP), ribonucleic acid (RNA) molecules and other. Therefore, the consent follows the sample together with all data related to it, including finding or sequenced DNA code that gives much useful knowledge for the researchers.

[726] Dara Hallinan and Michael Friedewald, 'Open Consent, Biobanking and Data Protection Law: Can Open Consent Be "informed" under the Forthcoming Data Protection Regulation?' (2015) 11 Life Sciences, Society and Policy 9.

[727] Article 4(11) of GDPR.

Donors usually have an interest in who and for what purpose will use their samples. Therefore, donors shall trust the biobank they are participating in. From the legal point of view, I see the informed consent document as an agreement between the data subject and the institution processing personal information. One party of such document is data donor, another party – a biobank, and both of them has duties and obligation.

As we saw before, the legal regulation of biobanks is very fragmented, composed of international soft law instruments, or national legislation. But not even all countries have national legal acts explicitly dedicated to biobank activities. As there is no standard regulation, there is also no single rule how the consent form in the biobanks should look like, and what questions it must include. As far as the informed consent form does not contradict main principles established in international or national legal acts, every biobank is free to prepare their consent form according to their understanding and needs.

The consent requirement is understandable, and the protection of privacy is crucial. The biggest problem is not about the doctrine of informed consent as such, but with the limitations such consent form creates. First, once the informed consent form is signed, it cannot be changed, amended or its scope broadened. Second, different consent forms put a legal burden to share samples between biobanks. The informed consent doctrine in biobanks must ensure a balance between the individual's rights and the interest of society from the perspective of a common good.

1. Costs of informed and explicit consent

The first problem with informed consent is that there is a high demand for different informed consent templates, as for every new research project a new form must be prepared. Once the informed consent form is signed, it already puts limitations on samples' use and reuse. Application of informed consent and explicit consent requirements to population genetic databases faces severe difficulties since all possible research uses and researchers cannot be anticipated at the point when biological materials and data are collected. The informed consent documents are commonly signed for an explicit research purpose (eg. cancer studies). If a need for different research using the same data occurs, there is a necessity to recontact the donor and ask for a new consent. Moreover, what if there is no possibility to recontact the person?

As described before, if data is anonymised, the donor cannot be recontacted. Same applies if a donor has died, and his/her consent is given only to limited research. Even if the donors can be recontacted, imagining that some research uses tens or hundreds of samples, such recontacting becomes hardly possible and the costs of the research increase dramatically. Such situation creates a significant administrative burden for a biobank and also requires additional financial expenses (administrative costs, legal assistance, etc.). As an outcome, new essential research studies can never be started just because it becomes impossible to ask people if they wish to participate in a study.

The concept is that the biobanks' consent forms cannot be dynamic or general, but must clearly and narrowly indicate the research purpose. Costs related to preparing documentation and acquiring informed consent for every new research might prohibit researchers from setting up small and midsize biobanks. And when we look at the biobanks as at medical research institutions leading to public health benefits, and creating other intangible values, like public trust in health care, respect for citizens' privacy,[728] informed consent doctrine should not become an obstacle.

The informed consent must be specific. Which means that a person must be informed and must sign the document where all the uses of the sample are indicated. UBC CREB Biobanking Consent Form Template[729] proposes to include a short description about a particular study the samples are going to be used. The form explains the goal of the primary study (such as "One goal of the optional studies is to figure out why Drug X may work better in some people than others"), indicates the study title. The University of the Basque Country in its "Guide for the elaboration of documents"[730] for the investigations of biological materials, indicates that informed consent document must include a full description of the project (objectives of the study, duration of the study, place of the study, etc.).

The main idea is that a person who agreed that his samples are used for cancer research has not agreed that the same sample is used for heart disease research, or mental illnesses research, or similar. It is particularly relevant when the samples are collected at the medical facilities, rather than the premises of a population biobank. When population

728 Tobias Schulte, INDEN Bäumen and Daniele Paci, 'Data Protection and Sample Management in Biobanking – A Legal Dichotomy' (2010) 6 Policy 42.

729 'The Clinical Research Ethics Board of University of British Columbia Consent Form Template' <https://ethics.research.ubc.ca/sites/ore.ubc.ca/files/documents/Biobanking_Consent_Form.docx > accessed 8 May 2018.

730 Universidad del Pais Vasco, 'Guía Para Elaboración de Documentos' <https://www.ehu.eus/documents/2458096/2528821/CEISH_gia_elaboracion_CI.pdf> accessed 8 May 2018.

biobank collects samples from the people directly, it may ask donors for a broader use of tissues, however, disease biobanks are very much dependent on the medical centre's support. Such smaller biobanks, researching about specific rare disease are dependent on samples and data collected at the hospitals. If hospitals use very strict and narrow consent forms, later such smaller biobanks can be prevented from using same samples for modified research goal.

Even the UN International Bioethics Committee in its recommendations have stated that "it is essentially impossible to give donors specific information on the potential future use of their samples and data stored in a biobank as new technological advances are likely to provide totally new approaches regarding analysis of old samples and so a change of research on these samples. It is why informed consent, building on the premise of the respect for individual autonomy and self-determination, can also entail consent for broader future use of the samples and data."[731]

The problem with the narrowness of the informed consent is real. The UK Biobank analysed that there might be a *prima facie* case for treating tumour tissue as part of a participant's 'health record' (the tissue is used to look at molecular signatures of tumours. The existence of tumour tissue using information from people participating in biobank who had cancer can possibly help to identify different tumours and find risk factors only by looking at the genetic profile). However, the problem was raised that UK Biobank shall evaluate the scientific utility of the samples, along with consideration of the practical challenges. As one of the main challenges was pointed that the participants might well have given (or refused to give) consent for further research when they had the tissue removed in the clinical setting and samples would only be released if the patient consented for such specific use.[732] It would be a considerable manual effort to collect these consent records, check them, and use only the samples that have consent, while not use the ones, which do not.

Biobanks cannot choose on their own and use samples if the specific consent for a particular use is not given. This responsibility to use samples only for the purpose the consent covers bounds researchers and investigators. If a biobank approved research broader that the consent is given, it would infringe legal regulations and personal rights of donor, precisely the same situation like the use of the samples without any consent at all.

731 International Bioethics Committee, 'Report of the IBC on Updating Its Reflection on the Human Genome and Human Rights' (2015) 19.

732 UK Biobank Ethics and Governance Framework 2007 11.

An example of such situations is the Havasupai case in the US. The members of the Havasupai Tribe brought claims against the Arizona Board of Regents (ABOR) and other defendants arising out of the alleged misuse of blood samples. The samples were taken from the tribe in the early 1990s. The members claimed an invasion of their personal privacy and the cultural and religious privacy of the Havasupai Tribe.[733] The story begins when the Arizona State University ("ASU") researchers initiated research to discover if diabetes among tribal members was a genetical disease, created a script for presenting the blood-draw proposal to the Havasupai and also prepared informed-consent documents for the diabetes research. Blood samples were taken from more than 200 Havasupai.

Despite the fact that initial idea and the given consents were for the use of the collected blood samples to test diabetes, the samples were used for other purposes. In ASU and elsewhere, researchers continued to perform research and publish articles based on data from tribal members' blood samples. Some of the papers generated from the blood samples dealt with schizophrenia, inbreeding and theories about ancient human population migrations from Asia to North America. The latter body of work is contrary to the Havasupai belief that, as a people, they originated in the Grand Canyon.[734] Furthermore, ASU distributed Havasupai blood samples to third parties, which in turn performed additional genetics experiments using tribal members' confidential blood data. Havasupai tribe members brought to the court ABOR, ASU and others who used the samples infringing the scope of the informed consent given.

The court concluded that "although the Tribe's notices do not describe the nature of the injury incurred, *invasions of privacy relating to tissue samples such as the Tribe described in its claim notices naturally give rise to the subjective personal injury, even when, as here, the samples are given voluntarily* (emphasis added)."[735] The court added that "dignitary torts" such as those alleged by the Tribe do not require proof of physical manifestation of injury.[736] Therefore, the defendant was liable without any proof of physical or mental distress.

Neither the court nor the defendants brought an argument that the use of the samples was for the purpose of the public good. Indeed, the use of tribe members' blood samples lead to a new research analysis, assisted to anthropology studies. There was no analysis in

733 *HAVASUPAI TRIBE OF HAVASUPAI RESERVATION v ARIZONA BOARD OF REGENTS, Nos 1 CA-CV 07-0454, 1 CA-CV 07-0801 (November 28, 2008)*.
734 Ibid. para. 4.
735 Ibid. para. 43.
736 Ibid. para. 48.

the case if such use of the samples without consent could be lawful for the reasons of the public good.

The traditional concept of consent is unnecessarily restrictive for the biobanks. It looks like the stringent requirements of the traditional concept of consent in medical research stand in direct denial of the prospective collection approach – the requirement to specify specific research in advance is standing in the way of achieving highest research benefit from collected samples.[737]

2. Limitations on data sharing

The second problem caused by different consent forms and requirements is that it can become a burden to share samples between biobanks. The differences between informed consent documents and data protection laws can become a burden to share samples between biobanks. As already noted, biobanks are research institutions having a great variety of tools and knowledge about diseases and their causes. It is essential that biobanks could share data with other biobanks and not to repeat each other's findings or not to collect same data, as another biobank has already collected. It is common sense to affirm that to reinvent what has been already invented is at best a waste of time. To double the monetary, temporal, and human investment, in order to re-implement what already exists, is a clear system inefficiency, especially from a purely scientific standpoint. Informed consent is a standard ethical requirement in medical research and thus applies also to biobank-based research.[738] The consent requirements and related procedures vary widely among biobanks, depending on the national laws and guidelines applied, which may pose difficulties for collaborative research.

This problem can occur not only when sharing of samples or data is between biobanks from different countries, but also between biobanks established in the same country. A study from 30 German biobanks illustrated that consent documents differ widely in the range of issues that they address.[739] Only 50% of participating biobanks in their consent forms informed participants about possible future developments and changes, and only 20% mentioned the sharing of data and materials with other

[737] Dara Hallinan and Michael Friedewald, 'Open Consent, Biobanking and Data Protection Law: Can Open Consent Be "informed" under the Forthcoming Data Protection Regulation?' (2015) 11 Life Sciences, Society and Policy 4.

[738] ibid.

[739] Irene Hirschberg, Hannes Knuppel and Daniel Strech, 'Practice Variation across Consent Templates for Biobank Research. A Survey of German Biobanks' (2013) 4 Frontiers in Genetics 1.

researchers/policy and process and the possible International cooperation/trans-border use. Only 12 German biobanks from 30 think about sharing their donors' samples and data with other biobanks inside or outside Germany. As an example can also be taken the consents forms of two biobanks in the UK. The Avon Longitudinal Study of Parents and Children (ALSPAC) is a longitudinal cohort study which has been charting the health of 14,500 families in the Bristol area since the early 1990s. In its consent form, ALSPAC informs the donors that any information will be kept confidential and used for ALSPAC research purposes only.[740] The consent form of the Wales Cancer Bank, collecting tissue and blood from patients where cancer is a possible diagnosis, informs the participants that medical information may be passed to other organizations involved in the research (keeping the data confidential).[741] The consent forms of these two institutions are so different, that Wales Cancer Bank could never receive samples from ALSPAC, even if both biobanks operate in the same country under the same legal provisions.

Of cause, much more significant dissimilarities arise between biobanks from different countries. Sharing of personal data is a form of data "processing" following national and international regulation such as GDPR in EU or HHS Regulations for the Protection of Human Subjects and the Health Insurance Portability and Accountability Act (HIPAA), Privacy Rule in the US. Data sharing in biobanks must comply with the data protection laws.

Before 2015, the biobanks in Europe could send the data to US entities under the Safe harbour provisions. European Commission's Decision 2000/520[742] based on the Article 25(6) of Directive 95/46, foresaw that "The adequate level of protection for the transfer of data from the Community to the United States recognised by this Decision, should be attained if organisations comply with the safe harbour privacy principles for the protection of personal data transferred from a Member State to the United States" (Recital 5 of the Decision). However, on October 6, 2015, the Court of Justice of the European Union ruled that the Decision 2000/520 is invalid.[743] As a result of the decision, EU

740 'University of Bristol Consent Form of 2012' <http://www.bris.ac.uk/alspac/external/playyourpart/consent-form.pdf> accessed 8 May 2018.

741 'Wales Cancer Bank Consent Form for Patient, Version 8 (2016)' <https://www.walescancerbank.com/getfile.php?type=site_documents&id=Patient Consent v8.pdf> accessed 8 May 2018.

742 Commission Decision 2000/520/EC of 26 July 2000 pursuant to Directive 95/46/EC of the European Parliament and of the Council on the adequacy of the protection provided by the safe harbour privacy principles and related frequently asked questions issued by the US Department of Commerce, Official Journal L 215.

743 *C-362/14 Maximillian Schrems v Data Protection Commissioner [2015] ECLI:EU:C:2015:650.*

biobanks, registries and researchers who transfer personal data (which under the circumstances could include coded or pseudonymised data) of EU citizens to the United States can no longer validly do so on the basis of the Safe harbour provisions.

BBMRI-ERIC suggested that the BBMRI members would advise all associated biobanks and principal investigators to check whether they operate under the Safe harbour provisions. If they were working under the provisions of the Decision, they can no longer validly do so and must construct their transfers of personal data of EU citizens to the US on another legal ground, such as informed consent or the use of contractual clauses.[744]

The study performed by M. Capocasa[745] and others revealed that most of the surveyed biobanks adopted specific legal frameworks that researchers should take into consideration to gain access to samples and data. The information collected highlighted that biobanks follow different standards and procedures regarding the sharing of their biological samples and data. The different modalities of resource accessibility seem to be highly influenced by social context and legislation of the countries where the biobanks operate. In the European context, privacy laws make the possibility to reuse data and samples extremely difficult. GDPR Recital 33 notes, that data subjects should have the opportunity to give their consent *only to certain areas of research* or *parts of research projects* to the extent allowed by the intended purpose. Furthermore, GDPR seems to protect the free flow of health-related information within the Union, but clearly leaves the regulation of the flow of such information between the Member States and the third countries to the national laws. Recital 53 states that the Member States can maintain or introduce further limitations, concerning the processing of genetic data, biometric data or data concerning health. However, this should not hamper the free flow of personal data within the Union when those conditions apply to the cross-border processing of such data. So even if European biobanks could raise objections against biobanks implying more restrictive criterion than GDPR in the data sharing, it could hardly be used by the US or other third country's biobank.

Furthermore, GDPR puts confirmation requirement for third countries, to provide evidence that such country has appropriate data protection rules. The first way of such confirmation is when the Commission monitors a third country and later approves in the

744 Jasper Bovenberg and Irene Schlünder, 'The Court of Justice of the European Union Has Declared the Transfer of Personal Data to the US on the Basis of "Safe Harbour" Invalid – What Is the Impact of This Ruling, If Any, on European Biobanks?' [2015] BBMRI CS ELSI Newsletter.

745 Marco Capocasa and others, 'Samples and Data Accessibility in Research Biobanks: An Explorative Survey' [2016] PeerJ.

implementing act that the level of data protection is adequate (procedures regulated in GDPR Article 45). If any third country is not in the Commission's list as ensuring the adequate data protection, a controller or processor may transfer personal data to such third country only if the controller or processor has provided appropriate safeguards, and on condition that enforceable data subject rights and effective legal remedies for data subjects are available (GDPR Article 46). Such safeguards can be given in the form of legally binding instruments, binding corporate rules, standard data protection clauses adopted by the Commission, or other means established in GDPR.

As the regulations of sensitive personal data are different in US and Europe, it leads to a problem of data sharing between these countries biobanks. The US laws give broader powers to the ethical committees to allow to use data without informed consent. Under the HIPAA Privacy Rule, covered entities may use or disclose protected health information from existing databases or repositories for research purposes either with individual authorization (as required at 45 Code of Federal Regulation §164.508 „Uses and disclosures for which an authorization is required"), or with a waiver of individual authorization (as permitted at 45 Code of Federal Regulation §164.512(i) „Uses and disclosures for which an authorization or opportunity to agree or object is not required").

US law clarifies the ways and means how the waiver of individual authorisation may be done and data used without person's consent. The HIPAA Privacy Rule requires documentation of waiver approval by either an Institutional Review Board (IRB) or a Privacy Board. A possibility of waiver is also foreseen in OECD Guidelines on Human Biobanks and Genetic Research Databases. Article 4.5 of the Guidelines reads as follow: "Where subsequent use of human biological materials or data is envisaged that would not be consistent with the original informed consent, a new consent should be obtained from the participant or from the appropriate substitute decision-maker, ***or a waiver of consent should be obtained from a research ethics committee or an appropriate authority, in accordance with applicable law and ethical principles pertaining to the protection of human subjects*** (emphasis added)." The European law does not prohibit broader consent in the research field, but if an explicit consent is given for a single use, no other use of the data can be made. From the stated case law of the European courts, it seems unlikely that biobank's research purposes could override the general requirements to protect personal data and individual's privacy.

It causes a problem – if data is collected in Europe and the consent is given only to a specific purpose, and such data is needed for a US biobank to perform a different study, European biobank should refrain from sharing the samples and information with US entity. If the processing data for another purpose is not compatible with the purpose for which the personal data are initially collected (the compatibility test[746] under GDPR), further processing is not allowed or will have to rely on a separate legal basis (e.g. re-consent of the individual). The biobank is held responsible for relying upon data protection rules and must ensure that the privacy of a participant (human subject) is protected following all applicable laws, regulations and policies.

Protections and restrictions of using personal data are substantial and essential. However, one must agree that researching a disease on individual's samples are much less harmful than direct medical interventions. The diversity exists in the literature on the importance associated with the informed consent in research using human biological materials compared with research carried out directly on the subject. The reason for this is related to three principal factors: the minimal risk of direct physical harm involved in biological research; the possibility to anonymise material; and the opinions and attitudes of research participants, who occasionally do not perceive informed consent as an important issue and do not read information provided to them.[747]

A patient must exert his/her autonomy when choosing whether to accept to undergo treatment, as well as to enter a clinical trial. However, when research is done retrospectively on patient's data and remaining tissues (i.e. tissues which have not been explicitly collected for research purposes but are left over after all clinically useful diagnostic assessments), there are wide disparities as to whether a patient's consent is needed.[748] Consent is essential for clinical or behavioral studies that amount to experimentation in which participants are asked to voluntarily take on some risks to body or mind. But consent serves less well in conventional terms for some large cohort studies,

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[746] Article 6(4) and Recital 50 of the GDPR. According to Article 6(4), the controller willing to reuse the data will have to consider, inter alia, 'any link between the purposes for which the personal data have been collected and the purposes of the intended further processing; the context in which the personal data have been collected, in particular regarding the relationship between data subjects and the controller; the nature of the personal data, in particular whether special categories of personal data are processed' […], or whether personal data related to criminal convictions and offences are processed […]; the possible consequences of the intended further processing for data subjects; the existence of appropriate safeguards, which may include encryption or pseudonymisation

[747] L Caenazzo, *Biobanche* (libreriauniversitaria.it 2012) 171–183.

[748] PG Casali, 'Risks of the New EU Data Protection Regulation: An ESMO Position Paper Endorsed by the European Oncology Community' (2014) 25 Annals of Oncology 1458.

like biobanks, in part because of the communicative distance between the data-subject and the data user.

First, the scientists who eventually study the data or biospecimens will never meet the physicians or other intermediaries who contributed the materials to the resources, much less meet the data subjects, and they may be far away physically. Also, some studies may commence a decade or two after the data and biospecimens were originally collected, and the uses of collections may shift over the time, as may the privacy issues.[749]

Biobank research presents hazards different from other types of medical research, for example, pharmacological or interventional clinical trials. The risk of bodily harm is very small or even non-existent in biobanks. The perils regarding biobank research could be: the knowledge/communication of a specific disease (for example, in case of mental/infectious diseases), the disgrace of individuals, or the misuse of scientific health data for other purposes.[750]

The consent exercise in clinical studies and genome research situations just cannot be viewed as pursuing the same ethical and legal ends. Despite the differences in medical and biobank research, the same consent rules apply to both research fields.

It is often reasoned that not simply the private sphere of patients or specimens require protection since they are essential for a self-determined life, but medical progress must also somehow be protected to the equal degree as a globally public good[751]. The US court in Havasupai case stated, that there was a violation of tribe's members' dignity, but it was also found that no direct or indirect physical or mental harm was caused. The negative consequences to a person for the use of his/her samples for different purposes that the consent was given in a research field are minor and, I would say, hardly imaginable. The additional use can help to indicate the causes of the diseases, find better treatment methods, help to heal the human population. Under such circumstances, it seems that the general informed consent doctrine requirements do not assist the biobanks in reaching their primary goal – advance medical research. Therefore, academic community proposes that other consent forms must be available for the biobank research.

749 Lowrance WW, Privacy, Confidentiality, and Health Research (Cambridge University Press 2012), 85.

750 L Caenazzo, P Tozzo and R Pegoraro, 'Biobanking Research on Oncological Residual Material: A Framework between the Rights of the Individual and the Interest of Society' (2013) 14 BMC Med Ethics 1.

751 Bartha Maria Knoppers and Claudine Fecteau, 'Human Genomic Databases: A Global Public Good?' (2003) 10 European Journal of Health Law 27.

III. Open consent for biobanks

1. Open consent definition

The sharing of data and accompanying information in the biobank-based research is crucial. The ability to reuse the samples for another research is also vital. Norwegian ethicists and researchers argue that Norwegians have an economic interest in undertaking biobank research and, on top of that, even have an ethical obligation to establish biobanks and perform genome research to benefit the health of the global community. There is a perception of the need for collective action for the different advantage of all and to benefit from the potential of existing biobanks and health registers. Also, to gain advantage from the relative ease of gathering Norwegians to take part in new research biobanks in the future.[752] Therefore if biobanks have broader possibilities to use the consent doctrine, that assists the better and more comprehensive research, the scientific research would proliferate.

D. Mascalzoni and others express an opinion that to help people with rare diseases, individuals should not be given a possibility to choose if they want or not to have their health records and specimens used in rare disease research[753]. Others also propose that cancer registries should be able to register cancer cases and patient data without the requirement of patient consent, in order to provide social and health administrators with exhaustive health data for public health policy decisions[754]. According to the authors, the collection of samples for rare diseases should be obligatory and not voluntarily.

The statement that for the people to have better health care, a possibility that imperatively persons should give their data and tissue samples for research is welcomed and understandable. However, it is hardly possible in near future perspectives. Article 8 of the Helsinki declaration[755] says that "While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects". Knowing the history lessons, when people were used for cruel scientific examinations and having in mind a legal precedents finding research

752 Lars Oystein Ursin, 'Privacy and Property in the Biobank Context' (2010) 22 HEC Forum 217.
753 ibid.
754 PG Casali, 'Risks of the New EU Data Protection Regulation: An ESMO Position Paper Endorsed by the European Oncology Community' (2014) 25 Annals of Oncology 1461.
755 World Medical Association, 'WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects' 1.

institutions liable for using samples without proper informed consent, I believe, that biobank's will continue to be bound by the consent doctrine.

However, there should be a reasonable scope of freedom for the researchers. A survey performed on the focus groups with medical researchers in the UK in 2010-2011 found, that researchers support broad consent, as they do not know and cannot be aware of the future research the samples can be useful. The researchers also indicated that broad consent is particularly important if a patient is being treated for a life-threatening illness. In such circumstances, a repeated consent cannot be even asked, if a person is deceased.[756] Consent should not be used to restrict or limit valid research based on legitimate grounds and approved by ethics or research committees. The consent rules and requirements must be adopted to ensure a fair balance between the individual rights and researchers' needs. In my opinion, this objective can be better reached by the using a broader consent form.

On the back of these arguments, some novel consent models were proposed as more suitable alternatives for biobanking. Some countries allow using the samples without donors consent for medical research purposes.

Norwegian Health Research Act has the aim to remove bureaucratic obstacles for health research and make the application and approval process of new health research projects better and less cumbersome for researchers. The measures of the new Act includes approving the research without participants specific consent if it is difficult to obtain new consent, and the research in question is of significant interest to society and the participants' welfare and integrity are ensured.[757]

German law guarantees the freedom of science according to article 5, para. 3 of the German Constitution.[758] German courts have ruled that the conflicting constitutional

[756] EA Whitley, N Kanellopoulou and J Kaye, 'Consent and Research Governance in Biobanks: Evidence from Focus Groups with Medical Researchers' (2012) 15 Public Health Genomics 238.

[757] Norway ACT 2008-06-20 no. 44: Act on medical and health research (the Health Research Act): § 28. Right to use biological material collected by the health service for research The regional committee for medical and health research ethics may rule that human biological material collected by the health service in connection with diagnosis and treatment may or shall be used for research purposes without the patient's consent being obtained. It may only be applied if the research in question is of significant interest to society, and the participants' welfare and integrity are ensured. The committee for medical and health research ethics may specify conditions for use. The patient must have been informed in advance that in some cases the human biological material may be used for research and must have been given the opportunity to refuse to be involved in research on the human biological material. An electronic register must be established with the details of the patients that have stated that they do not wish their biological material to be used for research.

[758] Grundgesetz für die Bundesrepublik Deutschland vom 23. Mai 1949 (BGBl. S. 1), zuletzt geändert durch Artikel 1 des Gesetzes vom 13. Juli 2017 (BGBl. I S. 2347)

values shall, if possible, be balanced. If a balance is not possible, then the decision which interest must outweigh the other should be made on a case by case basis. German court rulings expresses, that when collecting and processing personal data is necessary for scientific use, then the interests of research in regard to the use of the data outweigh the interests of the donor concerning the privacy. German law grants the freedom of science a higher position than the donor's right to informational self-determination.[759] Therefore, under the German law the broad informed consent is not only possible, but also could guarantee a constitutional balance between the freedom of research and the right to informational self-determination.

Spanish legislation also seems to allow a broader scope of consent. The new Spanish model also uses a "flexible, middle way" approach to the regulation of the samples already collected and stored in existing biobanks. According to the Law on Biomedical Research, consent can be obtained upon the collection of the sample, or at a subsequent time (Article 60(1)). In the Preamble it is explained that the law had to make provisions concerning "biological samples obtained for any purpose before the passing of this law, so as to make possible their use for research, while at the same time protecting the donors' interests" (IV). The law lays out the situations in which current samples may be used for biomedical research. This is when the donor has consented; they have been anonymised; the process of obtaining consent entails an "unreasonable effort" (this key concept is defined in Article 3(i) as "a disproportionate amount of time, work or other expenses"); or when the donor is deceased or cannot be located.[760]

Even if the general rule in the Spanish law is that informed consent must be obtained before a sample is collected, the law provides a number of exceptions. If obtaining consent for the new use was not feasible or entailed an "unreasonable effort", the requirement of consent may be waived. The use of the samples for all of these situations only requires the approval of a ethics committee, which will examine whether the following conditions are met: (a) the research is of general interest; (b) lack of data would

[759] J Taupitz and J Weigel, 'The Necessity of Broad Consent and Complementary Regulations for the Protection of Personal Data in Biobanks: What Can We Learn from the German Case?' (2012) 15 Public Health Genomics 265.

[760] Antonio Casado da Rocha, 'Biobank Governance in Spain: From the Autonomy of Research Ethics Committees to the Autonomy of Lay People' in Deborah Mascalzoni and others (eds), *Ethics, Law and Governance of Biobanking. National, European and International Approaches* (Springer Science 2015), 233.

make research impossible or less effective; (c) there is not an explicit objection to it; and (d) the confidentiality of personal data is guaranteed.[761]

Apart from a possibility to "waive" consent requirement, an idea for a dynamic consent is proposed. A dynamic consent shall use IT tools and digital interfaces for a 'personalised, digital communication' which allows biobank/researchers to establish a continuous communication with research subjects.[762] Research subjects would be presented with specific projects and information and, in turn, continuously tailor their consent preferences according to their desires and needs through the digital tools. Authors also mention the sectoral consent, extending the limited boundaries of the informed consent. Sectoral consent means that a research subject may give consent to research in a given area. For example, a data subject would be allowed to consent to all cancer research.[763]

Similar to a sectoral consent is an open consent, also known as broad consent, general consent and even blanket consent. Open consent is a comprehensive agreement method when biospecimens and data can be used in any research application without prior specification at the time of donation with a later opt-out for individual research uses and a guarantee of withdrawal.[764] Some authors suggest that in relation to population biobanks open consent is equal to the research subject's affirmative approval to participate in a population genetic research and projects that use tissue and data from that database.[765]

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761 Ley de Investigación Biomédica 14/2007, Art. 58(2): „*El consentimiento del sujeto fuente será siempre necesario cuando se pretendan utilizar con fines de investigación biomédica muestras biológicas que hayan sido obtenidas con una finalidad distinta, se proceda o no a su anonimización. No obstante lo anterior, de forma excepcional podrán tratarse muestras codificadas o identificadas con fines de investigación biomédica sin el consentimiento del sujeto fuente, cuando la obtención de dicho consentimiento no sea posible o represente un esfuerzo no razonable en el sentido del artículo 3.i) de esta Ley. En estos casos se exigirá el dictamen favorable del Comité de Ética de la Investigación correspondiente, el cual deberá tener en cuenta, como mínimo, los siguientes requisitos: a) Que se trate de una investigación de interés general. b) Que la investigación se lleve a cabo por la misma institución que solicitó el consentimiento para la obtención de las muestras. c) Que la investigación sea menos efectiva o no sea posible sin los datos identificativos del sujeto fuente. d) Que no conste una objeción expresa del mismo. e) Que se garantice la confidencialidad de los datos de carácter personal.*"

762 Jane Kaye and others, 'Dynamic Consent: A Patient Interface for Twenty-First Century Research Networks' (2015) 23 European Journal of Human Genetics 141.

763 'ASHG Report. Statement on Informed Consent for Genetic Research. The American Society of Human Genetics.' (1996) 59 American Journal of Human Genetics 471.

764 RG De Vries and others, 'The Moral Concerns of Biobank Donors: The Effect of Non-Welfare Interests on Willingness to Donate' (2016) 12 Life Sci Soc Policy 1, 2–3.

765 Nõmper 83.

Dara Hallinan and Michael Friedewald[766] gives specific core features of open consent: 1. the research participant actively gives his agreement (unlike presumed consent) only once to the biobank (differently from the dynamic consent); 2. the research subject is not requested to consent to a specific research project (unlike traditional specific informed consent) or an particular area of research (differently from sectoral consent). The sample donors agrees with the use of their sample and data for all future research purposes. When the collection of tissues occur, the research projects or research areas, in which samples and data will be used, are not specifically defined; 3. the researchers wishing to research samples will apply to the biobank for the opportunity to use stored tissue and data. The biobank and its governance systems (most likely the ethics committee) will then decide whether a research project will be permitted, and material given. The research participant plays no role in this decision.[767]

In an influential article, Hansson et al. argue that broad consent and consent for future research are valid ethically and should be proposed for biobank research on the following conditions: personal information is handled safely, donors of biological samples are granted the right to withdraw consent; and new research studies or changes to the legal or ethical authority of a biobank are approved by an ethics review board.[768]

In open consent, the ethics committees play a significant role. Presuming, that the committee composes best researchers, having a good knowledge about different genetic research, having high ethical standards and not biased, such competences seems reasonable and trustful. It would also prevent the situations, where individuals do not agree to donate the samples because of some fake facts, or gossips about the research or a biobank.

2. Allowability of open consent

Dara Hallinan and Michael Friedewald explain that applying open consent doctrine to biobanks is complicated under the new GDPR rules. The authors doubt if open consent can meet the requirement under the Regulation for consent to be 'specific and informed', as defined by the Regulation. They point some specific problems the open consent faces:

766 Dara Hallinan and Michael Friedewald, 'Open Consent, Biobanking and Data Protection Law: Can Open Consent Be "informed" under the Forthcoming Data Protection Regulation?' (2015) 11 Life Sciences, Society and Policy 5.

767 Ibid.

768 Mats G Hansson and others, 'Should Donors Be Allowed to Give Broad Consent to Future Biobank Research?' (2006) 7 Lancet Oncol 266–269.

the biobank has a dury to provide the data subject with information as to 'the purposes of the processing for which the data are intended' (GDPR Article 13(1)(c)); the biobank must provide the participant with information as to 'the recipients or categories of recipients of personal data' (Article 13(1)(e)). Of cause, the open consent is used for the all future researches so describing the exact purpose of use would not be an open consent, but an informed one.

The article by Dara Hallinan and Michael Friedewald have been written before the GDPR was adopted and is mainly based on the Commission's proposal. Today's GDPR some other aspects can be mentioned as being a burden to open consent. For example, Article 13(2)(a) states that the controller shall, at the time when personal data are obtained, inform the data subject **about the period for which the personal data will be stored**, or if that is not possible, the criteria used to determine that period. Therefore, the Regulation implicitly requires establishing a term line to use personal data. Furthermore, the exception of using generic data under Article 9(2)(a) is allowed only if the data subject has given explicit consent to the processing of such personal data for **one or more specified purposes**. So giving his/her consent for the use of genetic data the data subject must agree on specific research or analysis, and cannot, according to the Regulation, allow the use of his/her samples for any future research.

A quite old Article 29 Working Party's opinion, which was issued long before the new GDPR initiative was proposed by the Commission and negotiated in the European Council, has expressed the opinion, that blanket consent is not acceptable as valid consent. Consent must be specific, so it is legal. In other words, blanket consent without specifying the exact purpose of the processing is not acceptable.[769] Consent cannot apply to an open-ended set of processing activities. It means, in other words, that the context in which consent applies is limited.

However, when we look at the new Regulation, Recital 33 of the GDPR notes that "It is often not possible to fully identify the purpose of personal data processing for scientific research purposes at the time of data collection. Therefore, data subjects should be allowed to give their consent to certain areas of scientific research when in keeping with recognised ethical standards for scientific research. Data subjects should have the opportunity to give their consent only to certain areas of research or parts of research projects to the extent allowed by the intended purpose." Thus, the GDPR seems not to

[769] Article 29 Data Protection Working Party. Opinion 4 / 2007 on the Concept of Personal Data (2007) 17.

forbid the broad consent for scientific research if the donor has given an opportunity to consent only for a smaller part of a research. This exception can be used for biobank's open consent. The samples and data can be collected for extensive research, for example, focusing on heart diseases, cancer, mental diseases or similar. However, without clear interpretation and explanations are given of this recital by the official institutions, hardly any biobank in Europe would dear to rely on it.

The long-standing tradition to inform the research participants about the exact purpose and scope of the research initiated by the Nürnberg Code (1947) is prevailing not only in international but also the vast majority of national laws. Spanish Royal Decree 1716/2011 Article 23 and the Spanish Law on Biomedical Research Article 59 foresees that the consent form must indicate the scope, time, purpose of the research, also place of the investigation, inform who will use the samples, inform about possible economic benefits, etc. Under such requirements, the broad consent is not possible.

The only way, to adopt the broad consent for the research purposes could be the use of GDPR derogations under Article 89. However, such derogations must be implemented either by in the Union's or Member State's law. Which most likely means a national act, valid in only one country. It would not ensure the free flow of data between biobanks. Also, it is hardly likely that small countries (such as the Baltic states) would legislate additional documents for a few biobanks that operate there.

If a derogation act would be legislated at the Union level, this would more likely allow biobanks to use open consent. It would ensure that biobanks have more trust in using open consent templates and will have no fear to violate privacy rights. However, such legislation most likely will be stubborn, will require implementation into the national legal systems, will take much time to legislate. Furthermore, it would not solve the sharing question between European and third country's biobank.

Academics, on the other hand, expresses the support for the use of open consent. Ants Nomper talks about open consent that is understood as a form of informed consent. He explains that "given that obtaining a tissue sample constitutes an intervention, the subject agrees to interference with his bodily integrity. This aspect of open consent is probably the least dubious, given that the risks to bodily integrity can be explained to participants to the extent that also satisfies the criteria advocated by the proponents of the traditional informed consent concept. In that sense, open consent constitutes informed consent."[770]

[770] Nõmper 82.

The author also writes that open consent is under no circumstances consent to every kind of future research. What is explained, is that open consent can be applied only when research participant is informed about all the conditions of the participation (that is, the purpose of the use of the sample, the user of the sample, the possibility to withdrawn and other). Nomber's opinion is that each population genetic database has its objective that, albeit in quite a broad manner, it imposes limits on the research. For instance, the purpose of the UK Biobank is to study the interplay between genes, lifestyle and common diseases. The Estonian Geenivaramu aims to improve public health through research on genes, genealogies and phenotype. In author's view, such a broad objective is sufficient to fulfill the condition of law.

Consent is the expression of the right to self-determination. If it is agreed that a person has self-determination right in choosing the treatment, medicine and right to decide if he/she wants to be cured, then person's decision for a broad consent must be accepted on the same self-determination grounds. My opinion is, if we look at the data protection law as something, that can be derogated from by the person himself, and if we agree that a consent form is a contract between the donor and the biobank, then we should allow the research participant to give a broad consent if he wishes.

A consent form looks more like a contract between the donor and the biobank, giving a biobank the rights to use donor's samples and data. In such contract, a person clearly states its opinion to give the samples for particular research or broad scope of researches. Precisely in the same way, donor could agree to donate the samples for any future research.

It does not mean that the biobank is less responsible for the personal data when the broad consent is given rather than when a specific consent is provided. Susana Navas Navarro talks about the double effect of the informed consent. She presents that first, informed consent is a contractual relationship between the data owner and data uses, but second, and more importantly, it is a consent to treatment and use of data ("*asentimiento al tratamiento de los datos*"). This second part of the consent proposes higher standards than a simple contract, and it does not change depending on the needs for which the data is used, but instead creates additional responsibilities for the data controller.[771]

If the research participant understands all the consequences of giving the DNR samples to a biobank, wishing that the samples are used not only for current but also for

[771] Navas Navarro and Camacho Clavijo, *Mercado digital principios y reglas jurídicas* (Tirant lo Blanch 2016), 78-79.

future research, he/she must have an opportunity to do so. Neither the GDPR not another legal instrument can prohibit a person to give the samples to any research he/she wishes. Of cause, a person must be protected: first, the consent document must clearly explain all the circumstances of the donation, explain the withdrawal possibility. Other safeguards – such as anonymity, research approval by the ethics committee – must also be ensured.

Open consent has proven particularly popular with population biobanks. The donor's consent form of the Estonian Genome Center, University of Tartu (The Estonian Biobank)[772] states: "I have been informed of and am aware of the following: Article 1: <...>Research carried out with the help of the Gene Bank shall not be limited to the present scientific level. <...> 4) If I wish, I may submit additional information about myself to the chief processor. The chief processor of the Gene Bank has the right to receive information about my state of health from other databases. I have the right to prohibit the supplementation, updating and verification of descriptions of my state of health stored in the Gene Bank". The donor consent form for the UK biobank states: "I give permission for long-term storage and use of my blood and urine samples for health-related research purposes (even after my incapacity or death)" (UK Biobank 2013).[773] Therefore, if a person, having all the knowledge about a biobank, agrees to give his samples to a future research, no violation of GDPR shall occur.

The quite recent study performed by Canadian researchers have found, that research participants are willing to give their leftover samples for a broad scope of researches. 42% of the respondents (n = 48) preferred to provide a one-time general consent.[774] Another research performed in 2017, found similar results.[775] The statement that the open consent regime and free data sharing will be used in the research had limited relevance to participants' decision making if they want to participate in the biobank scenario presented in the study. The findings are consistent with previous research reporting that overall

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772 Annex 1 to the Ministry of Social Affairs Decree No 36 'GENE DONOR CONSENT FORM' 2007.Available at: https://www.geenivaramu.ee/sites/default/files/gene_donor_consent_form.pdf accessed 2018 May 8.

773 Consent Form for the imaging assessment: UK Biobank <http://www.ukbiobank.ac.uk/wp-content/uploads/2016/06/consent_form_imaging.pdf> accessed 2018 May 8.

774 Yann Joly and others, 'Fair Shares and Sharing Fairly: A Survey of Public Views on Open Science, Informed Consent and Participatory Research in Biobanking' (2015) 10 PLoS ONE 1.

775 Saskia C Sanderson and others, 'Public Attitudes toward Consent and Data Sharing in Biobank Research: A Large Multi-Site Experimental Survey in the US' (2017) 100 American Journal of Human Genetics 414.

acceptance of full consent is similar to that of specific or tiered consent, although some factors may influence this preference.[776]

3. Proposal for common templates

A unification of consent templates would reduce the administrative costs and advance the sharing of biological samples and data. To avoid inequalities and doubts, if data or samples can be shared between different biobanks, a template consent form could be used. The same form using the same language, same terminology, describing the same purpose of use, would ensure that any biobank is well informed about the limits of the use of the samples. Also, a biobank could easily trust sending a sample if a receiving biobank uses the same consent template form. It would assure, that the sending and the receiving biobanks grant the same protection. Digital and IT technologies could also assist in creating, managing, comparing which samples are collected using common consent template.

There are already ongoing initiatives to create common consent templates. The biobank's online tools P3G-IPAC ("Public Population Project in Genomics and Society: International Policy interoperability and data Access Clearinghouse") and the BioMedBridges, provide templates for consent, research participant information, and material or data transfer agreements. P3G-IPAC has prepared template consent agreements that can be used to facilitate data sharing.[777]

Another initiative, the BioMedBridges project "WP5 – Secure access",[778] has a goal to develop a security framework that will ensure that services provided by BioMedBridges are compliant with local, national and European regulations and privacy rules. The developed legal framework will allow the use of data bridges, which consider among other the EU regulations, national data protection acts, laws about biobanking, laws concerning genetic data and stem cell research, data access approval rules (by informed consent), regulations for intellectual property and license rights.

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776 David J Kaufman and others, 'Public Opinion about the Importance of Privacy in Biobank Research' (2009) 85 American Journal of Human Genetics 643, 643–654; Jodyn Platt and others, 'Public Preferences Regarding Informed Consent Models for Participation in Population-Based Genomic Research' (2014) 16 Genetics in Medicine 11, 11–18; Christian M Simon and others, 'Active Choice but Not Too Active: Public Perspectives on Biobank Consent Models' (2011) 13 Genetics in medicine : official journal of the American College of Medical Genetics 821–831.

777 P3G, 'Clauses / Agreements Templates' <http://www.p3g.org/node/1042> accessed 8 May 2018.

778 'The BioMedBridges Project' <http://www.biomedbridges.eu/workpackages/wp5> accessed 8 May 2018.

Creating templates will have to take on the challenges to generalise consent forms and provide templates that are comprehensive to the extent that different research purposes and legal unpredictabilities are taken into account. Common templates would help to ensure that the current intended use of the samples or data is covered by the scope of the consent under the relevant law. As the concept of broad consent for medical research has many advantages, this kind of templates would assist in making future use of biosamples and data possible.[779]

The proposal is, that to ease the consent requirements, lower the administrative and financial burden, some specific template forms can be created for the joint use by the biobanks. The analogy and success of the Creative Commons licenses,[780] or Open Source licenses[781] can be taken. Open source licenses allow software to be freely used, modified, and shared. Creative Commons licenses use four principal usability terms, that can be mixed together composing six basic licenses. Moreover, such licenses are used by adding the simple Creative Commons marks on the copyrighted content, eliminating a need to include long licensing agreement terms.

If biobanks commonly agree on specific terms and condition, the consent template could include such clauses as sample storage, benefits, risks, confidentiality, communication of search results to the patients, genetic counselling, possibilities of transfer or commercialisation, the scope of consent, sharing possibilities. There are several biobank's umbrella organisations: such as BBRMI-ERIC, the International HapMap Project, the International Cancer Genome Consortium, that could start the initiative of creating commonly used and acceptable consent template forms. As a suggestion, such forms could ask participants' agreement: 1) to use samples/data for the undefined number of researches; 2) use samples/data for future researches; 3) share samples/data with other biobanks, for their studies; 4) re-contact possibilities. All the data collected under such consents could be placed and available online for all cooperating biobanks. It would allow the data processing institution (the one that collected the samples and data) to make corrections, adjustments, modifications, or, if requested, remove the information. IT sharing possibilities and tools can ensure that the information is always updated, that data controller can correct errors, remove the information if a participant wishes to withdraw.

779 Murat Sariyar and others, 'Sharing and Reuse of Sensitive Data and Samples: Supporting Researchers in Identifying Ethical and Legal Requirements' (2015) 13 Biopreservation and Biobanking 263.

780 'Creative Commons' <https://creativecommons.org/> accessed 8 May 2018.

781 'Opensource.com' <https://opensource.com/resources/what-open-source> accessed 8 May 2018.

Data collected using proposed templates would be anonymised or pseudonymised. It would give more trust to the donors, but in most cases, would have no negative aspects to the research. Also, the biobanks ethics committees would take their role under such open data sharing initiative. The approval of a study by an ethics committee is a basic practice in the biobanks. Once a researcher finds out that the dataset does indeed contain relevant information, the next step is to gain access to it. The relevant ethics committee will read each proposal and decide whether to grant access. The approval by the committee would also help to calm sample donors that their data are not misused, that it is provided to researchers with caution and applying adequate standards. There are initiatives to digitalise and make more accessible the process of the approval by the committee. EMBL-EBI (the European Bioinformatics Institute)[782] is working with its partners to develop resources and tools to streamline the approval of the research projects. ELIXIR[783] has developed an Authentication and Authorisation Infrastructure[784] (AAI) to authenticate bona fide researchers based on their organisation's credentials. ELIXIR AAI services can connect data archives to authorised cloud services, making it easier for the committee to grant and control access to sensitive data.

If all these premises are accomplished, no threat remains that the personal rights of the data donor could be violated. Conditions for open consent are needed to overcome the inattentive nature of informed consent. Informed consent is always limited (not all the conditions for carrying out a population genetic database project can possibly be set out in consent form), ego-centric (as opposed, for example, to community consent), and absolute (i.e., this form of consent creates an all-or-nothing situation).[785] There is a large scope of academic literature on biobanking that is highly relevant to the ethico-legal framework for Big Data in healthcare. A notable similarity is a difficulty in gaining consent when future projects cannot be predicted but the risks to individuals remain low.[786]

782 The European Bioinformatics Institute (EMBL-EBI) shares data from life science experiments, performs fundamental research in computational biology and offers an extensive user training programme, supporting researchers in academia and industry. We are part of EMBL, Europe's flagship laboratory for the life sciences. More information at 'EMBL-EBI' <https://www.ebi.ac.uk/> accessed 8 May 2018.

783 ELIXIR is an intergovernmental organisation that brings together life science resources from across Europe. These resources include databases, software tools, training materials, cloud storage and supercomputers. The goal of ELIXIR is to coordinate these resources so that they form a single infrastructure. More information at 'ELIXIR' <https://www.elixir-europe.org/> accessed 8 May 2018.

784 <https://www.elixir-europe.org/services/compute/aai> accessed 8 May 2018.

785 Ants Nõmper, 'Open Consent – A New Form of Informed Consent' [2005] PhD dissertation, University of Tartu 115.

786 Ibid.

There are already ongoing initiatives for the Open biotechnology movement in the biobanks, but such initiatives must have legal support and approval of not violating data protection laws. The goal of the biobanks should be to give for the researchers as transparent as possible guidelines when, and if, the data can be used. It is reasonable to suppose that biomedical researchers cannot be expected to have detailed knowledge about all ethical and legal requirements concerning the use of sensitive data and samples in their research. Even researchers who have had the basic training or previous experience cannot always have up to date knowledge of complex and changing requirements. Hence, if similar to proposed open consent templates are adopted, it would assist researchers to understand their responsibilities and legal requirements in a way that is clear and comprehensible.

4. Right to withdraw

Following the idea that open consent is the most suitable form of consent for the biobanks, a participant's right to withdraw plays a very important role. Understandably, a research participant is much more willing to donate the samples when he/she is sure that at any time has a right to withdraw from the future research. No force or obligation can be used to convince participant to continue sharing his samples or provide additional samples or information.

The right to withdrawal in general means the research participants right to remove the samples and data from all the researches the samples are or will be used. But there are other alternatives of the withdrawal. For example, a partial withdrawal is another alternative. Henry T. Greely argues that research participants should have the right to withdraw their consent both in general or with respect to specific research topics.[787] As rightly stated by Nomper, withdrawal from certain types of research mirrors a situation in which only certain types of research are allowed.[788] An individual wishing to limit the scope of research to be carried out on his tissue can do so by placing limits on the research from the beginning by authorising only a limited scope for the research, or by imposing limits afterwards by modifying the previous authorisation. Such partial

[787] Henry T Greely, 'Breaking the Stalemate: A Prospective Regulatory Framework for Unforeseen Research Uses of Human Tissue Samples and Health Information' (1999) 34 Wake Forest Law Review 737, 755.

[788] Nõmper 111.

withdrawal could be mentioned on the consent form, or, if given later, a biobank storing the information, should make the relevant corrections.

The withdrawal can be also regarding the future contacts of the donor, but all before collected information can be used as was before. Such withdrawal possibility is foreseen, for example, in the UK biobank's consent form. No further contact means that whilst participants would not be contacted again in the future, samples and information previously provided could continue to be used, together with information that would be obtained in the future from the medical record.[789]

The general right of withdrawal is explained in Article 7(3) of the GDPR. The article states that "The data subject shall have the right to withdraw his or her consent at any time. The withdrawal of consent shall not affect the lawfulness of processing based on consent before its withdrawal. Prior to giving consent, the data subject shall be informed thereof. It shall be as easy to withdraw as to give consent." The interpretation of the article leads to the conclusion that withdrawal right cannot be used in reverse, that is, the investigations started before the withdrawal took place, can be finalized, or if already published, such publication can remain accessible to the public. The right to withdraw consent does not imply a right to withdraw results that have already accumulated, rather it implies that new data cannot be obtained, and that existing data must be maintained in an impersonalised form.[790] The right to withdraw consent after the samples have already been given includes a realistic practical possibility to exert this right, perhaps even many decades after the original consent as given. But such right shall not be related with an unrealistic approach to remove data that has been published as part of an aggregated data set and is in the public domain. Such reverse withdrawal cannot meaningfully or practically be possible at all. In effect, past uses of data and samples cannot be undone and therefore withdrawal must by necessity focus on activities that have are not yet started. Therefore, rather than referring to the cessation of an intervention, withdrawal should relate to prohibiting the future use of previously collected materials and data.[791]

Should this restriction – not to be able to withdraw from research that occur in the past scare the potential donors? I would answer this question negatively. Privacy is closely associated with autonomy, liberty, and individual freedom. Every person can have a right to change one's minds, to decide, that he/she does not wish to participate in a

[789] ibid 9.

[790] Hansson and others (2006) 269.

[791] Karen Melham and others, 'The Evolution of Withdrawal : Negotiating Research Relationships in Biobanking' 6.

research anymore. Reciprocity and trust in the biobanks activities are crucial. It is a matter of building a culture of care for the study participants and transparency that is integral to a biobank. Mutual trust and feeling that your donation is needed to the World are particularly important for study participants so that they acquire a sense that they are making an extraordinary contribution to researchers of high social relevance and that their act of giving is greatly appreciated.[792] When the nature of the relationship between participant and biobank is the one of a partnership, mutual collaboration, transparency and understanding, then donors should not be worried that the withdrawal possibility will not apply retroactively.

Another problem with withdrawal is that it is hard to detect third parties where the samples have been shipped and information shared. As is identified by the CIOMS guidelines,[793] it is in relation to the use of data that the seriously challenge extends to the withdrawal from biobanking infrastructures. Melham and others write about the drawbacks of withdrawing data, once it is transferred to third parties. Different data commonly contained in biobanks, such as participant medical histories, genetic or genomic sequences and sample characterisation metrics are regularly digitised, making them easily replicable, distributable and subject to modification, aggregation, and integration into larger data sets. Once data is shared with third parties outside the biobank it can be extremely difficult to track and control, what is done with a particular set of data derived from a specific research participant. It can be practically impossible to ensure that a particular piece of data is removed entirely, especially if the data has been incorporated into a larger data set where individual contributions can no longer be isolated.[794] The withdrawal possibility must be reasonable, and research participants must be clearly explained where and how the withdrawal can be used, and what data can be removed when requested. The withdrawal can become complicated in the biobank-based research that can last for many decades (eg, problems may arise to find contact information of the biobank after several years). To cope with such problems the Swedish national biobanking programme has established regional biobank registries that act as contact

[792] Herbert Gottweis, George Gaskell and Johannes Starkbaum, 'Connecting the Public with Biobank Research: Reciprocity Matters' (2011) 12 Nature Reviews Genetics 739.
[793] Council of International Organizations of Medical Sciences, 'International Ethical Guidelines for Epidemiological Studies' (2009) 45–47.
[794] Melham and others 5.

points for withdrawal of consent for all biobanks established within defined geographical regions (www.biobanks.se).[795]

The internet, could storage and sharing IT tools can play a very important role in ensuring withdrawal right. If biobanks use a global network, common sharing tool, where one biobank sees which information can be used, which information is withdrawn from future uses, such common communication would ensure the better protection of donors rights and a higher rate of satisfactory withdrawals. Biobanks would get the newest information about the samples and their use possibilities are established, it would be easy to follow which samples/data are allowed to use and which are not.

There is an international initiative to share biobanks' resources and information. The main resources for storing and distributing sequence data are three large databases: the NCBI database,[796] the European Molecular Biology Laboratory (EMBL) database,[797] and the DNA Database of Japan (DDBJ) database.[798] These databases collect all publicly available DNA, RNA and protein sequence data and make it available for free. They exchange data nightly, so contain essentially the same data.[799] The information about how these biobanks update data are not expressed. But if they update all the information automatically, the removed data would be also updated (at least it is clear, that such possibility exist). Therefore, if particular data and samples are withdrawn from one biobank, in 24 hours the other biobanks also would withdraw same data while updating their databases. A possibility for the submitting institution to remove data every time a need occurs, and for receiving institution or researcher to receive such information basically without no delay in time, gives an invaluable trust for the donors and ensures the smooth protection of participants right to withdraw.

Another similar initiative is started by the Central Research Infrastructure for molecular Pathology (CRIP). CRIP has created a model, that would enable biobank networks to form operational ''meta biobanks'' whilst respecting the donors' privacy, biobank autonomy and confidentiality, and the researchers' needs for appropriate

795 Mats G Hansson and others, 'Should Donors Be Allowed to Give Broad Consent to Future Biobank Research?' (2006) 7 Lancet Oncol 268.

796 National Center for Biotechnology Information, 'Welcome' <https://www.ncbi.nlm.nih.gov/> accessed 8 May 2018.

797 'EMBL-EBI' <https://www.ebi.ac.uk/> accessed 8 May 2018.

798 'DDBJ Center' <https://www.ddbj.nig.ac.jp/index-e.html> accessed 8 May 2018.

799 Avril Coghlan, 'Sequence Databases' <http://a-little-book-of-r-for-bioinformatics.readthedocs.io/en/latest/src/chapter3.html> accessed 8 May 2018.

biospecimens and information.[800] The Inhouse Research Database (a biobank participating in the meta biobank experiment) imports pseudonymized data, stores it into the CRIP database. However, data is not exported automatically to a researcher that has requested it – the export must be authorized on each occasion and triggered by the Inhouse Research Database. If a sample donor withdraws his/her consent, the Inhouse Research Database allows for deletion of the pertinent dataset before the whole data is anonymized and updated in the CRIP database. In other words, to make the withdrawal of consent effective, the CRIP partner deletes the withdrawing donor's dataset in the Inhouse Research Database and uploads all the respective (updated) data to the CRIP database, thereby completely replacing all data previously exported to the CRIP database. Such tool could be a good working environment for the proposed open consent regime because the information about the withdrawal would be shared on a timely base, or every time the need to correct/amend data occurs.

Common consent forms could also play an important role to ease the management of right to withdraw. Today, withdrawal forms differ in the biobanks. As an example, the P3G-IPAC[801] template consent agreements ensure that "You can withdraw your data at any time by contacting [name of relevant person] free of charge at [information]. Data sent to other researchers around the world cannot be withdrawn if already used or published." The HUNT longitudinal population health studies[802] in Norway guarantees that a participant can withdraw from the bank at any time and without giving a reason. It also explains the practical limits to withdrawal: "The present practice at HUNT Research Centre is that withdrawal of consent will lead to the deletion of data and the destruction of the biological material. However, a withdrawal of consent will not have retroactive effect, i.e. ongoing projects keep the de-identified data and material. This practice provides a reliable framework for collaboration partners and guarantees the realization of projects without restrictions". Common conditions of withdrawal would make it clear for all parties – the research participant, the biobank and the final researcher – what is the scope of withdrawal (total, partial, withdrawal from future contact, etc.), when the information cannot be used anymore and when the research can continue, it would answer other relevant questions. Today ethical boards of the biobank or researcher himself/herself must

800 Christina Schröder and others, 'Safeguarding Donors' Personal Rights and Biobank Autonomy in Biobank Networks: The CRIP Privacy Regime' (2011) 12 Cell and Tissue Banking 233, 233.

801 P3G, 'Clauses / Agreements Templates' <http://www.p3g.org/node/1042> accessed 8 May 2018.

802 The Nord-Trøndelag Health Study, 'HUNT Research Centre' <https://www.ntnu.edu/hunt> accessed 8 May 2018.

read the consent form, the withdrawal rules and decide about the scope of the use of information. This gives grounds for different interpretations and also, puts more responsibilities for the researchers and members of the ethics committee.

And at the final mark, in the proposed open consent doctrine, the correct right to withdrawal ensures people participation. Persons knowing that they are free to withdraw from participation will be much more willing to give their samples/data in the first place, even if as explained the withdrawal is never absolute. Furthermore, a Swedish study revealed that, even with an especially elaborate system for opting out of consent (where detailed information and consent forms were offered at sampling that patients could take home and fill in), only 1 in 19,000 actually did opt out.[803] Even among young to middle-aged women in the cervical screening subgroup, the rates of refusal to consent were only about 0.1%. According to the study results, people are willing to participate in the research broadly and give their samples and data for a future research.

In the suggested broad consent regime, the consent is valid until further notices are given by the donor. Of cause, under such a broad scope of the consent, there should be a real and valid opportunity for withdrawal. The biobanks should not try to minimize or negate the withdrawal possibilities, but rather allow the withdrawal as far as possible and ensure this right as fully as applicable sharing tools allow. It is important under the open consent regime to have a better trust of the participants and higher participation rates.

5. Responsibilities of researcher

Biobanks must respect the personal rights and confidentiality of research participants. It is the least obligations a research institution must follow. But besides the obligations to respect the consent of research participants, the biobank and its researchers also have additional responsibilities and must respect other ethical norms resulting from the activities performed. As general guidelines, ethical responsibilities and obligation of a biobank have been already described in this chapter. This part will concentrate on the researcher's ethical obligations and duties. Usually, a biobank foresees the ethical rules bounding the researchers its internal policies, or such obligations are foreseen in the material transfer agreements, establishing rules for the transfer of samples and/or data.

[803] Gert Helgesson and Linus Johnsson, 'The Right to Withdraw Consent to Research on Biobank Samples' (2005) 8 Medicine, Health Care and Philosophy 345.

Some authors express the opinion that the research ethics committees or reviewers are not the ones authorized to give legal advice, nor are they liable for any of their decisions in this respect. It is the researchers and the health or social care organisations who have the responsibility not to break the law.[804] A set of ethical norms at its core, guiding researchers, research ethics committees and other stakeholders engaging in biomedical research plays an important role in biobank's everyday activities. The main rules bounding researchers, or investigators, other assisting personnel, can be generalized into following groups: I) responsibility to report research and return its results; II) responsibility to perform and follow only the approved research and do not depart from what was approved; III) responsibility to keep information confidential and do not identify or contact the participants.

5.1. Responsibility to report research and return results

Norwegian Health Research Act foresees that "The project manager must submit a final report to the regional committee for medical and health research ethics when the research project is finished. The final report must present the findings objectively and methodically, ensuring that both positive and negative findings are presented. The regional committee for medical and health research ethics may stipulate requirements regarding the content of the final report. The regional committee for medical and health research ethics may order the project manager to submit annual or extraordinary reports if the Committee deems it necessary."[805] Similarly the reporting question is regulated by the Finish Biobank Act 688/2012. Section 27 of the mentioned act establishes an obligation to publish the results of biobank research based on the samples or information received from the biobank, otherwise, the access to samples or information should not be granted.

The rules of the material transfer agreement of Medische Biobank Noord Nederland(the Netherlands), requires the researcher after the termination of the agreement, provide Biobank with a written report, describing in reasonable detail (i) the activities executed, (ii) the results obtained in the course of the Research (including any new algorithms developed) and (iii) the methodologies used in the research (the latter to allow Biobank quality control and uniform approach by the users of data and material).[806]

[804] Research governance framework for health and social care (Second edition, 2005).
[805] ACT 2008-06-20 no. 44: Act on medical and health research (the Health Research Act) 2008.Article 12.
[806] The Medische Biobank Noord Nederland B.V., 'MATERIAL TRANSFER AND / OR DATA ACCESS AGREEMENT' 1. Available at <https://www.lifelines.nl/uploads/fckconnector/e37dbc4f-1288-51fa-

UK Department of Health also states in its "Research Governance Framework for Health and Social Care" that investigator's or researchers must be accountable for arranging to make findings and data accessible following expert review.[807]

This responsibility to give back the research results is related to the biobanks' wish to provide the research outcomes as broad as possible and do not repeatedly research for the information that is already known. Researcher, using biobank's materials, cannot withhold the new findings only for his/her own good, but must share such findings with other researchers.

5.2. Responsibility to perform only approved research

The transfer of samples and sharing of data raises several ethical questions. If samples and data are physically transferred outside the biobank, the recipient might use the material for purposes other than those to which the sample donors have consented, or the samples might be transferred to third parties, thus putting the privacy of donors at risk. Transfers of existing biobanks to third parties with the inclusion of personalized donor data should be possible only with the approval of a REC or IRB.[808] If a project is approved by the ethics committee, a Material Transfer Agreement (MTA) is signed between the biobank and researcher. The MTA foresees the scope of how the transferred data can be used, and the boundaries cannot be overstepped.

Iceland Biobanks and Health Databanks Act sets the rule that an "individual <is> responsible for the implementation of the study in accordance with a research protocol which has been approved by the National Bioethics Committee or an institutional review board."[809] UK Department of Health provides guidelines that biological researches must be conducted according to "the agreed protocol (or proposal), in accordance with legal requirements, guidance and accepted standards of good practice." The welfare of the participants' must be ensured while in the study.[810]

9d06-160823c09460> accessed 2018 May 8.

807 Research governance framework for health and social care (Second edition, 2005).

808 Brian Salter and Mavis Jones, 'Biobanks and Bioethics: The Politics of Legitimation' (2005) 12 J. Eur. Pub. Pol. 710.

809 Article 3 of Iceland Biobanks and Health Databanks Act No. 110/2000, as amended by Act No. 27/2008, No. 48/2009 and No. 45/2014.

810 Research governance framework for health and social care (Second edition, 2005) 2005 1. Similar rule is also foreseen in UK Biobank, 'Annex II: Material Transfer Agreement for Data And/or Samples' <http://www.ukbiobank.ac.uk/wp-content/uploads/2012/09/Material-Transfer-Agreement.pdf> accessed 8 May 2018. Rule 2.1. *The Applicant agrees that the Materials may only be used for the Permitted Purpose, namely: 2.1.1 solely to conduct the Approved Research Project in the manner and timeframe*

This responsibility of the researcher to respect the scope and follow the goals of the approved research is related with the protection of individual's personal data and data protection rules. Naturally, the researcher cannot overstep the decision of the ethics committee and to use samples or data for other purposes than was allowed.

5.3. Confidentiality

Material transfer agreement of Stichting Katholieke Universiteit (the Netherlands) Radboud university medical center[811] Article 4.1 states, that the partner shall treat as confidential information, for the duration of the agreement including any extension thereof and thereafter for a period of three years following termination or expiry of the agreement. Iceland Biobanks and Health Databanks Act[812] established that all staff of biobanks and those who have access to them, (including monitoring bodies), are subject to a duty of confidentiality regarding matters relating to their work which should be kept confidential, by law or by their nature. The obligation of confidentiality remains in force after employment, research or tuition ceases.

The researcher should also not try to identify or contact the participants. UK Biobank's rules state that the applicant shall not attempt: to identify any participant from the materials provided by UK Biobank; or to contact any Participant, save only as may be permitted under an Approved Research Project involving re-contact by the Applicant.[813]

The rules of confidentiality and prohibition to contact research participants is related with the protection of personal data and also with intellectual property rights of the biobank (such as commercial secrets, database rights, and others). If not followed, violation of such requirements can precipitate the internal or even external sanctions to the researcher.

Some national laws implicitly describe sanctions for the biobank as an institution or for its workers and researchers, if ethical rules are violated. Iceland Biobanks and Health Databanks Act allows the Minister to revoke the biobank's license, if the licensee or its

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set out in Annex A (namely the Permitted Purpose); and 2.1.2 solely by the Applicant PI and the related Applicant Researchers (and, in particular, are not to be shared with any other person without UK Biobank's explicit written approval).

811 'Material Transfer Agreement of Radboud Biobank Version 4.0, October 2015' <http://www.radboudbiobank.nl/media/2583/material_transfer_agreement_def.docx> accessed 8 May 2018.

812 Article 11 of Iceland Biobanks and Health Databanks Act No. 110/2000, as amended by Act No. 27/2008, No. 48/2009 and No. 45/2014.

813 Aritcle 4 of UK Biobank's Material Transfer Agreement for data and/or samples.

employees violate the terms of the Act or government directives on the basis of the Act, if the conditions of the license are not fulfilled, or if the licensee proves unable to operate the biobank.[814] The Spanish Biobank's act foresees that the administrative, civil or even criminal sanctions can apply if the investigators or biobanks' representatives violates the rules of the act intentionally or without due care and attention.[815]

For the reasons briefly explained below, there is an international consensus that the operator of a population genetic database should not be a purely for-profit organization, but rather should resemble a trust, foundation, or charitable company.[816] Primary medical ethical principle of "do no harm" must be followed by the operating biobanks. Ethical norms binding researcher should ensure this medical principal and a clear goal to balance medical benefits and privacy risks of participants.

6. The role of ethics committees

If we accept the proposal, that broad consent is applicable to the biobank's activities, then the wide powers will be given to the biobank's ethics committee. Research Ethics Committee (REC) is a local authority that evaluates research projects involving human beings, including genetic research. In general, no research can take place and no samples are provided until the project is approved by such committee. The primary function of a REC is to protect the welfare and rights of human participants in research. Depending on the jurisdiction, such committee may also be referred to as Ethics Review Board (ERB) or Institutional Review Board (IRB).[817] If scientists wish to do research on sufficiently detailed data they must go through the proper access procedures and having their applications approved. UK Biobank's Data Showcase[818] contains anonymous summary information about the data that are held in the resource, but not specific and individual

[814] Article 14 Article 11 of Iceland Biobanks and Health Databanks Act No. 110/2000, as amended by Act No. 27/2008, No. 48/2009 and No. 45/2014.

[815] LEY 14/2007, de 3 de julio, de Investigación biomédica*, Art. 73. 1. De las diferentes infracciones será responsable su autor. 2. Cuando el cumplimiento de las obligaciones previstas en esta Ley corresponda a varias personas conjuntamente, responderán de forma solidaria de conformidad con lo dispuesto en el artículo 130.3 de la Ley 30/1992, de 26 de noviembre, de Régimen Jurídico de las Administraciones Públicas y del Procedimiento Administrativo Común. La misma norma será aplicable a los directores de los centros o servicios por el incumplimiento de las referidas obligaciones por parte de los profesionales biomédicos dependientes de aquéllos.*

[816] Ants Nõmper, 'Open Consent – A New Form of Informed Consent' [2005] PhD dissertation, University of Tartu 103.

[817] The definition provided in ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT, 'OECD Guidelines on Human Biobanks and Genetic Research Databases'.

[818] UK Biobank, 'Online Showcase of UK Biobank Resources' <http://biobank.ctsu.ox.ac.uk/crystal/> accessed 8 May 2018.

information. In some situations, a biobank may decide not to show summary information on the website for some types of sensitive data and may instead only provide such information to approved researchers.

The biggest genetic information databases (NCBI, EMBL and DDBJ), collect all publicly available DNA, RNA and protein sequence data and make it available for free, also uses REC's assistance. The data to these databases are submitted by a researcher to the biobank. Before accepting new data, such data is approved by the Data Access Committee (DAC). When uploading the data, a confirmation that such data has the required consents and/or ethical approval must be made. The protection measures are taken by these genetic databanks before releasing the information.

The option of broad consent and future consent does not imply once-and-for-all permission to use collected samples and data. Additional safeguards exist to protect private data through medical codes of ethics. In regard to research projects, their approval by independent review boards and/or ethics committees is universally required. The ethics-review board remain responsible to assess the risk–benefit relation for a donor, it must review the coding measures, information security, and other potential risks for the donor that might arise from, for example, changes in legal status, principal investigators, or organisation of the original biobank.[819] The REC plays a role in ensuring that biobank or particular research respects ethical norms and comply with legislative acts. The UK Ethics and Governance Council, to give an example, oversees the UK Biobank's adherence to its regulative act the Ethics and Governance Framework. To perform its functions, REC has continuous access to an overview of the review process for all applications and can review the detail of any individual application.

Research ethics committees have emerged as an essential element in European biobank governance. It can act as an independent body from the biobank (for examples, the UK biobank's Ethics and Governance Council is independent of the biobank[820]), having a main function to protect the interests of the participants. It acts as a critical friend of the biobank, with the main task to protect the rights of the donors. The involvement of REC and the need for its favourable opinion is intended to ensure that a consent in broader terms is not inappropriately given an even wider interpretation and that exceptional situations in which consent may be waived are not illegitimately invoked.[821]

819 Hansson and others (2006) 269.

820 UK Biobank, 'Ethics' <http://www.ukbiobank.ac.uk/ethics/> accessed 8 May 2018.

821 R William G Watson, Elaine W Kay and David Smith, 'Integrating Biobanks: Addressing the Practical and Ethical Issues to Deliver a Valuable Tool for Cancer Research' (2010) *Nature Review Cancer* 10,

The OECD Guidelines[822] also establishes that in cases where human biological materials or data **are to be used in a manner not anticipated in the original informed consent process,** the governance, management, and oversight of such use must include the review processes done in accordance with applicable law, including research ethics committees or comparable oversight mechanisms being set up in place. Guidelines give examples of when the actions of such authorities are necessary: • for previously collected human biological materials or data where the user might deviate from the original consent; • for cases where informed consent may not have been obtained at the time of collection; • for determining when to seek re-consent; • *for use of human biological materials or data where consent was obtained using a broader or layered format for uses unspecified at the time of collection, especially in the case of large-scale genetic epidemiology studies*[823] (emphasis added). The Guidelines give the exact case that a trust shall be based on the ethics committee when samples are obtained using a broader consent regime. The members of the REC must also be trustworthy, competent and have the highest understanding about the biobank's activities.

The Spanish Law 14/2007 allows for the initial act of consent to include further use, related to the consent given. The law allows that specific act of consent to include consenting to the use of data and samples in other research projects, "related to the one initially proposed", by the same team or another one (Article 60.2). The "degree of relationship" between the two projects remains unspecified and open to interpretation by the relevant body, which is usually the REC supervising the biobank.[824] In such situation, RECs will have to decide about this issue of "project relatedness" and will have to produce appropriate guidelines and criteria. REC will have a possibility to waive the lack of informed consent and give a researcher requested information. REC will examine whether the following conditions are met: (a) the research is of general interest; (b) lack of data would make research impossible or less effective; (c) there is not an explicit objection to it; and (d) the confidentiality of personal data is guaranteed.[825] The new law relies heavily on decision making by RECs.

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822 OECD Guidelines on Human Biobanks and Genetic Research Databases (2009).

823 OECD Guidelines Article 3(1).

824 Antonio Casado da Rocha, 'Biobank Governance in Spain: From the Autonomy of Research Ethics Committees to the Autonomy of Lay People' in Deborah Mascalzoni and others (eds), *Ethics, Law and Governance of Biobanking. National, European and International Approaches* (Springer Science 2015) 231.

825 Ibid. 233.

To ensure the trustworthiness of the REC, its members must obtain the necessary education, have the highest ethical standards, so that the committee's decisions are lawful and correct. Generally, the members of the ethics committee are coming from different backgrounds (law, medicine, theology…). For example, the UK biobank's ethical committees included individuals with expertise in the use of genetic-epidemiological research resources. The Board has overall responsibility for the access procedures and all access decisions. It delegates oversight of the review process to its Access Sub-Committee. The Access Sub-Committee of the UK Biobank Board is responsible for making the key access decisions, notably those regarding the use of depletable samples or potentially contentious research. It is constituted as follows: it is chaired by a "non-scientist" member (with a legal and/or ethics background) of the UK Biobank Board and includes three further Board members with appropriate scientific expertise.[826]

A survey performed by Brian Salter and Mavis Jones showed that in UK, Iceland, Estonian, Latvian biobanks, the UNESCO International Bioethics Committee, plus the European Group on Ethics, the dominating characteristics of membership background in REC are medical science, particularly medical genetics, and law with a total number of 55 people (equal to 62 percent) of all the members.[827] The authors argue, that even if the expertise in science and law is regarded as an appropriate qualification for being able to make ethical judgements about the interests of citizens in the regulation of biobanks and other health technologies, such disciplines as philosophy may be called upon to deliver a degree of ethical sophistication and political functionality unavailable to medical science and law.[828] Therefore, the authors propose that people with ethical studies and studies of philosophy shall also become members of biobank's REC.

The members of the ethics committee have better knowledge about the research object and purposes. They can also contact the researcher, ask questions, in order to establish a better knowledge about the project and make a fair decision. From this perspective, the donor can have less knowledge and understanding about the specific uses of samples and make the incorrect decision about sample donation. The decision of the donor can be easily influenced by the personal perspectives or prejudices, what is different from the decisions made by the ethics committee, based on reasoning and analysis.

826 UK Biobank, 'Access Sub-Committee' <http://www.ukbiobank.ac.uk/access-to-the-resource/> accessed 8 May 2018.
827 Salter and Jones 728.
828 Ibid. 710.

Some authors express the opinion REC members cannot be really trusted and being humans they can also fail. Linus Johnsson and others[829] shows the limitations of the REC: rigidity – RECs have been found to rely more on local precedents than on theoretical frameworks; idiosyncrasy – no matter how competent its members, the REC is not always ideally positioned to evaluate the scientific merits of research projects, especially when they deviate from the paradigm; dependency – usually, at least some member in REC comes from the same research community and REC is not able to prevent harmful researches as they do not have any power to audit the research performed and how the samples/data were actually used. The authors propose that to ensure better reliance on the REC, first and foremost, RECs should be required to rationally justify their decisions. Face-to-face meetings are also noted to be preferable since they allow REC members to become familiar with the applicants and their capacities for ethical decision-making.[830]

Of cause, members of the ethics committee are persons. So, the possibility of error can never be eliminated. However, the REC is usually composed from more than one member, the decision it gives are reached in negotiation by people having different backgrounds and perspectives, not related with the study or the donor. Therefore, impartiality and professionalism must give confidence to the donors and the biobank. Nevertheless, the international, regional or even national guidelines could help REC to perform better and more accurate. Such guidelines one the one hand could have specific advice on how to evaluate the research, while on the other hand should leaving a sufficiently high level of abstraction to give room for deliberation, and not provide a narrow checklist point in making a decision. A member of the ethics committee must be taught and prepared to handle unexpected ethical problems.

The guidelines would be an important direction the REC could follow when making its decision. In Spain, as of 2008, there were 136 Research Ethics Committees, working mostly in the assessment of clinical trials, and some of them will have to act as review boards associated with biobanks.[831] There is also established the Coordinator Centre (known as CC-CEIC) that is acting as a contact point for further information on the network of RECs in Spain. The institution receives criticism for failing to provide

829 Linus Johnsson and others, 'Making Researchers Moral: Why Trustworthiness Requires More than Ethics Guidelines and Review' (2014) 10 Research Ethics 29.

830 Ibid. 15.

831 Adam M Hedgecoe, 'Trust and Regulatory Organisations: The Role of Local Knowledge and Facework in Research Ethics Review' (2012) 42 Social Studies of Science 662-83.

guidelines for all the other RECs.[832] Ambiguities make room for many possible outcomes and legal certainty here is same important as in any other decision.

This lack of guidelines also influences REC's members' psychological strength to make up their own decision. Especially, when the broad consent comes into play, and REC must decide to approve the research or not, many can have fears to make such a responsible decision. The study performed in Italian biobanks showed, that REC prefers to show a clear preference for partially restricted consent - which allows the use of biological specimens and related data for specific current research and future investigations directly or indirectly associated with current projects (50% of respondents). The large majority of the other RECs expressed a preference for specific consent (73%). Broad consent is regarded as acceptable by a low number of RECs (8%), as is presumed consent (4%).[833]

The decisions of research ethics committees can vary between committees, regions and countries and their powers of enforcement are limited to their own jurisdiction. Furthermore, there is currently no mechanism for the mutual recognition of research ethics committees or a pan-European research ethics approval.[834] The cultural and political differences in the countries can also play a crucial role in the approval or denial of scientific research by the committees. Approved guidelines would be a suitable mean to equalize the standards for the approved research and also would make for the work of the ethics committees more transparent. The members would be bound not by the national trends or political influences, but by commonly agreed standards.

To some extent, this process of unifying REC is already ongoing. The European Forum for Good Clinical Practice (EFGCP).[835] is an example of the development of common policies and standardized procedures for European RECs. Such initiatives need to be encouraged and supported for biobanking integration so that IRBs and RECs can work from a common set of standards, procedures and documentation that will streamline ethical applications without compromising the underlying ethics.[836]

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832 Jiménez PN and Casabona CMR, *Controles Éticos En La Actividad Biomédica: Análisis de Situación Y Recomendaciones* (Instituto Roche. Eucalipto, 33. 28016 Madrid 2009) 124.

833 Corinna Porteri, Elena Togni and Patrizio Pasqualetti, *The Policies of Ethics Committees in the Management of Biobanks Used for Research: An Italian Survey*, European Journal of Human Genetics vol 22 (2013) 260–265.

834 Clare Shelley-Egan, 'Ethics Assessment in Different Fields Internet Research Ethics', Project Stakeholders Acting Together on the Ethical Impact Assessment of Research and Innovation – SATORI (2015) 11.

835 The European Forum for Good Clinical Practice, 'Welcome' <http://efgcp.eu/> accessed 8 May 2018.

836 Watson, Kay and Smith 6.

The UN International Bioethics Committee recommended "to include all existing biobanks in an international registry with clear rules for access and sharing, in particular for cross-border and industrial access. <...> The rules governing data confidentiality and ethical review should also be harmonized."[837] By giving an overseeing body—in our case, research ethics committees (RECs)—the task of distrusting researchers, the public will not have to; they can go on cooperating, confident that the necessary control systems are in place. But to ensure effective oversight and maintain the legitimacy of the overseeing body, we also need clear rules or performance standards against which deviations can be spotted.[838] Guidelines, once intended to provide guidance, today shall be designed with this regulatory need in mind: to ensure higher trust by the research participants and better cooperation between the biobanks.

[837] International Bioethics Committee, 'Report of the IBC on Updating Its Reflection on the Human Genome and Human Rights' (2015) 20.
[838] Johnsson and others (2014) 32.

CHAPTER VI

OPEN BIOBANKS

In the previous chapters, I have talked about different types of biobanks, types of intellectual property rights that can be created by biobanks and the protection of the personal information of the donors. All these elements are unavoidable in biobanks management and functioning. Intellectual property rights and data protection have been developed throughout history, promoting innovation, giving the market powers and monetary incentives to companies, ensuring that rights are not misused. It is common to see IP rights applied to new technologies, that protects the invention and gives obligations to other parties. It is not a private firms business, public entities are also involved in the patenting game.

Universities encourage its students to apply for patents: technology transfer centres manage and license university's IP rights, take care of patenting proceedings, request students to fill in IP forms before disclosing to the public the research results. It seems that patenting is becoming not a choice, but rather an obligation that everybody must follow. Not always all the circumstances are evaluated before the patenting takes place, it has become a natural way – to patent. As was presented, on the one hand, intellectual property protects the investment of researchers or research institutions, but on the other hand, if misused, IPR can easily create a burden to share data and restrict progress in the genetic medicine. Every potential increase of protection might raise the cost of, or reduce access to, the raw material from which one can create something new. Therefore, in my thesis, I propose to question the monopolization of new discoveries by granting intellectual property rights in biobank field.

Professor James Boyle writes that "more property rights, even though they supposedly offer greater incentives, do not necessarily make for more and better production and innovation – sometimes just the opposite is true. It may be that intellectual property rights slow down innovation, by putting multiple roadblocks, multiple necessary

licenses, in the way of subsequent innovation."[839] This thesis promotes the soft-laws and multilateral agreements between biobanks to reach better improvements and to make biobanks more useful in genetics. In the final part of my thesis, I will disclose the initiatives, advantages and prospects of the openness in the biobanks. The presumption is that the more openly biobanks will share the samples and data with each other, the more valuable research outcomes to the society will be reached, and the work of biobanks will not go into the dustbin of academic literature.

I. Open biotechnology

1. Open biotechnology movement

The openness is a new but appealing concept. We do not create things from scratch. Professor James Boyle has very rightly stated: "information products are often made up of fragments of other information products; your information output is someone else's information input. Such input in biobanks is genetic information, databases of single nucleotide polymorphisms, sequences of DNA. The opponents of enclosure have claimed that the human genome belongs to everyone, that it is literally the common heritage of humankind, that it should not and perhaps in some sense cannot be owned, and that the consequences of turning over the human genome to private property rights will be dreadful, as market logic invades areas which should be the farthest from the market."[840]

The trend of free and open ideas is expanding in different fields. Richard Stallman first started the open source movement in computer software field. However soon enough similar ideas were adopted in the other areas. Thought the Creative Commons licensing schemes the authors can choose terms for general licensing of their copyrighted works: photos, music, videos, literature, academic articles and other. Similarly, open sharing is trying to find its way in the biotechnology.

Antonio Marturado explains that Open Source Initiative (OSI) philosophy can be applied to the biotechnology. He states that although the OSI definition's main criteria are referring to software, one protocol could suggest that the concept of open source may be

839 James Boyle, 'The Second Enclosure Movement and the Construction of the Public Domain' (2003b) 66 Law and Contemporary Problems 43.
840 Boyle (2003a) 98.

predicated on any individual technology or style of interface.[841] In the software world, open source refers to the ability to see the source code of programs. However, "open source" also embodies a set of cultural practices, licenses, and innovative collaboration methods.[842] Open source biotechnology initiatives have been proposed in the areas of bioinformatics software, genomic databases, and "wet lab" biology.[843]

Robin Feldman talks about open movement in biotechnology as offering a structure for cooperative exchange in the development of life science products that are either bioengineered or produced as a result of techniques that involve biotechnology. The projects and their design are varied, but a common theme is the desire to make biotechnology advances available to a broad research community and to ensure that such open access continues.[844] He explains that the open biotechnology does not reduce downstream rewards. It gives other than monetary incentives to the inventor, and participants are motivated by non-economic factors such as a desire for prestige and a desire to satisfy altruistic goals. Open access also cuts through patent thickets, it does not generate the monopolistic effects that the patent system produces typically, and does not produce the same level of restriction of supply and does not increase of prices of products as the patent system does.

Janet Hope explains the differences between intellectual property ruled biotechnology world and the biotechnology were open access is taking place. Differently from IPR ruling, where big companies having strong economic powers can restrict smaller companies using patented downstream technologies, in open biotech everybody has equal competitive power, independent on the company's size or economic powers.[845] Where open biotechnology is taking place, the use of the property is for promoting distribution and sharing of the object, oppositely, to the use of intellectual rights to control assets. Also, players in the open biotechnology have no obligations. Everyone can put as much input as he or she wants, nobody is forced to create-invent-patent, and therefore there are no deadlines, no push from outside. Differently, when IPR is licensed, the parties have their obligations: to pay remuneration fee, do not disclose confidential information, do not

841 Antonio Marturano, 'When Speed Truly Matters, Openness Is the Answer' (2009) 23 Bioethics 390.

842 Hassan Masum and others, 'Open Source Biotechnology Platforms for Global Health and Development: Two Case Studies' (2011) 7 Information Technologies & International Development 66.

843 Arti K Rai, 'Open and Collaborative Research: A New Model for Biomedicine' [2005] Intellectual Property Rights in Frontier Industries 140–145.

844 Robin Cooper Feldman, 'The Open Source Biotechnology Movement: Is It Patent Misuse?' (2004) 6 SSRN Electronic Journal 122.

845 Janet Hope, *Biobazaar: The Open Source Revolution and Biotechnology* (Harvard University Press 2008) 107–111.

license/sell in particular territories and similar. Furthermore, the licensing contract can be terminated by one party (eg. the licensor), and so another party is left without any possibility to use protected technology.

The main idea behind the open biotechnology is a joint contribution by different peers. As in open source programming, in biotechnology the same rule applies – one must give back to the community the new findings. The term open biotechnology has been used to refer to such different projects as open journals (e.g., Public Library of Science[846]), the new bioinformatic tool (e.g., the BioMoby messaging standard[847]), open databases (e.g., NIH db GaP[848], the International Stem Cell Forum[849]), big science project (e.g., HapMap or the Human Genome Project), or even project to facilitate access to biotech research tools (Cambia BiOS).[850] Such open projects are nothing but ideas built on ideas – a cooperative strategy against the monopolistic nature of the intellectual property regime.[851]

Hassan Masum and others present open biotechnology movement in Australia.[852] Cambia is a private, nonprofit institute in Australia that in 2006 launched the Biological Innovation for Open Society (BiOS) Initiative. BiOS aimed to create a "protected commons" to allow users to access, improve, and modify enabling technologies without infringing on proprietary rights. The BiOS project required that participants give back improvements in the core technology and made such improvements freely available to everyone.

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846 Public Library of Science (PLOS) was founded in 2001 as a nonprofit Open Access publisher, and advocacy organization that had a mission to speed up progress in science and medicine by promoting a transformation in research communication. PLOS database is available at PLOS, 'Official Webpage' <https://www.plos.org/> accessed 8 May 2018.

847 The MOBY system for interoperability between biological data hosts and analytical services. The MOBY system defines an ontology-based messaging standard that helps client automatically discover and interact with task-appropriate biological data and analytical service providers, without requiring hand-operated use of data formats as data flows from one user to the other. More information at Bio-Moby, 'Official Webpage' <http://biomoby.open-bio.org/> accessed 8 May 2018.

848 The database of Genotypes and Phenotypes (dbGaP) developed to collect and archive the data and results from studies that have investigated the interaction of genotype and phenotype in Humans. Available at National Center for Biotechnology Information, 'The Database of Genotypes and Phenotypes (dbGaP)' <https://www.ncbi.nlm.nih.gov/gap> accessed 8 May 2018.

849 The International Stem Cell Forum (ISCF) has a goal to encourage international collaboration and funding support for stem cell research, with the overall aim of promoting the global good practice and accelerating progress in this vitally important area of biomedical science. More at International Stem Cell Forum, 'Official Webpage' <http://www.stem-cell-forum.net/> accessed 8 May 2018.

850 Yann Joly, 'Open Biotechnology: Licenses Needed' (2010) 28 Nature Publishing Group 417.

851 David Koepsell, *Who Owns You? The Corporate Gold-Rush to Patent Your Genes* (Wiley-Blackwell 2009) 150.

852 Hassan Masum and others, 'Open Source Biotechnology Platforms for Global Health and Development: Two Case Studies' (2011) 7 Information Technologies & International Development pp. 61.

The Cambia's BiOS licenses are designed to nurture collaboration. BiOS licensee is granting to Cambia, a worldwide, non-exclusive, royalty-free, fully-paid license, with the right to sublicense the made technological improvements.[853] BiOS licensees must sign a detailed legal contract to preserve the right of others to use the technology (eg. to agree not to assert IP rights against others). The following advantages of the open BiOS licenses: ability to access the intelligence, creativity, goodwill, and testing facilities of a larger and broader community of researchers and innovators; decreased transaction costs relative to out-licensing or obtaining technology via bilateral license agreements; gives potential to expand the portfolio through synergies gained by combining segments of technology that may, by themselves, be too small to make a profit or lack satisfactory freedom to operate or implement; gives high leverage of expensive investments in obtaining proofs of concept, developing improvements, and obtaining governing and service data; and provides the ability to market products without an additional royalty burden.[854]

Secondly, Cambia together with the Queensland's University of Technology with some other partners,[855] has developed open tool "The Lens". "The Lens" is a free patent and academic literature informatics resource. "The Lens" is building an open platform for Innovation Cartography. Specifically, the "The Lens" serves nearly all of the patent documents in the world as open, annotating digital public goods that are integrated with scholarly and technical literature along with regulatory and business data. "The Lens" allows to collect documents, aggregate, and analyse them to be shared, annotated, and embedded to build an open mapping of the world of knowledge-directed innovation. Eventually, this should restore the role of the patent system as a teaching resource to motivate and inform entrepreneurs, citizens and policymakers.[856] One of "The Lens" open source software, the "PatSeq",[857] enables to perform search and analysis of DNA, RNA and protein sequences found in patents. The tool allows to search efficiently and access patents disclosing genetic sequences. A bulk downloads of disclosed sequence data based on jurisdiction, document type, and either sequence type or sequence location can be

853 CAMBIA BiOS, 'The CAMBIA BiOS License for Plant Enabling Technology' <http://www.bios.net/daisy/PELicense/751/383.html> accessed 8 May 2018.
854 CAMBIA BiOS, 'BiOS-Compatible Agreement Listing' <http://www.bios.net/daisy/bios/mta/agreement-patented.html> accessed 8 May 2018.
855 All participating institutions at Lens, 'Which Institutions Are Behind the Lens' <https://www.lens.org/about/which/> accessed 8 May 2018.
856 Available at <https://www.lens.org/about/what/> accessed 8 May 2018.
857 Available at <https://www.lens.org/lens/bio> accessed 8 May 2018.

performed. It also serves as a public, open repository for national systems to enable public sharing of sequenced data associated with patents.

There are of cause more open source approaches or tools used in the biotechnology. Like the Tropical Diseases Initiative, that is trying to solve the problem of the lack of samples related to tropical diseases and to encourage collaboration among scientists in this field. A new open source tool was created next to this initiative for predicting structures of protein sequences by comparative modelling, localising small molecule binding sites on the surfaces of the models and predicting ligands that bind to them. Investigators are encouraged to use the tool and to make the testings within the open source context.[858]

The tool was offered according to the Protocol for Implementing Open Access Data. The protocol is created by the Science Commons, an offshoot of the Creative Commons initiative. Science Commons was launched in 2005. Its main goal was to bring the openness and sharing to the world of science. Science Commons helped explore the intersection of the web, legal devices, and scholarly publishing for the benefit of scientific discovery, innovation, and collaboration. It is today re-integrated with Creative Commons and is no longer a discrete project.[859] The Science Commons implemented the initiative – the NeuroCommons, which is a beta open source knowledge management system for biomedical research that anyone can use, and anyone can build on. The NeuroCommons project seeks to make all scientific research materials as available and as usable as they can be. Such materials as research articles, knowledge bases, research data, physical materials, are made available.[860] The NeuroCommons ensures that the general data and knowledge sources used in computational biology, as well as sources specific to neuroscience and neuromedicine, are freely available to the science community.

Another case study presented in the same Hassan Masum's and others paper[861] is OSDD[862] (Open Source Drug Discovery) in India. OSDD aims to achieve affordable health care through a platform retaining patent protection alongside with the open source developments. In OSDD the drugs for masses, which shall be sold cheaply (such as

858 Leticia Ortí and others, 'A Kernel for the Tropical Disease Initiative' (2009) 27 Nature Biotechnology 320, 320–321.

859 Creative Commons, 'Open Science' <https://creativecommons.org/about/program-areas/open-science/> accessed 8 May 2018.

860 NeuroCommons, 'The NeuroCommons Project' <http://neurocommons.org/page/Main_Page> accessed 8 May 2018.

861 Masum and others 65-66.

862 Open Source Drug Discovery, 'Home Page' <http://www.osdd.net/> accessed 8 May 2018.

Hepatitis or TB drugs) are patent-free, while drugs that have high market affordability are patented.[863] Like the BiOS license, OSDD allows users to commercially or non-commercially use improvements, additions, or modifications of an invention – a drug. Users must grant back an unencumbered worldwide, non-exclusive right to OSDD for the use of any IP rights acquired for their improvements or modifications. OSDD approach to open source is to add it to the toolkit next to patent protection.

Another and probably one of the most known open biotech projects is the HapMap project. The target of the International HapMap Project was to develop a haplotype map of the human genome. Often referred to as the HapMap, it gives a description of the characteristic patterns of human genetic variation.[864] Concerning making the HapMap data available to users, the International HapMap Project emphasised its commitment to "rapid and complete data release, and to ensuring that Project data remain freely available in the public domain, at no cost to users."[865] The project released all the data it produced into the public domain, enabling any researcher worldwide to use the information for free. The project did not include "specific utility" studies to relate genetic variation to particular phenotypes, such as disease risk or drug response. Participants in the project have no goal and beliefs that SNP, genotype or haplotype data for which a specific utility has not been generated are appropriately patentable inventions. On the other hand, the project's policy did not prevent researchers from applying for patents on SNPs or haplotypes, as long as they do not prevent others from obtaining access to project's data.[866]

Until the HapMap Project was ongoing, it implemented "a free, non-exclusive, non-royalty-bearing licensing agreement to obtain access to certain types of data the project had collected on individuals' DNA sequences, specifically the genotypes."[867] The HapMap project's open license was titled as a 'click-wrap' license until the full genotype data was produced by the project and was sufficiently dense to allow derivation of

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863 Mrinalini Kochupillai, 'SPICY IP Interview with Dr. Samir K Brahmachari' *SPICY IP* (2008). Available at <http:// spicyipindia.blogspot.com/2008/03/spicy-ip- interview-with-dr-samir-k.html> accessed 8 May 2018.

864 NIH, 'About the International HapMap Project' <https://www.genome.gov/11511175/> accessed 8 May 2018.

865 Ibid.

866 Ibid.

867 NIH, 'International HapMap Consortium Widens Data Access' *NIH News Release* (2004).Available at <https://www.genome.gov/12514423/2004-release-international-hapmap-consortium-widens-data-access/> accessed 8 May 2018.

haplotype information.[868] Basically, the only condition of the license was that "users agreed not to prevent others from using the individual genotype data and to share data only with those who had also agreed to this condition." If this condition was followed, there were no restrictions for the user to access information in the HapMap. The consortium was concerned that other groups might combine some of the HapMap data on individual genotypes with their data to generate patentable inventions on haplotypes and then use these patents to exclude researchers from using the HapMap data, which some call 'parasitic' patents. The HapMap Consortium explained that its data access policy was formulated to avoid the filing of intellectual property claims that would impede other users' access to the data.[869]

After the project was finished, the HapMap Consortium removed a defensive 'click-wrap' license. In the view of the consortium, derivation of haplotypes and 'haplotype-tag SNPs' from HapMap data should be considered obvious and thus not patentable. Therefore, the original reasons for requiring to obtain a license to see the data no longer exist, and the licensing requirement has been dropped by the HapMap consortium.[870] Today the HapMap gives more than 5,5 million freely accessible and available studies on genome and gene variations.[871]

The HapMap project received several criticisms that the licensing terms of 'click-wrap' were not perfect.[872] However, despite the critics, the use of the open license in the HapMap policy demonstrates that the idea using open source license, similar to the ones used in software, in biotechnology are real and that it can help to compel users to give

868 'In formulating its data release policy, the HapMap Project had to address the potential problem of other parties filing, and being awarded, patents claiming certain of the data that the Project will produce. This concern arises because the genotype data produced during the early stages of the Project will not be sufficiently dense to allow derivation of haplotype information. During this time, however, it would be possible for others to combine the public HapMap Project's genotype data with their own, to construct haplotypes, to file for patents on those derived haplotypes, and in doing so potentially restrict others from using those haplotypes and underlying data. Therefore, the current licensing strategy has been adopted as a safeguard to prevent any such third-party patents that might otherwise use Project data being obtained or enforced in a way that would prevent others from using data generated by the Project, while at the same time allowing anybody who agrees to not use the data this way to have access to the data soon after they are generated.' Donna M Gitter, 'Resolving the Open Source Paradox in Biotechnology: A Proposal for a Revised Open Source Policy for Publicly Funded Genomic Databases' (2007) 43 Houston Law Review 11.

869 Ibid.

870 NIH, 'International HapMap Consortium Widens Data Access' *NIH News Release* (2004).Available at <https://www.genome.gov/12514423/2004-release-international-hapmap-consortium-widens-data-access/> accessed 8 May 2018.

871 NCBI, 'The HapMap Database' <https://www.ncbi.nlm.nih.gov/probe/> accessed 8 May 2018.

872 The relevant provisions were somewhat ambiguous, a tension was caused between the public-sector data users, who ultimately want their additions to the database to result in low-cost, innovative therapies, and those of commercial players acting in pursuit of proprietary business models. More about this in Janet Hope book *Biobazaar: The Open Source Revolution and Biotechnology* (2008).

back technology improvements and other downstream developments without legal encumbrance.

One more worldwide known example of open biotechnology is the Human Genome Project (HGP). HGP refers to the international 13-year effort, formally begun in October 1990 and completed in 2003, to discover all the estimated 20,000–25,000 human genes and make them accessible for further biological study. It was the international, collaborative research program whose goal was the complete mapping and understanding of all the genes of human beings.[873] The sequence of the human genome was obtained ultimately by 20 centres in six countries: China, France, Germany, Great Britain, Japan, and the United States. All the centres played a critical role in the overall effort, and the involvement of scientists from diverse nations provided a wonderful global sense to this investigation of our shared inheritance.[874]

The project wanted to determine the sequence of bases that make up human DNA, and to store such information in accessible databases, to develop tools for analysing the sequenced bases and information. The outcome of the project was the publication of the first complete human DNA sequence and has resulted in significant advances in biochemistry, bioinformatics, and genetics.[875] A "first draft" of the human genome sequenced by HGP was published in the public GenBank database in 2001. Moreover, the HGP disclosed not only the human genome sequences but also allowed to compare them with the sequenced genes of other species. In this way, it has provided users with additional and valuable sources of information concerning early human history, notably by considering the genome of others species (such as dogs, horses, rice, cereals, maize, etc.) as historical archives for bioarchaeological research.[876]

The HGP catalysed enormous technological progress in DNA-based methods that astonishing decreased the cost of sequencing and mapping of genes.[877] Within few years after the end of the HGP, the perspective of genome sequencing developed. By January 2000, HGP in 20 sequencing centres could collectively sequence 1000 base pairs a second, 24 hours a day, seven days a week, whereas, in the mid-1980s, even the best-

873 NIH, 'An Overview of the Human Genome Project' <https://www.genome.gov/12011238/an-overview-of-the-human-genome-project/> accessed 8 May 2018.

874 Francis S Collins, Michael Morgan and Aristides Patrinos, 'The Human Genome Project: Lessons from Large-Scale Biology' (2003) 300 Science 286.

875 Francis Collins, 'Has the Revolution Arrived?' (2010) 464 Nature 674–675.

876 Hub Zwart and Bart Penders, 'Genomics and the Ark: An Ecocentric Perspective on Human History' (2011) 54 Perspectives in Biology and Medicine 217.

877 Monika Gisler, Ryan Woodard and Didier Sornette, 'Exuberant Innovation: The Human Genome Project' (2010) 10–12 Swiss Finance Institute Research Paper Series, 17.

equipped laboratories could produce only about 1000 base pairs a day.[878] New revolutionary DNA sequencing technologies were introduced, and genomics groups continued to refine the basic methodologies used during the HGP and continued lowering the costs for genome sequencing.[879] The price drop has completely changed the way human-genomics research can be carried out. Based on the data[880] collected from the National Human Genome Research Institute's funded genome-sequencing groups, the cost to generate a high-quality 'draft' whole human genome sequence in mid-2015 was just above $4,000; by late in 2015, that figure had fallen below $1,500. In 2016 the cost to generate a whole-exome sequence was generally below $1,000.[881] The sequence of the genome for such a low price enables new studies identifying rare genetic variants linked to common diseases. It also gives prospect opportunities to open up the sequencing demand to diagnostic and pharmaceutical companies and incorporates genome sequencing in every day clinical drug testing.

A more recent open research project is 1000 Genomes Project. It was projected to generate 200,000 gigabases of data (approximately 20,000 times the quantity generated by the HGP) between 2008 and 2015. The objective of the 1000 Genomes Project was to find most genetic variants with frequencies of at least 1% of the populations studied.[882] The 1000 Genomes Project developed further on the sequencing technology. It was the first project to sequence the genomes of a large number of people, to provide a comprehensive resource on human genetic variation.

Information from the 1000 Genomes Project was quickly made available to the worldwide scientific community through freely accessible public databases.[883] Cell lines and DNA are available for all 1000 Genomes samples. This information can be obtained from the non-profit Coriell Institute for Medical Research.[884] A complete list of the populations available can be found in 1000 Genomes Project's Cell lines and DNA page.

878 Collins, Morgan and Patrinos 289.
879 NIH, 'The Cost of Sequencing a Human Genome' <https://www.genome.gov/27565109/the-cost-of-sequencing-a-human-genome/> accessed 8 May 2018.
880 NIH, 'DNA Sequencing Costs: Data' <https://www.genome.gov/sequencingcostsdata/> accessed 8 May 2018.
881 NIH, 'The Cost of Sequencing a Human Genome'.
882 EMBL-EBI, 'About IGSR and the 1000 Genomes Project' <http://www.internationalgenome.org/about> accessed 8 May 2018.
883 Ibid.
884 'Coriell Institute for Medical Research Official Page' <https://www.coriell.org/> accessed 8 May 2018.

The DNA samples can be ordered for a fee varying from $55 for a 50 μg sample of DNA isolated from cell cultures, up to $1000 for panels with 100 or more samples.[885]

Data from the 1000 Genomes Project are used to study and screen variants discovered in exome data from individuals with genetic disorders[886] and in cancer genome projects.[887] The enhanced catalogue presented in the project allows more accessible and more accurate analysis of the different diseases. Moreover, such data provides a new hypothesis for the number of rare, low-frequency and common variants with different functional consequences typically found in randomly sampled individuals from different populations. The studies that used data generated by the 1000 Genomes Project found that the data is assisting in the interpretation of the genetic-association studies, and also provides lessons on how best to design and analyse sequencing-based studies of particular disease.[888]

The possibility to access genetic data easily and freely is crucial for the better understanding of the disease, to build on already existing information when performing further researches. The named projects are the examples how genetic data can be made available for free to anyone with the ability to download it from the websites. The public availability of this data over the past decade has yielded significant advances in medical genetics, molecular biology, and bioinformatics; reduced research costs; and enabled greater reproducibility of results, all of which have contributed to the acceleration of scientific discovery and biomedical research.[889] Fortunately, the worries that genomic data would be placed in proprietary databases, protected by intellectual property rights, trade secrets or confidentiality restrictions never came true.

The HapMap, Human Genome Projects and 1000 Genomes Project all released information very quickly into the public domain and made it freely available. From the beginning, it was one of the operating principles of the HGP that the data must be publicly released well before publication (far more rapidly than is standard in the scientific community). The goal of releasing the key pre-competitive information was for

885 The Coriell Institute for Medical Research ordering information. Available at <https://www.coriell.org/1/page(0afd1ac6-61ea-45b4-b39e-a3fdf2f3f8be/> accessed 8 May 2018.

886 Michael J Bamshad and others, 'Exome Sequencing as a Tool for Mendelian Disease Gene Discovery' (2011) 12 Nature Reviews Genetics 745.

887 The Cancer Genome Atlas Research Network, 'Integrated Genomic Analyses of Ovarian Carcinoma' (2011) 474 Nature 609–615.

888 The 1000 Genomes Project Consortium, 'An Integrated Map of Genetic Variation from 1,092 Human Genomes' (2012) 491 Nature 56.

889 Jorge L Contreras, 'Constructing the Genome Commons' [2014] Governing Knowledge Commons 100.

promoting the best interests of science and helping to maximise the public benefit to be gained from research.[890]

The rapid data release was crucial for the development of the genetic sciences. In 1992, the federal co-managers of the project approved joint guidelines for the sharing of data by investigators performing HGP-funded activities, acknowledging that the rapid sharing of HGP materials and data was "essential for progress toward the goals of the program," and that such sharing would avoid unnecessary duplication of effort and expedite research in other areas.[891] Francis Collins notes, free and open access to genome data has had a profoundly positive effect on progress. The radical ethic of immediate data deposit, adapted by the Human Genome Project is now the norm for other community resource projects. It empowers the best minds in the World to begin working immediately in analysing the massive amounts of genomic data that is being produced.[892]

The commitment to release all human genome sequence freely rather than allowing it to become a commercial commodity of the enterprise was entirely useful decision for the scientific community and the general public. The alternative open commons model prevailed over propriety interest in the 'race for the genome'. All this openness in genetics and general medical science, started by HGP, was later strengthened in Bermuda's and associated meetings.

2. Bermuda principles of accelerated release

From the start, the Human Genome Project had a vital issue – to promote and encourage the rapid sharing of the data generated.[893] Sharing was considered essential to foster the project, to avoid duplication and to expedite research in other areas and it has never been a purpose of the project to keep the information secret or to sell it making the profit. The project decided to publish information as fast as possible, not only that everyone interested could access such data, but also prevent possible patenting by other private companies of DNA related information. Therefore, every part of the genome

890 Collins, Morgan and Patrinos 288.

891 Jorge L Contreras, 'Data Sharing , Latency Variables, and Science Commons' (2010) 25 Berkeley Technology Law Journal 1643.

892 Collins 674–675.

893 Jasper A. Bovenberg 'Accessibility of biological data: a role for the European database right?' in David Castle (ed), *The Role of Intellectual Property Rights in Biotechnology Innovation* (Edward Elgar Publishing 2009).

sequenced by the Human Genome Project was published immediately after revealed.[894] As it was an international project, so different participating entities needed to share data rapidly to coordinate their research efforts and not to analyse the already known information repeatedly. Such a fast release was also coupled with the desire to expedite scientific advancement as quick as possible and to establish a broad data sharing principles in the community.[895]

In 1996, at the summit in Bermuda, the leaders of the HGP settled that all human genomic sequence information generated by centres funded for large-scale human sequencing should be made freely available and published in the public domain within 24 hours after generation.[896] Before these principles were accepted, the standard practice was that the scientific research experimental data was available only after its publication and data were suspended for six-month "holding period" before release.[897] The Bermuda principles reshaped the practices of an entire industry and had established rapid pre-publication data release as the norm in genomics. The Bermuda Principles were drafted to encourage research and development and to maximise the Human Genome Project's benefits to society.[898]

In the meeting was agreed that finished annotated sequence should be submitted immediately to the public databases. It was agreed that these principles should apply for all human genomic sequence generated by public centres, that are funded by the state. It should prevent such centres establishing a privileged position in the exploitation and control of human sequence information.[899] Even the Celera Genomics, being in direct competition with HGP, eventually agreed to make the data from their competing effort to sequence the human genome available to the public.[900] Since their adaption, the Bermuda Principles have been used as a point of reference for publicly funded large-scale

894 NIH, 'The Human Genome Project Completion: Frequently Asked Questions' <https://www.genome.gov/11006943/human-genome-project-completion-frequently-asked-questions/> accessed 8 May 2018.

895 Heather L Harrell and Mark A Rothstein, 'Biobanking Privacy Laws in the United States' (2016) 44 Journal of Law, Medicine and Ethics 119.

896 The Bermuda Statement is an international agreement favouring release into the public domain of genetic databases achieved through public funding. See HUGO, 'Summary of Principles Agreed Upon at the First International Strategy Meeting on Human Genome Sequencing' (1996). Available at http://www.ornl.gov/sci/techresources/Human_Genome/research/bermuda.shtml#1 accessed 2018 May 8.

897 Robert Cook-Deegan and Stephen J McCormack, 'A Brief Summary of Some Policies to Encourage Open Access to DNA Sequence Data' (2001) 293 Science.

898 The Bermuda principles.

899 The Bermuda principles.

900 Jorge L Contreras, 'Bermuda's Legacy: Policy, Patents, and the Design of the Genome Commons' (2011) 12 Minnesota Journal of Law, Science & Technology 85.

sequencing projects. The attendants observed that these projects have become increasingly important and that they drive the progress in biomedical research better than keeping information secret.[901]

One of the most significant challenges was to show that data release policy does not conflict with the Bayh-Dole Act. The Bayh-Dole Act of 1980 provides that researches supported by public funds can and should seek patent protection, when appropriate. The US NIH shall also follow this act as it is public organisation. The Bayh-Dole Act encourages to patent the inventions made using government funds and to license those inventions with the goal of promoting their utilisation, commercialisation and public accessibility. The similar provisions are also followed in Europe and public research institutions more and more often patent their inventions in different fields.

The US National Human Genome Research Institute (NHGRI) has, following Bayh-Dole Act, encouraged grantees to seek patent protection for genomic technologies that have been developed with grant funds. However, on the other hands, the Institute expressed concerns about the patenting of large-scale genomic data sets and supported the broad accessibility of the large-scale genomic data. To solve this double problem, not to go against the Bayh-Dole Act, NHGRI communicated its opinion that raw data, in the absence of additional experimental biological information, lacks the specific utility and therefore are inappropriate materials for patent filing.[902]

The Bermuda principles were agreed between HGP participants and leaders. After they were adopted such community resource projects as International Human Genome Sequencing Consortium, the Single nucleotide polymers (SNP) consortium, the International HapMap Project or the Encyclopaedia of DNA elements (ENCODE) adopted same principles to their working methods. The rapid release of data became a visible 'driver of progress in biomedical research' serving the scientific community best.[903] Even if the fears, that rapid release of data can be re-used by other third party and published in a scientific article before such article is prepared by a person who indeed discovered or disclosed the information, such threats did not reduce the positive aspects

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901 Kshitij Kumar Singh (ed), *Biotechnology and Intellectual Property Rights. Legal and Social Implications* (Springer India 2015) 181.

902 NIH, 'ENCODE Project Data Release Policy (2003-2007)' <https://www.genome.gov/12513440/encode-project-data-release-policy-20032007/> accessed 8 May 2018.

903 Bovenberg, Jasper A. 'Accessibility of biological data: a role for the European database right' in David Castle (ed), *The Role of Intellectual Property Rights in Biotechnology Innovation* (Edward Elgar Publishing 2009) 338.

of accelerated data sharing. Therefore, public genome projects commonly concluded that immediate pre-publication release of the project data served the scientific community best and implemented such policies.

Same policies later were implemented in the internal rules of different biobanks. For example the UK Biobank (while not an open source project, in that it does require and review applications for data access before allowing academic institutions, nonprofits, and commercial companies non-exclusive data access) has implemented a grant-back policy.[904] All users of the information are "required to put results from all analyses made on participants' data and samples, and any relevant supporting information, in the UK Biobank database so that they are subsequently available to all researchers with appropriate scientific and ethics approval" and must give back all research findings generated using biobank's data into the public domain (a limited period of exclusivity is allowed, however).[905]

The Bermuda meeting was a first meeting seeking rapid publication of scientific data. However, the principles were later supported and reconfirmed in 2003 in the meeting in Ft. Lauderdale, Florida. In the Ft. Lauderdale meeting the participants reached a consensus that the Bermuda Principles should apply to each "community resource project" (CRP). The CRP was defined as any "research project specifically devised and implemented to create a set of data, reagents or other material whose primary utility will be as a resource for the broad scientific community."[906] Such definition includes all large-scale projects generating non-human sequence data (e.g., the Mouse Genome Consortium), other basic genomic data maps (e.g., the SNP Consortium and International HapMap Consortium), and other collections of complex biological data, such as protein structures and gene expression information.[907]

Follow on the Bermuda and Ft. Lauderdale meetings and decisions other similar initiatives began. One prominent example occurred in 2008 in Amsterdam. The NCI convened a meeting of proteomics[908] to "identify and address potential roadblocks to

[904] UK Biobank Ethics and Governance Framework 2007.

[905] Ibid.

[906] Wellcome Trust, 'Sharing Data from Large-Scale Biological Research Projects: A System of Tripartite Responsibility' (2003). Available at <http://www.genome.gov/Pages/Research/WellcomeReport0303.pdf> accessed 2018 May 8; Contreras (2011) 90.

[907] Contreras (2011) 90.

[908] Proteomics is the study of protein structures. Today, two definitions of proteomics are presented. The first definition is more classical, that restricts the large-scale analysis of gene products to studies involving only proteins. The second definition combines protein studies with analyses that have a genetic readout such as mRNA analysis, genomics, and the yeast two-hybrid analysis. However, the

rapid and open access to data."[909] Outcome of the meeting in Amsterdam was the agreement on six Principles for Proteomic Data Release and Sharing: 1) data generated by individual investigators should be released into the public domain at the latest upon publication while data generated by community resource projects should be released upon generation following appropriate Quality Assurance (QA) and Quality Control (QC) procedures. 2) Data must be released in a format that, as comprehensively as possible, captures the results of an experiment and the conditions under which the experiment was run. 3) Open access to proteomic data requires community-supported standardised formats, controlled vocabularies, reasonable reporting requirements, and publicly available central repositories. 4) Data shall be stored in the central repositories, and they should make it attractive for depositors to use them. 5) Main repositories should develop threshold metrics for evaluating data quality. These metrics should be developed in a coordinated manner, involving the participants from the research community and biobanks, to ensure interoperability. 6) Scientists, funding agencies, and journals share joint responsibility for ensuring that all parties adhere to community standards for data release.[910]

Another meeting dedicated spreading the open access principles took place in 2009. More than a hundred scientists, journal editors, legal scholars, and representatives of governmental and private funding agencies met in Toronto to assess the current state of rapid pre-publication data release.[911] One goal of the Toronto meeting was to reaffirm the existing principles as agreed in Bermuda, Ft. Lauderdale and Amsterdam for early data release with a wider group of stakeholders, and to extend, if possible, similar data release policies to other types of large biological datasets – whether from proteomics, biobanking or metabolite research.[912] In Toronto, attendees endorsed the value of rapid pre-publication data release for large reference datasets in biology and medicine that have broad utility and agreed that pre-publication data release should go beyond genomics and proteomics studies to other datasets – including chemical structure, metabolomic, and

goal of proteomics remains the same - to obtain a more global and integrated view of biology by studying all the proteins of a cell rather than each one individually. See Paul R Graves and Timothy AJ Haystead, 'Molecular Biologist's Guide to Proteomics' (2002) 66 Microbiology and Molecular Biology Reviews 39.

909 Henry Rodriguez and others, 'Recommendations from the 2008 International Summit on Proteomics Data Release and Sharing Policy: The Amsterdam Principles' (2009) 8 Journal of Proteome Research 3689.

910 Rodriguez and others 3689–3692.

911 Contreras (2011) 109.

912 Toronto International Data Release Workshop, 'Prepublication Data Sharing' (2009) 461 Nature 168.

RNAi datasets, and annotated clinical resources (cohorts, tissue banks, and case-control studies). The Toronto statement encouraged to rapidly publish data for large-scale, broad utility projects that are creating reference data sets and associates with community buy-in. It also stated that the funding agencies should facilitate the specification of data-release policies for relevant projects by explicitly informing applicants of data-release requirements, ensuring that evaluation of data release initiatives is part of the peer-review process, proactively establishing analysis schemes and timelines for projects releasing data prepublication, taking other actions. Data producers should state their intentions and enable analyses of their data by informing data users and giving general information about the data being generated and related information (e.g., questionnaires, phenotypes, environmental conditions) that will assist other researchers in analysing the data. Data producers shall also ensure that research participants are informed that their data will be shared with other scientists in the research community. The Toronto agreement also established suggestions for data analysts/users[913] and the scientific journal editors.[914]

Discussions in Toronto also addressed issues of intellectual property. The doubts were expressed that when more and more information and data are subject to rapid pre-publication release, it expands way beyond purely genomic and proteomic "basic science". Therefore, the question was asked if greater functional content and the clinical utility will be subject to rapid publication, can it have consequences on the patentability of this information and if the early release of such information can have a more significant impact on the data generators' ability to secure patent protection?[915] As the issue of patents are quite controversial, and there was no consensus among the participants, the subject of intellectual property was never published in the meeting report. Some representatives participating in the Toronto meetings express views that intellectual property issues will play an increasingly important role in discussions of rapid pre-publication data release in fields of medical significance.[916]

[913] The data analysts/users should freely analyse released prepublication data and act responsibly in publishing analyses of those data by: Respecting the scientific etiquette that allows data producers to publish the first global analyses of their data set; Reading the citeable document associated with the project; Wholly and accurately citing the source of prepublication data, including the version of the data set; Being aware that released prepublication data may be associated with quality issues that will be later corrected by the data producers; Discuss the publication plans with the data producers in the case of overlap between planned analyses; Ensuring that use of data does not harm research participants and is in conformity with ethical approvals.

[914] The scientific journal editors should engage the research community about issues related to prepublication data release and provide guidance to authors and reviewers on the third-party use of prepublication data in manuscripts.

[915] Contreras (2011) 110.

[916] ibid 111.

The Bermuda and following meetings that encouraged the rapid publication of information and its principles are taking precedent in genetic research. Internal documents of genetic research institutions incorporate the open research data policies. For example in 2008 the United Kingdom's Medical Research Council (MRC) released a comprehensive set of guidelines surrounding the release of data from MRC-funded research. The guidelines state, that "responsible sharing of data allows testing of new hypotheses and analyses, linkage and pooling of datasets, and validation of research findings. These activities not only reduce duplication of data creation but also enhance the long-term scientific value of existing data. It benefits the wider research community and generates new opportunities for advancement towards the longer-term goal of improving human health."[917] The MRC guidelines also set a broad data access principle – data generated by publicly-funded research is a public good and, as such, "must be made available for new research purposes in a timely, responsible manner."[918]

The Welcome Trust has an open access policy and believes that global health can be improved by supporting bright minds in science, the humanities and social sciences, and public engagement. Therefore, the Welcome Trust supports the unrestricted access to the published works of research as an underlying part of its charitable mission and a public benefit to be encouraged wherever possible.[919] Specifically, the Welcome Trust expects authors of research papers, monographs and book chapters to maximise the opportunities to make their results available for free. It also requires electronic copies of all research papers that have been accepted for publication in a peer-reviewed journal, and are financed in whole or in part by Wellcome Trust funding, to be made available through PubMed Central (PMC) and Europe PMC. The electronic copies must be made available as soon as possible and in any case within six months of the official date of final publication. The Welcome Trust also stated that it would provide the grant holders with additional funding to cover open access charges, where appropriate, to meet open sharing requirements.[920]

Another leading player in genetic research, the European Molecular Biology Laboratory (EMBL), is also applying rapid data release policies. EMBL is one of leading

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917 Medical Research Council, 'Principles for Access To, and Use Of, MRC Funded Research Data'. Available at <http://www.peac-mrc.mds.qmul.ac.uk/> accessed 2018 May 8.

918 Ibid.

919 Wellcome Trust, 'Open Access Policy' <https://wellcome.ac.uk/funding/managing-grant/open-access-policy> accessed 8 May 2018.

920 Ibid.

research institutions for the life sciences in Europe. EMBL scientists publish the research results and technology development in high-quality, peer-reviewed journals. EMBL has committed to provide free and unrestricted access to published research. EMBL's Open Access Policy consolidates its adherence to open access to publicly funded research outputs. The policy develops towards open access to scientific literature in EMBL's member states and is in line with the open access mandates of several main external funders such as the European Commission, the Wellcome Trust and the UK Research Councils.[921]

The biggest genome databases are releasing the new data and information as fast as possible.[922] However, the most significant majority of collections of nucleotide sequences or other genetic data stored in the international databases are provided by individual researchers or research institutions. The International Nucleotide Sequence Database Collaboration (INSDC), the National Center for Biotechnology Information (NCBI's) does not create data. INSDC or NCBI provides a platform, computer space, hard drives, remote clouds to store such data and makes it freely available to any interested party. Organizations put the effort in creating a platform, supporting it, making it available, but it does little towards the creation of a content of a database.

NCBI administers one of the biggest genetic database, a GenBank. The most important source of new data for GenBank is direct submissions from scientists. GenBank depends on its contributors to help keep the database as comprehensive, current, and accurate as possible.[923] The genetic information – uploaded gene sequences, can usually be amended also only by a person who uploaded it to a database. Some sequences may be manually curated by biobanks personnel so that the associated entries contain extra

[921] EMBL-EBI, 'Internal Policy No. 66. EMBL Open Access Policy' (2015). Available at <https://www.embl.de//services/library/open-access-information/open-access-at-embl/IP-66-EMBL-Open-Access-Policy.pdf> accessed 2018 May 8.

[922] The main resources for storing and distributing sequenced data are three large databases: the NCBI database, the European Molecular Biology Laboratory (EMBL) database, and the DNA Database of Japan (DDBJ). These databases collect all publicly available DNA, RNA and protein sequence data and make it available for free. They exchange data nightly, so contain essentially the same information. All published genome sequences are available over the internet, as every scientific journal requires that any published DNA or RNA or protein sequence must be deposited in a public database.

[923] NCBI, 'How to Submit Data to GenBank' <https://www.ncbi.nlm.nih.gov/genbank/submit/> accessed 8 May 2018.

information, but the majority of sequences are uncurated.[924] GenBank sequence records are owned by the original submitter and cannot be altered by a third party.[925]

Without fast release and free access to information, there would be very little input from the scientific community, and the databases would not have new data and information. Moreover, as mentioned, raw gene sequence information or other raw genetic information available in the genetic databases does not have any copyright protection. So after an actual researcher uploads it, it belongs to the whole community.[926] Also, because human DNA sequence data cannot be invented around, downstream users of such data are often motivated to place upstream data in the public domain so as to thwart patenting that would impede the development of downstream products.[927]

The Bermuda principles and later initiatives that followed had a tremendous positive impact to genetic research and sharing of knowledge. Incentives to support the voluntary release of genetic data before publication, while recognising and protecting the interests of scientists who disclosed the data, is a definite benefit to all scientific community and people. Data and research sharing arrangement works best for data that is sufficiently upstream, as the genetic sequences databases.

II. Open licenses

1. Using IPR in open biobanks

I have already talked about patenting of genes and use of patent rights in biobanks. Patents are the most common intellectual property right when we talk about genetics and genomic research. Other IP rights, such as database rights, copyrights in software, can also play an essential role in the information sharing in the biobanks.

The private biobanks and biotechnology companies are still very much interested in patenting the human gene sequences or other information, protect their created databases.

924 Avril Coghlan, 'Sequence Databases' <http://a-little-book-of-r-for-bioinformatics.readthedocs.io/en/latest/src/chapter3.html> accessed 8 May 2018.

925 NIH, 'TPA Frequently Asked Questions' <https://www.ncbi.nlm.nih.gov/genbank/tpafaq/> accessed 8 May 2018.

926 But not to be confused with published papers, which also are available in genetic databases.

927 Matteo Pascuzzi, Giovanni; Izzo, Umberto; Macilotti, *Comparative Issues in the Governance of Research Biobanks* (Springer-Verlag Berlin Heidelberg 2013) 117.

As I was talking in the previous chapters, intellectual property rights can be a burden for the open research, sharing of knowledge, and can restrict innovation if downstream data is monopolised.

Patenting in genetics at the final point increases the price of medicine. High medicines prices is one of the reasons why roughly 2 billion people – one-third of the world's population – still lack regular access to essential medicines.[928] However, patenting or other IP rights will not cause any adverse effect for genetic research and gene-related inventions if such rights are not used in a restrictive manner and are used reasonably to promote open sharing. If the holders of the rights are allowing other researchers to use the patented invention, IP rights can be used in the open biobanks very positively. What I am trying to say is, if a company, indeed, has patented a human gene sequence, but is not intentionally restricting other companies, public bodies, researchers, to use that patented discovery, the free flow of information is not restricted and open biobank can be established.

Open biotechnology and open biobanks are not necessarily antagonistic to intellectual property, and patent rights, an open source project can be developed that makes use of the patent system. Yann Joly explains the possibility that open biotechnology could also include a mechanism to allow the initial researchers to recuperate reasonable production costs invested in its realisation. She, however, cautioned that such mechanism should not impede the open nature of the project. The author suggests that a variety of licensing schemes with or without IP (e.g. patent pool, non-assertion covenants, protected commons agreement, contractual licenses) can theoretically be used as the engine to support the open nature of the project.[929]

Another author, Janet Hope, explains why she believes open source is a better way to encourage dissemination of knowledge than a pure free revealing of information.[930] First, she says, in cases where intellectual property rights arise automatically, open source license may help to reduce the transaction costs of transferring the technology to other potential users by clarifying the owner's will to make the technology available on nonproprietary terms. Some biological innovations incorporate software code, data, written protocols, or other elements that may be subject to copyright protection. Similarly, many biological innovations in biobanks usually have tangible material components such

928 Jonathan D Quick, 'Essential Medicines Twenty-Five Years on: Closing the Access Gap' (2003) 18 Health Policy and Planning 1.
929 Yann Joly, 'Open Biotechnology: Licenses Needed' (2010) 28 Nature Publishing Group 417.
930 Hope (2008) 158–164.

as cell lines or germplasm, blood cells, that constitute institutions property. Irrespective of any intellectual property rights that may be associated with the technology, open source can assist in sharing such property with other researchers, delivering the samples.

Secondly, Janet Hope states that the approach to adopt open source licensing for a patent might be relevant when the patent is still valid, but its use is not so relevant anymore.[931] After patent's value as a generator of proprietary licensing revenue begins to decline, granting an open source license is then an alternative to abandoning the patent. It can help to promote the technology and can be used in company's advertising campaign.

The third positive aspect of protecting the technology is that simple free revealing of information without first asserting ownership leaves open the possibility that someone else will patent the technology and pursue a proprietary exploitation strategy. Even if a defensive disclosure is done before the patent application is filed, the possibility exists that patent examiner will not find such publication and the patent will be granted to a third party. Another user of the technology not only will be forced to search for such for preventing literature himself/herself but also will need to start legal patent invalidity proceedings. Even the original inventor can face challenges as the invalidity of the patent must always be shown in a courthouse, and it may be too burdensome to start invalidity actions for smaller companies. Straightforward free revealing is especially risky where there is a proliferation of overlapping intellectual property rights, or the field of innovation is exceptionally competitive or litigious.[932]

Another reason, why open source licensing can be preferred over merely revealing the information, is that ownership of rights gives the patent holder the ability to set up the terms of use. For example, the patent owner can establish that free use of a patent is allowed only if its user gives back under the same conditions all the new findings and disclosures. Those that do not agree with the proposed open license terms will not be allowed to use technology and will be excluded. In this case, the proprietor has a broader range of strategic options than mere publication or defensive disclosure. It is a particularly useful way to manage the "automatic" IP rights, such as copyrights, or database rights. Similarly to open software licenses, the owner of rights in biobanks can request any other users to share new findings under the same open source licensing regime, give back the research results.

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931 Ibid.

932 Hope (2008) 161.

Moreover, to add some more reasons, sometimes patenting is an inevitable outcome of a particular national research project. For example in Lithuania, the research institutions or universities foresee the patent application as an outcome of the state-funded project. National institutions give more credit and higher funding to such research projects that foresee IP protection and submitting the patent application during the investigation process. In this way, the project participants show, that the project was new, inventive and was worth public financial contribution. Presumably, such project is finalised by a patent issued. Would that not be great if such patent supported merely by public funding is available to anyone under the open license? The open licensing way would be a perfect solution to share the knowledge and value of such patented inventions.

As long as intellectual property protection in the biobanks field is playing an important role and is desirable by those who invest in genetic innovation, open source licensing is a suitable tool to establish a fair balance between the holder of rights, the researcher, and the final beneficiaries – the people. The development of the relevant technology will have much less to do with pure proprietary exclusivity, but rather with establishing networks of users, eliminating any possible flaws, and demonstrating the value of the technology.

National Institute of Health has published the best practices for the licensing of genomic inventions. The NIH makes a separation between inventions that require exclusive licenses as an incentive for commercial development and the inventions that can be best disseminated with the non-exclusive licenses. The practices say that whenever possible, non-exclusive licensing should be pursued as a best practice. A non-exclusive licensing approach favours and accelerates broad enabling technologies and research uses of inventions widely available and reachable to the scientific community. When a genomic invention represents a component part or background to commercial development, non-exclusive freedom-to operate licensing may provide a proper and sufficient complement to existing exclusive intellectual property rights.[933] The Best Practices also explains that exclusive licenses should be limited to the scope and territory, to use the invention better. For example, patent claims to gene sequences could be licensed exclusively in a limited field of use drawn to the development of antisense molecules in therapeutic protocols. Independent of such exclusive consideration, the same

[933] 'National Institutes of Health Best Practices for the Licensing of Genomic Inventions: Final Notice, Federal Register, Vol. 70, No. 68' (2005) 18415.

intellectual property rights could be licensed non-exclusively for diagnostic testing or as a research probe to study gene expression under varying physiological conditions.[934]

The Organization for Economic Co-Operation and Development has also published Guidelines for the Licensing of Genetic Inventions.[935] The Guidelines contain principles and best practices for the licensing of genetic inventions used for the human healthcare purposes. They are directed at all those involved with innovation and the provision of services in health and, essentially, at those involved in the licensing of such inventions. The Guidelines are for the genetic invention including nucleic acids, nucleotide sequences and their expression products; transformed cell lines; vectors; as well as methods, technologies and materials for making, using or analysing such nucleic acids, nucleotide sequences, cell lines or vectors.[936]

The Guidelines encourage the IP owners to license the technologies in such a way that the licensing terms and conditions maximise the utilisation of the genetic invention.[937] It also states that the rights holders should broadly license genetic inventions for research and investigation purposes.[938] The document also encourages the licensing for the freedom of research and that the licensing practices should increase rather than decrease access to genetic inventions for research purposes.[939] The Guidelines state that the licensing agreements should include terms that maintain low barriers for access to genetic inventions. It may mean that such agreements do not include, for example, excessive up-front fees and that license agreements should avoid reach-through rights to foster broad and unencumbered utilisation of the genetic invention and do not discourage or stifle subsequent innovations.[940]

The appropriate means of licensing of genetic inventions can play a critical role in the biobanks and sharing of knowledge. The licensing practices can promote a robust research environment and a market for healthcare products and services. The broad licensing of genetic inventions is preferable in order to maximise the chances that a genetic invention will be widely used. To support even further the sharing of genetic information, a possibility that open licenses can be applied in biobanks shall become real.

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934 Ibid.
935 OECD, 'Guidelines for the Licensing of Genetic Inventions' (2006). Available at <https://www.oecd.org/sti/biotech/36198812.pdf> accessed 2018 May 8.
936 Ibid. page 14 „General Terminology", Article 7.
937 Ibid. Article 1.6.
938 Ibid. Article 2.1.
939 Ibid. Article 3.A.
940 Ibid. Article 4.2 and 4.3.

I find it possible, that open licenses, already approved in the information technology field and now applied to any copyright object (with the help of Creative Commons licenses), can also find its way in the field of genetics and the biobanks.

2. Examples of open licenses

I have talked about open sharing, open biobank and possibilities to use IP rights in a non-restricting way. I have also mentioned that open licenses can be used in biobanks. Using the open licensing templates and forms already applied in the other fields, I will try to draw the main criterion of the open biobank's license. The open license is a license to an IP protected work, which applies to every person, confirming the licensing conditions. The open licenses in biobanks can represent an elegant use of contractual terms and property rights to create social conditions in which intellectual property rights in the genetic field are used and new rights created on a model of openness. Such license does not need to nullify the IP rights, but it allows to use such rights in a non-protective way.

The terms and conditions of an open license usually are presented next to the IP rights protected object. For example, the Creative Commons license is presented in the corner or front page of a copyrightable work. Open license means that anyone who agrees to use the work under the conditions specified in the license can use the work free of charge, in an unlimited territory and without additional approval from the owner. A license attached to work is a legal document that specifies what can and cannot be done with work. The open license can grant permission to access, re-use and redistribute a work with few or no restrictions. What is very important is that open source strategies do not rely on domestic or international law reform. It is a contract between the holder of rights and the user, so it is governed by the contract law and not the intellectual property law.

"Open Definition" describes open license as such that: allows free use of the licensed work; allows redistribution, modification, and compilation for any purpose of the licensed work, including sale; allows the creation of derivatives of the licensed work and allows the distribution of such derivatives under the same terms of the original licensed work; allows any part of the work to be freely used, distributed, or modified separately from any other part of the work or from any collection of works in which it was originally distributed; allows to make compilations; does not discriminate against any person or

group; the license is attached to the work and applies to all; is free of charge or any other payments.[941]

The initiative of open licenses started in 1983 when the free software movement was launched. Free software movement initiated open source licenses – a type of license for computer software that allows source code to be used, modified and shared under defined terms. From that time in the computer software world creators are widely developing and sharing computer codes through the open source licensing system. Other open licenses in the computer-related areas have been developed, such as open database licenses and open game licenses.

Currently, there are several initiatives – bigger or smaller, that dedicate their goals to promote free and open sharing of information, data, works. For example, the Open Knowledge International (OKI) is a global non-profit organisation focused on realising open data's value to society by helping civil society groups access and use data to take action on social problems.[942]

Creative Commons is another global nonprofit organisation dedicated to supporting an open and accessible Internet that is enriched with free knowledge and creative resources for people around the world to use, share and cultivate. Creative Commons (CC) helps authors to share their works, knowledge and creativity legally and to build a more equitable, accessible, and innovative world. Creative Commons provides free, easy-to-use copyright licenses to make a simple and standardised way to give the public permission to share and use the creative work – on conditions of author's choice.[943]

Creative Commons licenses are very easy to use. One can mix four different types of licenses to allow others to copy, distribute, and make some uses of their work. The licenses are presented in the clearly understandable format: such as  [944]. Every Creative Commons license works around the world and lasts as long as applicable copyright lasts.

The most remarkable feature of Creative Commons licenses is that they are understandable to every user. Public copyright licenses incorporate a unique and

941 'Open Definition 2.1' <https://opendefinition.org/od/2.1/en/> accessed 8 May 2018.
942 Open Knowledge International, 'About' <https://okfn.org/about/> accessed 8 May 2018.
943 'Creative Commons' <https://creativecommons.org/> accessed 8 May 2018.
944 The license called „Attribution". This license lets others distribute, remix, tweak, and build upon the work, even commercially, as long as they credit the author for the original creation. It is the most cooperative of offered licenses, recommended for maximum dissemination and use of authorized materials.

innovative “three-layer” design: 1-Legal Code, a traditional legal tool written in legal language; 2- Commons Deed, “human readable” version of the license, that is understandable for every normal user; 3-software code, a “machine-readable” version of the license (a summary of the key freedoms and obligations written into a format that software systems, search engines, and other kinds of technology can understand).[945] All these three layers allow creators easily apply the licenses, and users to understand and find the works covered by the Creative Commons. Such multi-layered format of licenses allows to adapt them to different international jurisdictions. Human-readable and machine-readable versions remain unchanged from one jurisdiction to another, while the lawyer-readable version is adjusted to take account of different legal environments.[946] Such platforms like Youtube, Google, picture platform Flickr, music platform Jamendo, allows to search for works with CC license in their search engines.

A similar approach to CC could be adapted in open biobanks. Amy Kapczynski and her colleagues at Yale University proposes an Equitable Access licensing, designed to improve access to biomedical innovations in low-income and middle-income countries, and Neglected Disease licensing, intended to facilitate research beneficial to people suffering from neglected diseases.[947]

Equitable Access licensing has similar woking methods like the licensing practices that govern free software. The Equitable Access licensing approach is designed to harness technologies developed through university technology transfers to the industry. It uses proprietary rights to secure freedom for an open class of potential users and to ensure the right of third parties to access and distribute the innovation and its derivative products. Under an Equitable Access license, a university would, for a fair royalty payment, grant to another party (such as a commercial firm) a non-exclusive license to use its patented technology to produce an item for sale in poorer countries and wealthier countries (territorial limitations are not applied). In return, the licensee would agree to grant back to the university any improvements it might make to the technology and to cross-license any other rights the licensee holds that might be used to block the production of the item in question.[948]

945 Creative Commons, ‘About The Licenses’ <https://creativecommons.org/licenses/>.
946 Janet E Hope, ‘Open Source Biotechnology’ [2004] SSRN Electronic Journal 110.
947 Amy Kapczynski and others, ‘Addressing Global Health Inequities: An Open Licensing Approach for University Innovations’ (2005) 20 Berkley Technology Law Journal.
948 Hope (2008) 319.

Equitable Access licensing terms would apply to all improvements to the technology. The licensing terms would follow the innovation no matter who uses it or what improvements are done. Such licensing terms would keep the competition high and lower the drugs prices in poorer countries. Lower prices can be reached for such critical pharmaceutical products like aspirin, cisplatin or insulin. On the other hand, the licensing territory would not be limited to only developing countries. The licensee would have a possibility to sell in any country, so it could compensate the less favourable aspects of the deal in developing countries, with revenues it makes in rich country markets.

Kapczynski and others favour the Equitable Access licensing for health-related technologies. Licensing clauses can be applied regardless of the type of health care, related to any technology that has health-related, or more broadly, human welfare, benefit. The focus by the researchers is in biomedical technologies, but it can be applied to any health-related technology with a demonstrated medical benefit. The idea behind such licensing agreements is to give help and assistance to poor people, living with very minimal or no income at all, and ensure such people can receive better health care and overcome the diseases. It is a very profound goal that open licensing can assure. Proposal of Equitable Access licensing does not seem to be different from the open licensing – everyone participating in such licensing scheme is sharing the benefits and improvement with each other.

The mechanism of operation for the Equitable Access licensing can be summarized in three steps: (1) cross-licensing and grant back of rights between the university and a licensee; (2) notification by a third party of intent to supply a drug to low and middle-income countries; and (3) grant back of rights for any subsequent developments made by the third party to the university.[949] If a generic supplier (or other entity, such as a ministry of health or an NGO) wishes to compete with a university's licensee in a low-income country to make or market a given product that is covered by the Equitable Access license, the generic supplier has only to write a letter to the university and the licensee, expressing this intent to invoke the Equitable Access license in the low income country. Such notification triggers the generic supply, it can automatically use open licensing provisions. Intellectual property and regulatory hurdles are immediately removed through

[949] Samantha Chaifetz and others, 'Closing the Access Gap for Health Innovations: An Open Licensing Proposal for Universities' (2007) 3 Globalization and Health 3.

the open licensing of any patented technologies and proprietary data for a requested party.[950]

The Equitable Access licenses are already in use. An example is an agreement between the Yale University and generic drug manufacturer. Yale University had given an exclusive license to the pharmaceutical company Bristol-Myers Squibb (BMS) to use the patent on the HIV-medication d4T (Stavudine). However, such agreement received strong opposition from the public pressure. Therefore, Yale asked BMS to grant "patent relief", and BMS agreed to allow Aspen Pharmacare, a leading South African generic manufacturer, to produce the AIDS drug locally. The price of d4T dropped by 96 percent within a year. It allowed to scale up HIV treatment programs across Africa.[951]

Another use of Equitable Access license was done by the foundation of UAEM (Universities Allied for Essential Medicines). The group developed the first standard form of an Equitable License, and inspired the so-called Philadelphia Consensus Statement in 2006. In this statement the university leaders acknowledged their institution's social responsibility in making accessible the essential medicines.[952]

Some examples show, how Equitable Access license would prevent the misuse of a patent. The Emory University, Gilead Sciences, and Royalty Pharma announced a deal in which Emory sold its 20% royalty interest in the antiretrovirals Emtriva (emtricitabine, FTC) and Truvada (emtricitabine+tenofovir, FTC+TDF) for an up-front payment of $525 million. The emtricitabine was a compound discovered and patented by the university. At the beginning it looked like a great deal for the parties, however, with this deal the University lost an opportunity to renegotiate the contract the upcoming year. It missed a second chance in the royalty buyout negotiated with Gilead and Royalty Pharma. If Emory would have included the Equitable Access license terms it could have received the same $525 million payment, while at the same time ensuring the access to Emtriva and Truvada to millions of patients in developing countries.[953]

Equitable Licensing is a better way to provide drugs to middle and low-income countries. It is useful not only to the people but also to the manufacturer. The reason for this is clear: those patients who need medicine will not be able to purchase them if the price will be too high, neither will be able companies to make any sales. Also, when

[950] Ibid.

[951] Christina Godt, Christian Wagner-Ahlfs and Peter Tinnemann, 'Equitable Licensing – Ensuring Access to Innovation' in David Bollier and Silke Helfrich eds. *'The wealth of the commons: A world beyond market and state'* (Levellers Press 2016).

[952] Ibid.

[953] Chaifetz and others 1.

Equitable Licensing is taking place, a manufacturer can be more or less sure, that the government will not impose a compulsory license on its product. Low licensing fee and the possibility for the competitors to come into market ensures (or at least reduces to a minimum) a risk that government will intervene in the competition and impose its price on a drug. For low-income countries, the Equitable Licensing sets the royalty rate as low as possible (it can be just one percent). It is better to negotiate an Equitable License than to pay high royalties and not to sell in poor countries when the prices are not reasonable, and people cannot afford a drug.

Another type of open licenses in biotechnology, presented by Kapczynski and the colleagues, is a Neglected Disease licensing.[954] Neglected diseases are conditions that inflict severe health burdens on the world's poorest people. Many of these conditions are infectious diseases that are most prevalent in tropical climates, particularly in areas with unsafe drinking water, inadequate sanitation, substandard housing and little or no access to health care.[955] Curing such diseases usually do not bring significant economic income to the manufacturer, but medicines are necessary to help the people in need. If intellectual property rights would additionally burden research tools or technologies to treat neglected diseases, barely any company would put effort to develop needed drugs.

The proposed Neglected Disease license would make an IP protection exception for neglected diseases research in the contract. The license agreement would ensure that no exclusivity is granted to the university or transferred by the university to a licensee, related to research, treatment or diagnoses of the neglected diseases. A Neglected Disease clause would allow a university to retain the right to license the use of the technology for research on neglected diseases anywhere in the world and for commercial purposes in low- and middle-income countries and no company would have the exclusive use of such technology.[956] There are various possible formulations of Neglected Disease license: the licensee might be required to grant back and cross-license its intellectual property, the research exemption might be confined to non-commercial institutions, or to a definite list of neglected diseases, or to diseases that meet a general standard can be made.[957]

The presented licensing agreements assist in providing poorer nations with better health care and access to medicine. If such open licenses are used more often, as

954 ibid.

955 NIH Genetic and Rare Diseases Information Center, 'Neglected Diseases' <https://rarediseases.info.nih.gov/files/Neglected_Diseases_FAQs.pdf> accessed 8 May 2018.

956 Kapczynski and others 1112.

957 Janet Hope, *Biobazaar: The Open Soure Revolution and Biotechnology* (Harvard University Press 2008) 319.

examples show, the prices for the essential drugs can drop radically. Hopefully, the same conditions can play an important role in the open biobanks.

3. Open licenses in genomics

The ESHG proposes to work with the existing patenting systems and find complementary mechanisms facilitating access to patents, such as new licensing models. ESHG underlines that changes in the regulation of patenting system cannot be done separately and only in genetics and gemonics. It would mean that the whole patenting systems need to change, which is very unlikely and also, unnecessary.[958]

The presented Equitable Access and Neglected Disease licenses originated as a licensing proposal for university's IP rights. However, it does not mean that similar initiatives cannot apply to other spheres, including biobanks. There are many similarities between universities and biobanks: both institutions usually receive high public financing, both have same primary goal – to perform researches on health conditions and to try to reach best possible results, both are using widely the work and analysis done by the partner institutions (neither a university nor a biobank wants to perform the same research another institution has already done). Therefore, similar licenses can be used in the biobanks.

In the open license for the biobanks, it could be agreed that participating biobanks are not restricting the use of their data to the other biobanks and that all new findings and discoveries should be returned and not monopolised by any IP right. It shall also be allowed for non-profit or profit institutions, even if they are not considered as biobanks, to use the information for research purposes – again, no IP right can be used to monopolise the information, and all the findings must be returned. Moreover, the findings from the use of such open resources would be available to anyone.

Let's imagine the 1st biobank has a haematological collection of samples and related data. The 2nd biobank stores information about lung cancer patients and relevant collection. The 3rd biobank wants to research about relations between smoking habit and a hear diseases, for which it needs information from the 1st and the 2nd biobanks.

[958] The ESHG Working Party on Patenting and Licensing, 'Patenting and Licensing in Genetic Testing: Recommendations of the European Society of Human Genetics' [2007] European Journal Of Human Genetics 3.

Under the current regulation, the 3rd biobanks needs to present its project to the other two biobanks, receive an approval from the ethics committees, confirm with the rules of all the national laws that are applicable to personal data, indicate clear and strict uses of the samples, pay all the fees, and only after these administrative procedures are confirmed it can receive the samples.

Under the open biobanks model, the 3rd biobank would present commonly approved Material transfer agreement template, indicating that it uses same restrictions and safeguards of the personal data as other biobanks, and confirming that it will give back all the samples that remain and will provide all the information about research outcome. No fees would be required from the open biobank as all biobanks would be sharing their information commonly, and so, theoretically, by sharing they are covering each others' expenses. It would mean that, once the 1st biobank needs information from the 3rd biobank, such information is given under the exact same conditions, like when the 3rd biobank needs information from the 1st biobank. Also, all the information generated by the researchers in the 1st and 3rd biobanks is shared between them and between the 2nd biobank as well.

The social relationships between the people would also assist in making such information sharing model working. People are the social beings, and they care about the wellbeing of others especially, the sick ones or people who cannot have normal living conditions, are inferior and vulnerable. Therefore we care about the positive impact a biobank can have, not necessarily for us, but for the humanity in general. I would be much more willing to buy medicine from a pharmaceutical company that I know is investing its profits in creating cures for underprivileged. In the same manner, I am more willing to become a sample donor in the biobank that is giving for free its finding and sharing its samples with other research institutions, having a common goal – to advance the research and improve medical conditions.

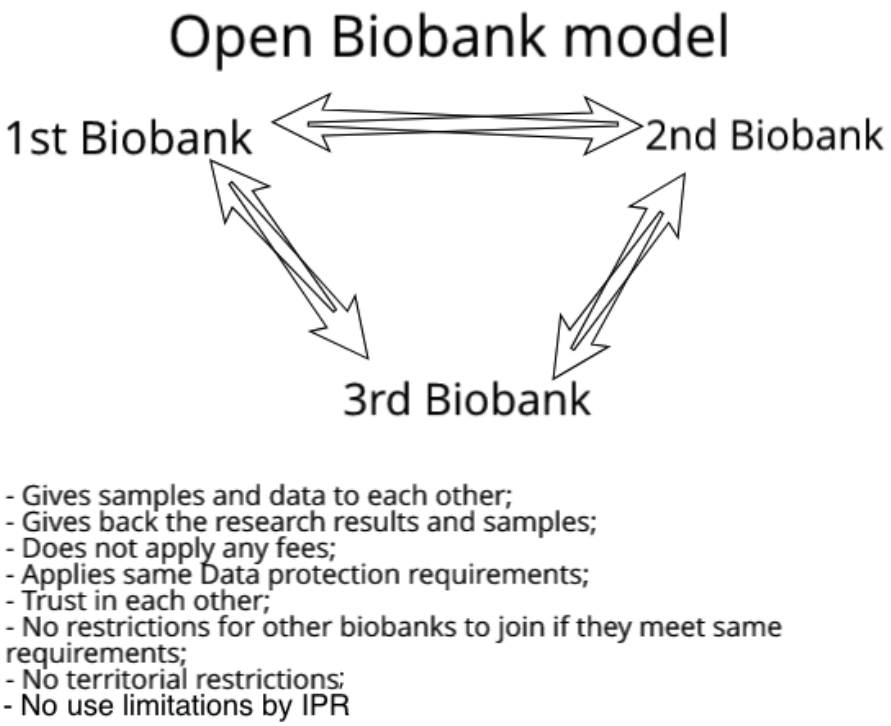

Figure 1. Open Biobank's model

In the proposed sharing scheme, not only biobanks could take place, but also other genetic research institutions. It should be no restrictions on other research bodies to join open biobanks if they can prove transparency and protection of personal rights. There also should be no restrictions if the biobanks or a company is private or public if it generates profit or is non-profit. The main idea is, that everything one institution receives from another must be given back with advancements – new research findings, improved samples information, even new intellectual property rights created.

Let's assume a biobank discloses a particular genetic variation that helps to foresee the onset of the disease. Then it wants to patent this genetic variation and successfully receives a patent. It would mean that such patent can never be used against other open biobanks or other participating institutions, and they shall be free to use the same information with no restrictions.

It is the general overview and not the only possible scheme, how the licensing of the open biobank could work. I have highlighted the most important aspects that must be established in the open biobanks' licenses so that the goals for more open research are reached. This part of the thesis has highlighted a series of institutional innovations that are currently used in other fields to promote sharing of knowledge and advancement of

medical inventions. These named tools could constitute the backbone of a new agenda for access to biomedical innovations and research in the field of biobanks. One substantial advantage of these approaches is that they can be undertaken in the absence of any changes to national or international IP regimes. By collectively adopting such an agenda, as well as clear and binding policies governing the use of these approaches, biobanks can maximise their collective potential to close access gaps of the genetic information and to improve the lives of people.

III. Open biobank

1. Definition of open biobank

In the first chapter, I have already defined the open biobank as a biobank that does not have any financial, technical, territorial, intellectual property restrictions or similar subjective limitations. Article 12(a) of the 1997 Universal Declaration on the Human Genome and Human Rights[959] underscores the need for shared benefits in research: "Benefits from advances in biology, genetics and medicine, concerning the human genome, shall be made available to all, with due regard for the dignity and human rights of each individual". The second part of the Article states that "Freedom of research, which is necessary for the progress of knowledge, is part of freedom of thought. The applications of research, including applications in biology, genetics and medicine, concerning the human genome, shall seek to offer relief from suffering and improve the health of individuals and humankind as a whole".

1.1. Collaboration

The first element of the open biobank is that such biobank must collaborate with other biobanks, research institutions and researchers. Biobanks must follow the goal to share the research benefits and seek together the progress in the health sector. Open biobank must apply the Bermuda and related principles in its data and information

[959] Universal Declaration on the Human Genome and Human Rights | United Nations Educational, Scientific and Cultural Organization 2016.

sharing policy. Such biobank must also share its information openly and easily by collaborative methods in online platforms.

Masum and others[960] talk about at least three linked senses of "open" biotechnologies: open access to underlying information, open licensing practices, and open collaborative methods and platforms. Open access to information by itself, as authors rightly point, is the first and most natural step to take, but it may be of little value if there is no freedom and collaborators with which to apply such information to create solutions. The same conclusion applies to biobanks. Open biobanks should not be a single biobank, but a collaboration of open biobanks. Only by sharing together their findings, researchers can reach a common goal.

Several initiative or projects encourage biobanks to share information. For example, the BBMRI-ERIC[961] is the Europe-wide platform for translational medical research with the aim to develop personalised medicine and disease prevention for the benefit of European citizens. Or B3Africa project[962] that aims to implement a cooperation platform and technical informatics framework for biobank integration between Africa and Europe. Such collaborative projects seek to harmonise the ethical and legal framework, biobank data representation and bioinformatics. The aim of the project is to create a common service pipeline for sharing data and knowledge among biobanks and allowing access for researchers.

The Public Population Project in Genomics and Society (P^3G) is a not-for-profit international consortium dedicated to fostering collaboration between population genomics researchers. This is done through the development of free and accessible research tools, resources and methods that help optimise and harmonise the design of biobank infrastructures and research projects.[963] P^3G primarily serves the research needs of biomedical researchers working with studies, biobanks, research databases and other similar health and social research infrastructures in the areas of human genomics, social science and environmental and epidemiological research. This international community includes biobankers, researchers, scientists and students working in the field of human

960 Hassan Masum and others, 'Open Source Biotechnology Platforms for Global Health and Development: Two Case Studies' (2011) 7 Information Technologies & International Development pp. 61.

961 BBMRI-ERIC, 'Home Page' <http://www.bbmri-eric.eu/> accessed 8 May 2018.

962 BBMRI-ERIC, 'B3AFRICA' <http://www.bbmri-eric.eu/scientific-collaboration/b3africa/> accessed 8 May 2018.

963 P^3G, 'FAQ' <http://www.p3g.org/about-p3g/faq> accessed 8 May 2018.

genomics. P³G brings the research community closer together, in person – at events held around the world – and online.[964]

The PharmGKB[965] is a pharmacogenomics knowledge resource that encompasses clinical information including potentially clinically actionable gene-drug associations and genotype-phenotype relationships. PharmGKB collects, curates and disseminates knowledge about genetic variants and gene-drug-disease relationships, summarise critical pharmacogenomic genes, associations between genetic variants and drugs, and drug pathways. PharmGKB grants use of its contents for research purposes. The knowledge and data held by PharmGKB is freely available to researchers in academia and industry for research purposes, however, non-academic users must negotiate an individual license to use the content.[966] The support for collaborative research is also established in Spanish biobank law. Article 83 para. 4 of the Law 14/2007 on Biomedical Research[967] foresees that the biomedical research can be also performed in collaboration with other international institutions. The same Article in the fifth paragraph states that biomedical research institutions can employ outside researchers and investigators for the research and development activities.

1.2. Broad territorial scope

Another restriction to give samples can be the territorial boundaries. A biobank may not ship samples to another country's biobanks if it believes other country's laws do not protect the rights of the donor or might use the samples for criminological investigation or state security reasons rather than for research. For example, the European Group on Ethics in Science and New Technologies to the European Commission published a document on the Ethical Aspects of Human Tissue Banking,[968] where it states that Public authorities should license tissue imports or exports in biobanks. Licensing should be subject to at least similar ethical and health rules to those outlined in the document. Therefore, open biobanks must not only know the relevant laws of another country but also a trust must be established between the two institutions and its fellow researchers.

964 Ibid.
965 PharmGKB, 'About Us' <https://www.pharmgkb.org/about> accessed 8 May 2018.
966 PharmGKB, 'Licensing' <https://www.pharmgkb.org/licensing> accessed 8 May 2018.
967 Ley 14/2007, de 3 de julio, de Investigación biomédica 2007 (BOE nú m) 28826.
968 The European Group on Ethics in Science and New Technologies to The European Commission, 'Ethical Aspects of Human Tissue Banking' (1998) 11.

The characteristic of the open biobank is that it should not limit access to data and samples based on territorial restrictions. As the biggest problem is different requirements for the protection of personal data in different jurisdictions, such restriction could be removed by applying equal data protection requirements in biobanks. It could mean, of course, that some biobanks would need to apply even stricter requirements for its data protection than national laws foresee when sharing data between open biobanks that have agreed on the same conditions. Open biobanks would have minimal standards for data protection between them (all biobanks would use the same Informed consent and Material transfer forms). Such equal rules would ensure the easier flow of data and samples.

1.3. Non-restrictive IPR

Thirdly, open biobank should never use intellectual property rights in a restrictive manner. If a biobank chooses to patent the findings it made, the patent rights shall not be used against other researcher or other biobanks using the same information. A biobank can be considered open only it does not to patent downstream data at all. As mentioned in the previous chapter, downstream data is crucial for any follow-on research. It is the essential information and must remain open for anyone to use.

Such IP policy is applied in UK biobank. Intellectual property and access policies are being developed to help ensure that the UK Biobank resource is accessible to all bona fide research users, but is not exploited improperly or used in any way that inappropriately constrains use by others. UK Biobank is not expected in itself to lead to patentable inventions that return significant income either to researchers or UK Biobank, but it is expected to become a valuable shared resource for research. On the other hand, UK Biobank does not prohibit others to patent their findings. Research conducted using the biobank's resource (which might be conducted by researchers in the public or commercial sector, as well as the academic and charity sector) can subsequently support the development of an invention that returns a profit and biobank cannot prevent or prohibit it. Commercial companies and other research endeavours that stand to make a profit are not restricted to access to UK Biobank's databases if their proposal falls within the UK Biobank purpose and complies with the usual scientific and ethics requirements.

UK Biobank also states that any income it secures from access fees or intellectual property are reinvested in the resource.[969]

1.4. Protection of personal data and use of pseudonymisation techniques

In the previous chapter, I have talked about personal data rights and the pseudonymisation of donor's information. Open biobank should ensure that the personal rights of a donor are respected, that the donor knows about data protection rights and the scope of protection. Open biobank must also apply pseudonymisation techniques. Pseudonymisation would ensure that samples can be used as broad as possible and shared between biobanks while the personal rights of the donor are respected.

Biobanks routinely apply some form of anonymisation of data and samples to protect the privacy of the research participants and the confidentiality of the information. In the HapMap project a complete anonymization was used, because of the nature of the project – to develop "a haplotype map of the human genome [and] describe the common patterns of human DNA sequence variation."[970] Samples were collected with population and sex identifiers, but without links to individual donors so that "it will be extremely difficult for anyone to link any genomic data in the HapMap database to a specific person". Pseudonymisation has a goal to prevent anyone "to establish that a specific DNA sequence came from a particular individual, other than re-sampling an individual's DNA and comparing it to the sequence information in the public database."[971]

Some projects, such as the CARTaGENE project, adopted a double coding strategy. Double coding is used when the independent body holds the code, linking the randomised number assigned by the project to data and biological specimens of each participant and the personal nominative data of the participant.[972] Or a strategy can be used to unidirectionally encrypt but yet allow the donor to be identified if needed. Iceland biobank uses such way. Personal information is "coded before entry on the database <...>.

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969 Ronald J Trent, 'Chapter 10 - Ethical, Legal and Social Issues (ELSI)' in *Molecular Medicine: Genomics to Personalized Healthcare (Fourth Edition)* (Elsevier 2012).

970 The International HapMap Consortium, 'Integrating Ethics and Science in the International HapMap Project' (2004) 5 Nature Reviews Genetics 467, 471.

971 NCHGR-DOE, 'Guidance on Human Subjects Issues in Large-Scale DNA Sequencing'. Available at <https://iop.vast.ac.vn/theor/conferences/smp/1st/kaminuma/HumanGenomeProjectInfor/nchgrdoe.html> accessed 2018 May 8.

972 Andrea Boggio and others, 'Comparing Guidelines on Biobanks : Emerging Consensus and Unresolved Controversies' [2005] Project Human Genetic Databases: Towards a Global Ethical Framework 20.

Personal identification <is> coded one-way, i.e. by coding that cannot be traced using a decoding key."[973]

1.5. Open consent

Already proposed open or broad consent should be adapted in the open biobank. The wide use of samples would confirm that the best results can be achieved using the genetic data.

Several guidelines have adopted the view that a broad consent that allows for the use of samples for genetic research in general, including future research, as yet unspecified research projects, appears to be the most efficient path to follow.[974] Ma'n H. Zawati, Yann Joly, Bartha Maria Knoppers[975] talks about the equilibrium between individual's autonomy and the social benefits generated by population biobanks. They present that the public engagement to participate must correlate with participants confidence of public biobanks. The higher confidence in biobanks leads to higher participation rate of individuals. The authors say that if research participant understands the value of population biobanks' research and trust the biobank then the broad informed consent must prevail in genetic research. The broad consent in no way negates the autonomy of participant; rather it creates individual autonomy that is socially responsible.

Broad consent also means that biobanks become more responsible for the personal data they collect and store. Susana Navas Navarro talks about the responsible treatment of personal data by data collector and controller. The author says, that responsible for the treatment is such entity, which has influence over the personal information and understands the contractual relationship between the parties. Besides, such responsible entity must determine the proper object, use and purpose, where and how the personal data is used.[976] Biobanks ensuring the requisite to use personal data responsibly, and protecting the research participants' information adequately, should be allowed to use broad consent forms.

[973] Icelandic Act on a Health Sector Database No 139/1998.Article 7.

[974] WHO Meeting on Ethical Issues in Medical Genetics (1997: Geneva, Switzerland) & WHO Human Genetics Programme. (1998). Proposed international guidelines on ethical issues in medical genetics and genetic services: report of WHO meeting on Ethical Issues in Medical Genetics, Geneva, 15-16 December 1997. Geneva: World Health Organization.

[975] Ma'n H. Zawati, Yann Joly, Bartha Maria Knoppers, 'L'autonomie basée sur l'individualisme libéral : les limites dans le contexte des biobanques populationnelles' in Hervé C, eds., Réflexion et recherches en éthique, (2018), 279-293.

[976] Navas Navarro and Camacho Clavijo, *Mercado digital principios y reglas jurídicas* (Tirant lo Blanch 2016), 67.

1.6. Free information

The sixth condition of an actual open biobank shall be free and easy access to its information databases. If we agree, that biomedical research is a public good, then the scientific community shall be able to access genetic materials and data that are stored in the various repositories. All genetic information that is free from personal identifies, the sequenced genes, scientific publications, research techniques, must be provided by online means and free of charge. Any researcher must be able to download such information and use for his research. It also means that a biobank should not protect its database by the copyrights or *sui generis* rights.

Lowrance indicates several impetus increasing data sharing: 1) reduced duplication of data and biospecimen collecting and management, and reduced competition for access to data; 2) compilation of masses of data on resource platforms, making statistically more powerful analysis; 3) ease access to data for use as statistical controls; 4) increased linking of data and biospecimens across projects; 5) scientifically more diverse interrogation of data for more purposes, including independent validation of findings; 6) more productive use, for the common good, of government and charity research funds and the data contributed by participants.[977]

There are genetic databases that allow its user to download and use information free of charge. The National Center for Biotechnology Information (NCBI) has a wide variety of different genetic databases. From literature databases to molecular and genome databases.[978] There are also many different types of nucleotide sequences and protein sequences in the NCBI database. Concerning nucleotide sequences, some may be entire genomic DNA sequences, some mRNAs, others lower quality sequences such as expressed sequence tags (ESTs, which are derived from parts of mRNAs), or DNA sequences of contigs from genome projects.[979] NCBI is not a biobank itself (as it does not store any biosamples), but it contains information extracted from biological samples provided by other biobank institution (like the Coriell Institute for Medical Research[980]

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977 Lowrance WW, *Privacy, Confidentiality, and Health Research* (Cambridge University Press 2012), 138.

978 NCBI, 'All Resources' <https://www.ncbi.nlm.nih.gov/guide/all/> accessed 8 May 2018.

979 Avril Coghlan, 'Sequence Databases' <http://a-little-book-of-r-for-bioinformatics.readthedocs.io/en/latest/src/chapter3.html> accessed 8 May 2018.

980 Coriell Biorepositories and Services is the international resource providing essential research specimens and custom services to the scientific community. More information at 'Coriell Institute for Medical Research Official Page' <https://www.coriell.org/> accessed 8 May 2018.

and ATCC[981]). It also combines information received from other genetic sequence databases (like GenBank[982] and the Sequence Read Archive[983]).

Such global genetic databases as NCBI does not have their researchers or sample storages. Genetic databases are created or supervised in different manners. Biological sample database represents an archival repository of all sequence; it stores submitter-supplied descriptive information, or metadata, about the biological materials from which data stored in NCBI's primary data archives are derived. Researchers typically initiate a deposit to BioSample as part of a submission to one of NCBI's primary data archives. Database staff respond to queries and report errors but, as with other primary data archives, submitted data are not subject to extensive curation.[984] Many different labs have sequenced the gene and submitted their sequences to the NCBI database.

One of NCBI managed databases is the RefSeq database. It contains a non-redundant set of reference standards derived from the International Nucleotide Sequence Database Collaboration (INSDC)[985] databases that include chromosomes, complete genomic molecules (organelle genomes, viruses, plasmids), intermediate assembled genomic contigs, curated genomic regions, mRNAs, RNAs, and proteins. The RefSeq sequences provide non-redundant curated data representing the current scientific knowledge of known genes. Records may include sequence, descriptive information, publications, or feature annotation. RefSeq records are owned by NCBI and therefore can be updated as needed to maintain current annotation or to incorporate additional information.[986]

One of the Database directive's goals is to ensure an attractive environment for investment in databases. However, if applied to biobanks, it would restrict sharing of knowledge in genetic research. As presented, databases containing genetic information

981 ATCC is the global biological materials resource and standards organisation that focuses on the acquisition, authentication, production, preservation, development, and distribution of standard reference microorganisms, cell lines, and other materials. More information at ATCC, 'ABOUT ATCC' <https://www.lgcstandards-atcc.org/About/About_ATCC/Who_We_Are.aspx> accessed 8 May 2018..

982 GenBank is the NIH genetic sequence database, an annotated collection of all publicly available DNA sequences. More information at NCBI, 'GenBank Overview' <https://www.ncbi.nlm.nih.gov/genbank/> accessed 8 May 2018.

983 The Sequence Read Archive (SRA) stores raw sequence data from "next-generation" sequencing technologies. In addition to raw sequence data, SRA now stores alignment information in the form of reading placements on a reference sequence. More information at NCBI, 'The Sequence Read Archive' <https://trace.ncbi.nlm.nih.gov/Traces/sra/sra.cgi>.

984 Tanya Barrett, 'BioSample', *The NCBI Handbook [Internet].* (2nd ed, Bethesda (MD): National Center for Biotechnology Information (US) 2018). Available at <https://www.ncbi.nlm.nih.gov/books/NBK169436/> accessed 2018 May 8.

985 International Nucleotide Sequence Database Collaboration, made up of GenBank, the European Nucleotide Archive, and the DNA Data Bank of Japan.

986 Ph D Kim Pruitt, Ph.D., Garth Brown, Ph.D., and Mike Murphy, *RefSeq Help [Internet]* (Bethesda (MD): National Center for Biotechnology Information (US) 2018).

are generated by its users each of which can claim to take a part, or being a creator of a database. The investment to such resources is influenced by a goal to spread the knowledge, share the research findings with the community.

1.7. Cost-free biological samples

The other condition of an open biobank would be the availability of the biological samples. One thing is to share sequenced genes or scientific publications, but open biobank shall also provide the samples. Biobank storing human genetic materials cannot be closed and keep those samples only to its use. Not only genomic data but also the samples shall be available without subjective restrictions in the open biobank.

The restrictions to provide samples can be monetary, territorial or related to the scope of research. Quite often a high fee for the samples is required. A fee that varies from few to several thousand euros can become a real burden for a small biobank or universities biobank. Open biobank should at least minimise the costs of the samples to cover only expenses related to the storage and shipping of samples. Another possibility to reduce sample sharing fee is public grants. As seen in this thesis, most significant majority of the biobanks are state funded. Therefore public funds can also cover sample storage and shipping expenses.

One European project was giving the free samples to researcher during the project time. The Biobanking and Biomolecular Resources Research Infrastructure – Large Prospective Cohorts (BBMRI-LPC) has declared to reach such goals as fair transnational access to samples and data. It agreed to provide free transnational access by users, through study proposals selected by an open, pan-European call. In the framework of the studies, the goal was to generate and provide access to whole genome sequences, transcriptome, proteome, metabolome and methylome data.

The project was going from February 2013 till October 2017. It was granted €8,000,000.00. The internet site of the project gives information about biobanks or researches that were participating in the project and offered free access to samples and data.[987] During the time it was operating, the BBMRI-LPC project supported innovative research projects conducted in large prospective cohorts (LPC) across Europe. The successful applicants were offered free access to samples and exposure data from the BBMRI-LPC network of 20 European cohort studies, involving over 2.8 million study

[987] BBMRI-LPC, 'Access Website' <http://bbmri-lpc.iarc.fr/mica/> accessed 8 May 2018.

participants with lifestyle information and samples collected at baseline. Not the monetary incentive was provided to the successful applicants but instead the cohorts, free shipment of samples, support for metabolomics and whole-genome genotyping/sequencing data.

The BBMRI-LPC also pointed the necessity to build new public-private partnerships involving large-scale prospective cohorts and strengthening existing ones, allowing transparent industrial access to academic expertise to build a network transferring the expertise of established European large-scale biobanks to new biobank initiatives under development in other countries.[988] The project was indeed open and implemented a lot of new perspectives of how the genetic resources can be better used. Unfortunately, as it was European project, the BBMRI-LPC Scientific Calls for Access was open to scientists and investigators who work in an institution located in an EU Member State or Associated State only.[989]

1.8. Use of open-source software

The next requirement for an open biobank is that it should use the open-source programmes in managing the samples, data, sharing the information, giving access to the samples. Of cause, if it is a publicly funded project, it should better invest its resources in the human capital, financial support to the researchers, and try to prevent high fees related with IT tools. An example of open source application that is created to manage biobank's activities is Acquire.[990] It is a robust, secure, web-based, database-backed open-source system that supports all major needs of a modern biobank. The system is freely available under an LGPL license.

Though banking protocols and processes may differ among institutions, all must have processes for identifying potential subjects and obtaining consent, collecting specimens and capturing data. Acquire supports the full biobanking lifecycle for specimen and data

[988] BBMRI-ERIC, 'COMPLETED PROJECTS' <http://www.bbmri-eric.eu/scientific-collaboration/completed-projects/> accessed 8 May 2018.

[989] BBMRI-LPC, 'Scientific Calls' <http://www.bbmri-lpc.org/access> accessed 8 May 2018.

[990] The Dan L Duncan Comprehensive Cancer Center's Biomedical Informatics Group in the Biostatistics and Informatics Shared Resource developed Acquire, a central, web-based data management tool for managing information on collection protocols, their participants, specimens, specimen inventory, clinical and pathological annotations, molecular biomarker data, and more. More information at Baylor College of Medicine, 'Acquire. Overview' <https://www.bcm.edu/centers/cancer-center/research/shared-resources/biostatistics-and-informatics/biomedical-informatics-group/acquire> accessed 8 May 2018.

collection. The system provides the capture of participants' data (consent, demographics and clinical annotations), specimen data (collection, accession, storage, maintenance, quoting or derivative creation and pathologic findings); workflow management (status checks on which key participant and specimen data are incomplete); data quality checks (reports to help identify data or specimen collection quality problems); helps to allocate resource (public researcher specimen requests, RAC request reviews and specimen distributions) or assists in making reports (data mining for biobank personnel and restricted-access searching for public researchers). Acquire provides comprehensive electronic support for public researchers to request specimens. It also records all documents relating to these requests and gives possibility to demonstrate that the biobank is sharing tissues per its grants. [991]

1.9. Openness to public scrutiny

The ninth requirement is that open biobank must be open not only for other researchers but also for the people. Individuals must have a possibility to visit biobank, to learn about the biobank's activities and to feel that their donation of samples and information is essential and useful. Public biobank must be transparent and report where it uses its resources.

The openness and trust are essential for people who are willing to donate. If biobanks are more open to the public, I believe their initiative and work would be much more appreciated and valued. Stacey Pereira analysed the principal motivations to share biological samples for research.[992] She describes that the most commonly observed motivation is the desire for collected samples to be used in research, and not being stored in freezers indefinitely. Another motivation is the desire to make samples more easily accessible for research, and keep the requirements and responsibilities of recipients of biobank materials not too high. The third motivation to share samples with other researchers is the desire to increase the value of banked materials with associated genomic data and the desire to increase the visibility of the biobanking group in the research community.

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991 Heidi Dowst and others, 'Acquire: An Open-Source Comprehensive Cancer Biobanking System' (2015) 31 Bioinformatics 1655–1622.

992 Stacey Pereira, 'Motivations and Barriers to Sharing Biological Samples: A Case Study' (2013) 3 Journal of Personalized Medicine 102–110.

Biobanks must assure reciprocity between them and society. The UK Biobank website relies heavily on the language of altruism and solidarity, making moral appeal for cooperation and assistance to enable a better society in the future. The study performed in the UK and Germany biobanks showed, that participants do not simply see their "donation" terminating after the initial conditions of acceptance. Rather, their "conditional gift" was seen to begin what was expected to be an ongoing and long-term mutual exchange of benefits between biobanks, society and the individual.[993] Reciprocity and trust can be viewed as a mode to deal with a range of main issues in biobanks activities, such as privacy concerns over future long-term studies.

Biobanks not only need to be linked to individuals as they participate in cohort studies or donate tissue. A daunting challenge is a question of how to link biobanks with society in general.[994] Biobank projects even can collapse due to social resistance. Therefore, the political-cultural context of any biobank project plays a significant role. Publics of biobanks can spontaneously develop, be shaped through a variety of activists that thematise a particular topic. Such publics emerge from civil society.[995] The biobank itself must take actions to show the society that it can be trusted, that it protects personal rights and works for the society's needs. Legal suits where people accussed biobanks of not respecting their privacy or family life, will never lead to a trustful relationship between the two. The UK Biobank realises that ethical considerations are one of the most critical biobank's concerns. The Interim Advisory Group (IAG) in the UK Biobank seeks to give best ethical decisions and practices to provide a sound basis for fostering public trust and confidence in the project. The goal of the IAG was as much about minimising the risk to the project of public rejection and ensuring public trust as it was in minimising the risks of harm to those participants involved in the research.[996] UK biobank also gives obvious indications for the donors regarding the repeat assessment: what questions will be asked, how to prepare for the visit, why the new assessment is needed, gives other explanations.[997]

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993 A Hobbs and others, 'The Privacy-Reciprocity Connection in Biobanking: Comparing German with UK Strategies' (2012) 15 Public Health Genomics 280-281.

994 Peter Dabrock, Jochen Taupitz and Jens Ried (eds), *Trust in Biobanking*, vol 33 (Springer Berlin Heidelberg 2012) 213.

995 Dabrock, Taupitz and Ried 214.

996 Ibid.

997 UK Biobank, 'Information Leaflet for Repeat Assessment Visit' <http://www.ukbiobank.ac.uk/wp-content/uploads/2012/09/Repeat-Measurement-Participant-Leaflet.pdf> accessed 8 May 2018.

From my point of view, the criteria numbered here are the most important to title a biobank genuinely open. Therefore, my definition of the open biobank is:

> **- The open biobank is a freely accessible biorepository using no IPR restrictions in its activities, working in close cooperation with other biobanks in sharing its collections of data and samples while ensuring adequate protection of personal data. It uses open source software in its everyday activities and ensures transparency and trust to its users and the general public.**

Some biobanks affirm several criteria of the given definition. UK Biobank seems to be one of the most open biobanks in Europe, and it does not protect its resources by IPR. UK Biobank's Data Showcase gives scientists and members of the public the possibility to view the valuable information that has been collected to help improve the health of future generations.[998]

However, UK Biobank's is not providing its resources free of charge. The biobank requires at least two payments for every application: an initial payment: due after application submission, before application review begins (£250)[999] and a main payment: due after the application is approved and before data is released (£1,500 – per application that requires access to data only; an additional cost of £500 for access to any "bulk" data files, genetic data, built environment data and raw accelerometer data).[1000] Other payments can also be requested: if the bulk data is requested that was not originally selected or further work is required after a project is underway.[1001]

There is hardly a biobank that would meet all of the requirements stated above. A research performed by Marco Capocasa and others[1002] showed that biobanks have a lot restriction forbidding the open sharing. The survey involved 46 biobanks. Most of them gave permission to access their samples (95.7%) and data (85.4%), but free and unconditioned accessibility was not a standard practice. 41 out of 46 biobanks (89.1%)

998 UK Biobank, 'Data Showcase' <http://www.ukbiobank.ac.uk/data-showcase/> accessed 8 May 2018.
999 UK Biobank, 'Scientists' <http://www.ukbiobank.ac.uk/scientists-3/> accessed 8 May 2018.
1000 Ibid.
1001 UK Biobank, 'UK Biobank Access Management System (AMS) User Guide: Getting Started' <http://www.ukbiobank.ac.uk/uk-biobank-access-management-system-ams-user-guide-getting-started/> accessed 8 May 2018.
1002 Marco Capocasa and others, 'Samples and Data Accessibility in Research Biobanks: An Explorative Survey' [2016] PeerJ 1.

stored data extracted from the analysis of their samples. 23 out of 41 biobanks (56.1%) additionally stored data produced by external research groups that have used their samples. Other biobanks did not accept data produced by external research groups. The majority of biobanks (35 out of 41; 85.4%) allowed external research groups to access their data in compliance with certain conditions (such as third-party authorization for data access (i.e., ethics committees, IRBs, scientific boards), criteria linked to the decision of a single researcher within the biobank institution, other criteria).

Reviewing the functioning biobanks, it seems that historically they are becoming more and more open with each other: the data is released more rapidly, disclosed sequences are made available in the internet, researchers can easier access the biobank. However, there are influential factors – such as funding bodies, applicable national laws or data protection legislation, that naturally create barriers for biobanks to be truly open. In fact, while data sharing culture in biosciences seems to be ongoing for several years among both researchers and policymakers, the same sharing of samples idea is still very new and is not accepted in such a broad scope.[1003]

2. Public opinion on free data sharing

2.1. Support of open sharing by research participants

In the previous chapter, I have presented the possibility to use a broad informed concept in the biobanks. The perception to accept broad concept can be strengthened by people's willingness to donate the samples to open biobanks.

The possibility to allow biobanks to work openly depends a lot on the participants perspective of the sharing of their data and samples. The studies performed shows that participants are not against the open sharing, on the contrary, the support can be acknowledged. Open data sharing model can be acceptable equally by the participants as the controlled data sharing model.

A research study that analysed people's willingness to give samples and data showed that basically the same level of participation was between two presented biobanks models. The first model was a biobank with controlled access and the second model was presented with the open data sharing. 68% of participants agreed to participate in the

[1003] Pereira 102.

controlled model biobank, versus 65% of participants that agreed to participate in the open model biobank.[1004] So in general, the study showed that the same amount of people would participate in the open biobank, compared with closed biobank.

Another study performed by Yann Joly and others showed that a majority of survey respondents reported they would be willing to participate in a project where their information and samples would be shared with the international community, provided the samples and data did not contain any personal identifiers (54%, n = 61).[1005]

Some socio-demographic groups differ in their readiness to participate in biobank research (better-educated people are more willing to participate than having a lower education; religious people are less willing to participate than non-religious, etc.),[1006] but the openness of a biobank seems to play little or no role at all.

People are willing to participate in a biobank not because they are expecting any financial gain. They are participating in a biobank because they believe their input and participation is essential and can help cure other people. Today's society is very social. People care about the wellbeing of others and are attentive to the social issues and problems. As much as we care about our Earth, recycling, global warming problems, we also care about curing diseases or helping other people to cope with the health issues, to be blood or organ's donors. If a person believes that his credit to give samples and information to a biobank is useful, the psychological satisfaction of doing good it is enough for a person to participate. If a person is informed that better results can be reached by sharing the samples between biobanks, it will not change a person's decision to participate.

And the additional argument is that, in my personal opinion, people are not so much attached to their body residues, blood cells, or their genes in general (as some might believe or claim). The human genome, and information relating to the human genome is not of much use without further information and technology. Particular machines generate gene sequences and the genomic data. Special tools and softwares[1007] are used to read the

[1004] Saskia C Sanderson and others, 'Public Attitudes toward Consent and Data Sharing in Biobank Research: A Large Multi-Site Experimental Survey in the US' (2017) 100 American Journal of Human Genetics 414.

[1005] Yann Joly and others, 'Fair Shares and Sharing Fairly: A Survey of Public Views on Open Science, Informed Consent and Participatory Research in Biobanking' (2015) 10 PLoS ONE 11.

[1006] Saskia C Sanderson and others 414.

[1007] An example is the sequencing device–known as the Polonator, created by George Church and his team. The device uses open source software and allows users to tinker with it in any way they wish. All the parts can be swapped out, and scientists can use different enzymes and chemicals. More information at Emily Singer, 'Rewriting Life: Gene Sequencing for the Masses. A Genomics Pioneer's Sequencing Machine Comes to Market.' [2008] MIT Technology Review.,

gene and provide the information about its data to the biologist and researcher. Not being able to use these machines or understand the information they disclose, little value a person can have from his/her tissues or samples. There is no prepared manual that everyone could use to sequence their genes, neither there is a manual of the creation of the databases where the information of the sequenced genes is stored. Without biobanks, no genetic information would be available for researchers use. Population biobanks are unique in the resources they have and the databases they create. Biobanks are seen as custodians of the data and samples for research to be performed by others seeking access.

2.2. Accepting genome databases as common goods

The second argument, supporting the open biobank's working model and already presented by several scholars is that genetic information shall be treated as a common and not a private good. I also believe that information received from a sample, will it be a gene sequence, RNA information or other downstream information from a gene, should not fall under the definition of personal good. It is quite a meaningful discussion if the information stored in genomic databases should be held common or private good?

The Universal Declaration on the Human Genome and Human Rights emphasise the need for benefit-sharing between developed and developing countries, stating that the "benefits from advances in biology, genetics and medicine, concerning the human genome, shall be made available to all".[1008] The HUGO Statement on Human Genomic Databases made in December 2002, implies that to prevent the potential risk of misusing genomic data' genomic databases, they should be seen as a common and not a private good. Genomic databases should be acknowledged as public rather than a private goods in order to encourage innovation, that is, "to rapidly place primary genomic sequences in the public domain."[1009]

The HUGO statement considered the benefits of sharing research information involving the human genome. The statement recommends, among other things, "that profit-making entities dedicate a percentage (e.g. 1–3 %) of their annual net profit to

<https://www.technologyreview.com/s/410055/gene-sequencing-for-the-masses/> accessed 2018 May 8. Other technologies can be mentioned such as Illumina, 454, IonTorrent, Complete Genomics, PacBio and OxfordNanopores.

[1008] Universal Declaration on the Human Genome and Human Rights | United Nations Educational, Scientific and Cultural Organization 1997.

[1009] HUGO Ethics Committee, 'Statement on Human Genomic Databases' (2003) 13 Eubios Journal of Asian and International Bioethics.

healthcare infrastructure and humanitarian efforts."[1010] In the same statement the HUGO Ethics Committee offered three arguments to justify benefit sharing: 1) 99.9 % of the human genome is common to all humans. It entails a responsibility, grounded on human solidarity, to share in the benefits of research based on this common good. 2) There is a long legal history of viewing global resources, such as the sea, air and space, as common goods, to be equitably available to all humans, and protected for future generations. The human genome can equally be regarded as a common heritage. 3) Vast differences in power and wealth between those conducting human genetic research and those providing genetic samples for such research, as well as the potential for substantial profits, raise concerns of exploitation.[1011]

The two key aspects that describe or define a good as a public are that it is 'non-excludable' and 'non-rivalrous'. A good is non-excludable if persons cannot be excluded from accessing it, and it is non-rivalrous, when one person's use of the good does not diminish the supply of that good. An example frequently cited is that of a lighthouse. Intentionally or not, a lighthouse lights the sea for everyone: no one can be prevented from receiving the benefits of the light, and the light cannot be diminished no matter how many persons are benefited by it.[1012] The internet is normally open to all (non-excludable) and downloading information does not diminish the information itself (non-rivalrous). Global public goods are public goods that possess such properties of publicness across national boundaries.[1013]

As we have seen, biobanks contain different information, and a lot of that information is principally about knowledge – DNA sequence codes, RNA transcriptions, scientific articles – which is commonly conceived to be the archetypal public good. Despite the fact that private enterprises owned the Icelandic database, there was also an acknowledgement of the "common ownership" nature of the enterprise, in that deCode, biopharmaceutical company owning a biobank, has acknowledged the genealogical information of Icelanders to be part of Iceland's "common heritage", and as such the genealogical database will be available for free.[1014]

[1010] The same is again repeated in WHO Human Genetics Programme of 2005 'Genetics, Genomics and the Patenting of DNA: Review of Potential Implications for Health in Developing Countries'.

[1011] Ibid. 33.

[1012] R Chadwick and S Wilson, 'Genomic Databases as Public Goods?' (2004) Res Publica 10, 125.

[1013] Inge Kaul, Isabelle Grunberg and Marc Stern, 'Global Public Goods' in *Global Public Goods: International Cooperation in the 21st Century* (Oxford University Press 1999).

[1014] G Pálsson and P Rabinow, 'The Icelandic Genome Debate.' (2001) 19 Trends in biotechnology 166–171.

Genomics knowledge is non-rivalrous in consumption (not depleted by use) and is generally made public by genomics databases on the internet and journal publication, as was the way how the Human Genome Project was funded and undertaken. It is a global public good in the sense of the knowledge not being bound by a national border, in discovery, transmission, or use.[1015]

Bayefsky present the view that human genome can be treated as a public good, because of its common nature. "*The most powerful sense in which our genome is common lies in the fact that all people belong to the human gene pool. The human gene pool contains the set of genes of the whole human species. It is a repository for our genetic history, as well as the source of future generations. Furthermore, as members of the human species, we all have a stake in what becomes of the human gene pool.*" – writes the author.[1016] The human gene pool is common to all people, and all people belong to this pool – that justifies a universal interest in using genetic information for the society's benefits.

Bayefsky also explains that if humanity has a common goal to protect human genome from any manipulations – especially the direct manipulation of an organism's genes using biotechnology; the common heritage concept, shall be accepted. As presented by the author, a comparison with other forms of common heritage (e.g. natural or cultural heritage), lets to transform the genome to *public* good by establishing that not only each person, but also collectively – humankind at large – has an interest in what becomes of the genome.[1017]

Ruth Chadwick and Sarah Wilson raise a question if treating genomic data as a private good do not create injustice of the growing genomics divide. What is expressed is that applying public good concept to the genetic databases could help to satisfy the demands of international justice, ensure that the benefits of genomics databases extend across geographical and socio-economic groups. Enhancing the status of such databases as global public goods, and anything that benefits across geographical and socio-economic groups would enhance international justice[1018].

Jeremy Rifkin talks about the genetic Commons and presents the history of enclosure movement, starting with the feudal enclosures of agricultural lands in Europe and ending

[1015] H Thorsteinsdottir and others, 'Genomics - a Global Public Good?' (2003) 361 Lancet 891.
[1016] Michelle J Bayefsky, 'The Human Genome as Public: Justifications and Implications' (2017) 31 Bioethics 212.
[1017] Ibid. 214.
[1018] Chadwick and Wilson 123.

with the enclosure of the genetic Commons with the conferring of patents on genes.[1019] Rifkin also says, that the intensification of genetic-Commons advocacy comes at a time when new IT and computing technology is speeding up genetic research. The marginal cost of some genetic research will approach zero in the not-to distant future, making valuable genetic data available for free, just like other information in the Internet. Biological and genetic research which just some years ago were available to only elite group of scientists, are no reachable for university students. In such circumstances and changes, the younger generation is going against companies wish to convert the biological information on the planet into intellectual property.[1020]

Bialobrzeski and others make the separation between "public goods" – related with the economic context; and the "common goods" – describing goods used for noneconomic settings, referring to goods that are identified as relevant for the community according to several normative factors.[1021] Authors state, that in the field of biobanks, a better definition is a common good and that we should question the structure, operation and output of the biobanks regarding normative values (as a result of public deliberation to participate) that will be handled and examined in public processes of carefulness. In this way, biobanks will be seen not as a non-rival and non-exclusive, but rather as institutions build on intentional people's wish to participate in creating commonly used knowledge.

If genetic information will ever be treated as a common good, depends a lot on the perspective of the biobanks and their adherence to the principles of sharing, collaboration and openness. The Human Genome Project adopted an important principle: the collaboration to the project is open to centres from any nation. Although potentially less efficient, in a narrow economic sense, than a centralized approach involving a few large factories, the inclusive approach in the HGP was strongly favoured because of the feeling that the human genome is the common heritage of all humanity, and the work should transcend national boundaries, and because of a belief that scientific progress was best assured by a diversity of approaches.[1022] Treating human genetic information as a public good may substantiate ideas such as "open science", sharing of knowledge between scientists. The concept of the public good can be perceived as a solidarity and be

[1019] Jeremy Rifkin *Zero Marginal Cost Society: The Internet of Things, the Collaborative Commons, and the Eclipse of Capitalism* (St. Martin's Press 2014) 167.
[1020] Ibid. 169.
[1021] A Bialobrzeski, J Ried and P Dabrock, 'Differentiating and Evaluating Common Good and Public Good: Making Implicit Assumptions Explicit in the Contexts of Consent and Duty to Participate' (2012) 15 Public Health Genomics 291-292.
[1022] ES Lander and others, 'Initial Sequencing and Analysis of the Human Genome' (2001) 409 Nature 864.

preserved by a community that finds it worthy to protect the shared interests of research.[1023]

I believe the most prominent force to encourage common good perspective for genetic information should come from the biobanks' umbrellas organisations, such as BBRMI-ERIC, non-governmental organizations, and other private initiatives. The BBRMI-ERIC incorporates together the vast majority of European biobanks and uses soft tools in encouraging more advanced cooperation. A non-profit organization, the Foundation on Economic Trends – whose mission is to examine emerging trends in science and technology, in 2002 has initiated a meeting of 250 organizations to agree on the Treaty Initiative to Share the Genetic Commons.[1024] The aim of the meeting was to express wishes of prohibiting all patents on plant, microorganism, animal, and human life. The organizations, including women's groups, biotech activists, organic food associations, environmental organizations, during the meeting agreed that genetic heritage of Earth is a shared Common.

Governmental bodies, such as NIH, can also play a significant role by regulating biobank's activities or establishing guidelines for the best practices. Moreover, such guidance can be applied not only for public biobanks, that dependent on state finances but also to private biobanks.

The US government encourages an open source approach to biotechnology, particularly for large-scale, publicly-funded genomic projects such as the International HapMap Project and the 1000 Genomes Project. Governmental funding bodies now require researchers to deposit their genomic data in centralised, openly accessible repositories. Moreover, the NIH Data Sharing Policy requires that all projects, receiving at least $500,000 in federal funding, would share data in a de-identified format.[1025]

However, despite some strong global common good characteristics, genomic databases as they are currently being developed are generally following a private good model. As described, biobank can have several restrictions to access its resources, imposed through either financial, intellectual or technological constraints. Treating human

[1023] Benjamin Capps and others, 'Falling Giants and the Rise of Gene Editing: Ethics, Private Interests and the Public Good' (2017) 11 Human Genomics 20.

[1024] Porto Alegre Treaty to Share the Genetic Commons 'Hundreds of NGOs from More than 50 Nations Announce Support of a Treaty to Establish the Gene Pool as a Global Commons', Press Release 1 February 2002. Available at <http://www.ukabc.org/genetic_commons_treaty.htm> accessed 8 May 2018.

[1025] Massimiliano Izzo, *Biomedical Research and Integrated Biobanking: An Innovative Paradigm for Heterogeneous Data Management* (Springer International Publishing Switzerland 2016) 167.

genome as a common resource can maximise its value, allow broader use of the genetic information.

All people have an interest in the genome and its proper use for the benefit of the public. Biobanks should support such views and the concept that the value of the human genome and its research is public and can never be private. The benefits from such researches shall be shared among all people. Although the personal and private nature of the human genome is undeniable, there is also an unquestionable common and public aspect of our DNA. Individuals have an interest in their genetic privacy, protection of personal data, but the public, on the other hand, has a legitimate interest in the structure and use of the human genome. Genetic research shall be developed in a way to pursue the public interest by maximising public health benefits while respecting individuals' autonomy. As it sounds challenging, and, indeed, it is, but such goals can be reached by putting global efforts together and enlightening people that their genetic information can provide various advantages to the society.

IV. The value of open biobanks

I have already mentioned some advantages of open biobanks. However, to strengthen them and to show all the benefits of open sharing to the innovation and wellbeing of the population, I will summarize the positive aspects of proposed perspective. The entire premise of the open biobank philosophy is predicated on sharing knowledge of technological advancements broadly and creating and advancing such technological knowledge for the good of the community.

According to technology journalist Glyn Moody, Celera Genomics changed its business model because it could not win in a race against companies that subscribed to the open source philosophy.[1026] There were two main problems why Celera failed: first, the availability of DNA code and, second, a free computer code in the form of open source software like GNU/ Linux that made high-performance computing available to anyone. "Science should be based on the 'economy of gift' rather than sold to the highest bidder, and the transformational approach looks beyond the satisfaction of the immediate needs of a scientist or group of scientists to the potential motives in scientific practice; it

[1026] Glyn Moody, *Digital Code of Life: How Bioinformatics Is Revolutionizing Science, Medicine, and Business* (John Wiley & Sons 2004) 135.

seeks to satisfy higher needs" – Antonio Marturano is writing.[1027] The main object of open sharing is to turn individuals' attention toward more significant causes, such as the development of science, and not to seeks satisfaction of the individual needs and benefits. Open technologies are using the knowledge to accelerate innovation and expand markets for the use of a product. Open approach proposes, that firms can and should use external ideas, not only internal ideas and that the ideas must be shared to advance commonly used technologies.

What open technologies guarantee, is that specialist will share their ideas with other specialists, innovators will share their ideas with other bright minds. Putting all effort together can mean that best solutions are reached, and all voices are heard. Most important – open licenses of the downstream technology aim to secure the freedom of all elements and levels of such technologies, not just the technology itself. They do this by requiring that any distribution of derivative works be licensed on the same terms as the original product. The goal of the biobanks is to increase the value of the sequenced data by incorporating additional information from other sources and encouraging the exploitation of such information by the maximum number of commercial and academic centres. Such centres should be keen to cooperate in the development of new therapeutic agents and maintain a non-exclusive environment. The best way to achieve this goal is to use an open source license that requires users of the data to grant back all newly revealed haplotypes and haplotype tag SNPs so that all other users would have the non-exclusive freedom to use this information as tools for their research.[1028]

The monopolisation of ideas can create barriers to create significant value not only to society but also to the firm itself. By having a closed monopoly, the company not only risks to be overruled by other, better technology, but it can also be forbidden to use the advancements of the technology in the future. Also, open license scheme in biobanks can minimise or perhaps even eliminate, parasitic patenting – when patent applications are filed only to prevent others from using the sequenced genes or other genetic info. Instead, a practice to use open information and research tools developed by different players and including contributions from numerous participants in the public, for-profit, and nonprofit sectors, would lead to a better-developed biobank and would ensure real value of these databases.

[1027] Antonio Marturano, 'When Speed Truly Matters, Openness Is the Answer' (2009) 23 Bioethics 393.
[1028] Donna M Gitter, 'Resolving the Open Source Paradox in Biotechnology: A Proposal for a Revised Open Source Policy for Publicly Funded Genomic Databases' (2007) 43 Houston Law Review 39.

The primary motives, why biobanks should choose open working methods, can be numbered the following: 1) it creates global value – not only a single biobank but everybody can benefit from open sharing; 2) it reduces R&D costs, as institution can take previously disclosed information; 3) it gives access to technologies to a much broader spectrum of biobanks; 4) the greater mass of researchers are working on the same question and sharing their findings; 5) the risks, liabilities and costs are shared between several institutions; 6) it allows to have better relations with partners, as all are reaching the same common goal; 7) it gives benefits of technology transfer; 7) new business can access the technology easier; 8) the market is accessible to a broader circle of companies; 8) it proposes standardization of some requirements (for example, informed consent forms).

Yann Joly[1029] describes the following benefits of the use of open source in biotechnology. First she describes the scientific benefits such as: a) the peer evaluation and validation of findings, when open development exposes new input and encourages an open, critical discussion in order to foster higher quality research; b) the increase in intellectual curiosity and motivation, where the exposure to new ideas, refining scientific skills, and being part of a community are essential elements of the innovation rewards; c) maximization of rational development, when each user becomes a potential source of new ideas for future directions in the product, and the workload for implementing change is shared between an expanded group of developers; d) the facilitation of sharing of technical information, when having learned about the technical details of the project, the collaborator can contribute more actively and effectively to the ongoing technical discussion; e) facilitation of technology transfer and access to health in developing countries, when new solutions to developing treatments for rare diseases or for diseases found in poor nations may come from open source search practices in biotechnology. Such approaches can foster biomedical innovation while significantly reducing research and development expenditures, which often pose barriers to new drug development for combating many neglected diseases[1030].

Secondly, Yann Joly numbers the economic benefits: 1) the reduction of duplication, greater overall transparency and a reduction in costs in research. Researchers will be able

[1029] Yann Joly, 'Open Source Approaches in Biotechnology: Utopia Revisited' (2007) 59 Maine Law Review 385.

[1030] Mrinalini Kochupillai, 'SPICY IP Interview with Dr. Samir K Brahmachari' *SPICY IP* (2008). Available at: <https://spicyip.com/2008/03/spicy-ip-interview-with-dr-samir-k.html> accessed 8 May 2018.

to learn more quickly and easily when they are working on open source projects, they will avoid the excess costs generated by the duplication of their research efforts;[1031] 2) development of market for complementary goods and services, where open source licensing can potentially foster a user base for the technology, thereby growing the market for complementary goods and services and perhaps even establishing a de facto industry standard;[1032] 3) enhance institution's reputation and public relations. Making the technology they develop freely available to the general public, these companies can boost their reputations for innovation and expertise, as well as user-friendliness and social-mindedness;[1033] 4) share financial risk in projects, it is often the case that in biotechnological research the only way to obtain the desired final product is to share the burden of innovation. By joining efforts each firm minimizes the risk of paying excessive prices for future licenses on important research tools while retaining the right to patent downstream innovations developed with the help of these tools;[1034] 5) attract volunteer labor. Volunteers respond to the "supply side" incentives of idealism, learning new skills, and impressing potential employers;[1035] 6) elimination of time-consuming and costly negotiations for the use of IP rights (patents, databases) and also eliminating the costs associated with patent protection;[1036] 7) customization, the improvements are driven from a bottom up approach where end-users both initiate and implement modifications based on real needs, making the invention more attractive and useful to its users;[1037] 8) production of usable output at a lower cost: if highly skilled collaborators use an open source approach to undertake the fundamental research, sponsors could avoid overpaying the research and development costs that are so difficult to estimate in the early stages. Moreover, because the intellectual property would be accessible to everyone, any

[1031] Joly (2007) 400; Jean-Michel Dalle and Paul a David, 'The Allocation of Software Development Resources in Open Source Production Mode' (2005) 94305 Perspectives on Open Source and Free Software 297, 300.

[1032] Joly (2007) 400; Hope (2004) 152.

[1033] Joly (2007) 400; Eric von Hippel and Georg von Krogh, 'Open Source Software and the "Private-Collective" Innovation Model: Issues for Organization Science' (2003) 14 Organization Science 209, 13–15.

[1034] Rebecca S. Eisenberg, 'Will Pharmacogenomics Alter the Role of Patents in Drug Development?' (2002) 3 PHARMACOGENOMIC 57 S1, 571-73 (as cited in Joly (2007) 401.).

[1035] Stephen M. Maurer 'New Institutions for Doing Science: From Databases to Open Source Biology' 13 (Nov. 19, 2003) paper presented to the European Policy for Intellectual Property Conference on Copyright and database protection, patents and research tools, and other challenges to the intellectual property system (as cited in Joly (2007) 401.)

[1036] Janet E Hope, 'Open Source Biotechnology' [2004] SSRN Electronic Journal 91.

[1037] Neil B. Niman & Brian T. Kench 'Open Source in the Pharmaceutical Industry' (2003) PROC. MIDWEST Bus. ECON. Ass'N 124, 127 (as cited in Joly (2007) 402.)

company could manufacture the good, and the resulting competition would likely keep down the market price for the completed product.[1038]

And thirdly, Yann Joly indicated the social benefits, such as: 1) the increased respect of peers – an open source environment fosters greater transparency, making it easier for peers to signal the production of a higher level of work since they can see each contribution made by individuals participating in a given project;[1039] 2) compatible with the scientific ethos of open science – the use of open source approaches could be the perfect way for academia to progress toward the "communalism" norm of science embraced by Merton; these norms recognize that scientific progress does not emerge from a void, but always depends on the body of knowledge accumulated by previous generations of researchers; 3) improve coordination – it facilitates effective collaboration within the research community-both nationally and internationally-by enabling the sharing of expertise, resources, and knowledge; 4) facilitate access to information for learning and educational purposes – open source biotechnology projects could enable students to benefit from the latest research tools without them or the university having to worry about possible infringement suits or the status of the common law research exemption; 5) increase motivation of employees – employees are usually motivated by such incentives as the desire to become well-known through the improved accessibility of their work.[1040]

There are initiatives to share the information more broadly. At a national level, there are a number of examples of coordinating activities. In Germany, biobank operators have been maintaining and interactively updating their data in the German Biobank Registry (GBR). In the USA, the Coriell Personalized Medicine Collaborative (CPMC) aims for better understanding the impact of genome-informed medicine by combining a biobank facility with modern microarray technology.[1041] In the USA the Office of Biorepositories and Biospecimen Research (OBBR) created the Biospecimens Research Network (BRN) and a Biospecimen Resource Database (BRD). Biospecimen Research Database is a free and publicly accessible database that contains peer-reviewed primary and review articles

[1038] Joly (2007) 403; Stephen M Maurer, Arti Rai and Andrej Sali, 'Finding Cures for Tropical Diseases: Is Open Source an Answer?' (2004) 1 PLoS Medicine 183, 184.
[1039] Joly (2007) 403; Josh Lerner and Jean Tirole, 'The Economics of Technology Sharing: Open Source and Beyond' (2004) 20–24.
[1040] Joly (2007) 304; Lerner and Tirole 16.
[1041] Don Chalmers and others, 'Has the Biobank Bubble Burst ? Withstanding the Challenges for Sustainable Biobanking in the Digital Era' [2016] BMC Medical Ethics 7.

in the field of human Biospecimen Science.[1042] BBMRI in Europe has the aim to develop an information technology concept for the exchange of data between biobanks (at national and European levels). It also seeks to present a positive and transparent image of biobanking. The BBMRI is now recognised as a European Research Infrastructure Consortium (ERIC), pulling together a broad range of biobanks operating to increase efficacy and excellence in research of European interest.[1043]

There can be other proposals on how to promote better use of biobanks' information and advance health care of higher quality, like compulsory licensing of patents, transparency between institutions, liability rules, etc. All of these possibilities have advantages and disadvantages, but open sharing and open licenses can be used as additional option to increase advances in medicine. Anne Cambon-Thomsen has stated, "many restricted uses and opposition to sharing bioresources are a result of intellectual property rights or the control that scientists want to exert on the biobanks they have established with great effort, rather than ethical issues related to respect for the individual rights of donors".[1044] And such restrictions can be easily overcome by open sharing.

Genomics holds the promise of individualised medicine, tailoring prescribing practices and management of patients to each person's genetic profile. A better understanding of the genetic factors could have an enormous impact on health in the developing world. The millions of people around the world who supports sequencing of the human genome have expectations that it would benefit humankind. It is critical to encourage the same intensity toward deriving medical benefits from the genome by sharing each others knowledge. If research support continues and sharing of information increases, genome science will begin revealing the answers to hereditary diseases and in this way assist in finding better cures for people.

[1042] National Cancer Institute, 'The Biospecimen Research Database' <https://brd.nci.nih.gov/brd/> accessed 8 May 2018.
[1043] BBMRI-ERIC, 'Home Page' <http://www.bbmri-eric.eu/> accessed 8 May 2018.
[1044] Anne Cambon-Thomsen, 'The Social and Ethical Issues of Post-Genomic Human Biobanks' (2004) 5 Nature Publishing Group 872.

CONCLUSIONS

This thesis faced the challenge of answering the question if intellectual property rights, that are created by the biobanks' activities, can be managed in a more open way to ensure the equitable distribution of knowledge and improvements in the medical research. Biobanks, being repositories of human genetic samples, has as their main task, to provide the scientific community with sufficient scientific data and genetic resources to advance the development of medical research. If we agree that genetic research can help to cure diseases and treat people, the human biorepositories, storing hundreds and thousands of tissue samples, are playing very important role. Therefore, the restrictions created by intellectual property rights might be inadequate and prevent the biobanks from performing their main goal. Sharing of scientific discoveries is crucial for the biobanks and the repetitive work naturally delays scientific improvements.

During my research I was investigating what types of intellectual property rights biobanks are creating and can own. The use of intellectual property rights in the biobanks was also discussed and proposals for the possible alternatives how IPR can better assist in advancing the distribution of genetic research outcomes, were given.

The first limitation to share biological resources, that I have discovered in my dissertation, is copyrights and database protection rights. Even if human gene, as such, cannot be protected by copyrights, the collection of biobanks databases can be, and all the data gathered by the biobanks is automatically protected by the *sui generis* rights in Europe. The database right is very much questioned by the legal scholars and economic operators does not seem to care much about such rights. The studies have shown that implemented database protection in Europe did not increase the creation of databases, what was the main goal of the Directive. Despite any legislative database protection, the growth and number of databases in US is much higher than in the EU. Between 2002 and 2004, the European share in databases decreased from 33% to 24%.[1045]

Also, no evidence was found that biobanks would ever use database rights to protect their genetic resources. But regardless these facts, as long as database rights are in force, the biobank's resources are protected automatically by *sui generis* rights and its protection

[1045] Commission of the European Communities, DG Internal Market and Services Working Paper 'First evaluation of Directive 96/9/EC on the legal protection of databases', Brussels, 12 December 2005, 22.

can be claimed according to the terms of the Database Directive. So far there is no better way to surrender database rights in biobanks than simply does not claim such rights or apply open licenses to such databases. If biobanks can enter into mutually beneficial relations with each other, and open their databases to global partners, the *sui generis* rights can be left behind in the biobanks activities.

Another IPR limitation that is extremely important for biobanks is patenting of human genes and other upstream discoveries in the genomics. The monopolization by patent of the basic scientific information can become a reason for the increase of prices in medicines and the decrease of useful products in the health sector. Biobanks cannot restrict their users or investigators to protect the research outcomes by IPR. It would not be accepted in general as IPR are established more than hundred year ago and these rights ensure the protection of intellectual assets in any technical field, including biotechnology.

Moreover, in Europe, the Biotechnology Directive foresees that genes can be patented. Also, the genes that exist in nature can have patent protection as long as its technical applicability is shown. In the Myriad decision[1046] the US Supreme court ruled that Myriad Genetics cannot own patent for the genetic information encoded in the BRCA1 and BRCA2 genes. But the case did not give a clear explanation when genes can be patented and when they fall under the product of nature doctrine. As a consequence, gene patents are still granted in US as well as in Europe.

In the thesis I propose, that to ease the transfer of knowledge between biobanks, the reflection to open licenses can be made. I see it being reasonable and acceptable to promote open licenses for genetic patents. I have presented in the thesis the open sharing model and described the possibilities to use IP rights in a non-restricting way. Open licenses, that are already used for decades in softwares, can be adopted to the biotech research and in the activities of the biobanks. Open licensing templates and frameworks (such as Creative Commons licenses) already working in the other fields, can become important tool in sharing genetic knowledge as well.

The open license is a license to an IP protected work, that applies to every person, confirming the licensing conditions. The open licenses in biobanks can represent an elegant use of contractual terms and property rights to create social conditions in which intellectual property rights in genetic field are used and new rights created on a model of openness. Such license does not need to nullify the IP rights, but it allows to use such

[1046] *Ass'N For Molecular Pathology v Myriad, 133 SCt 2107 (2013).*

rights in a non-protective way. Open license can grant permission to access, re-use and redistribute a work with few or no restrictions. What is very important is that open source strategies do not rely on domestic or international law reform. It is a contract between the holder of rights and the user, so it is governed by the contract law and not the intellectual property law.

The Equitable Access licensing has been presented as a possibility to share genetic patents more broadly. Under an Equitable Access license, a university would, for a fair royalty payment, grant to another party (such as a commercial firm) a nonexclusive license to use its patented technology to produce an item for sale in poorer countries and richer countries (territorial limitations are not applied). In return, the licensee would agree to grant back to the university any improvements it might make to the technology and to cross-license any other rights the licensee holds that might be used to block production of the item in question.[1047]

We cannot expect that biotech industry, which profits depends a lot on the patenting and licensing of technologies would agree to abandon these rights and disclose all the information to the public domain. But it is possible that big companies would agree with open licensing terms if they see it as a win-win solution between the industry and the society.

The third issue biobanks are facing in their everyday work is the protection of individuals' data. This is one of the most important issues, which must be taken into account when a biobank wants to share its information and resources more openly. There are already decisions of the national courts (Icelandic Supreme Court case No. 151/2003, *Ragnhildur Guðmundsdóttir* vs. *The State of Iceland*) where people have claimed that a biobank is not respecting their privacy and family rights.

The informed consent requirement is very strict in the biobanks, and a biobank cannot use the tissue of a donor more broadly than the person has implicitly stated. In M.S. v. Sweden,[1048] the European Court of Human Rights found that the lack of consent of the data subject to the disclosure of certain sensitive data was a key element in the finding of an infringement of Article 8 (the right to privacy) of the European Convention on Human Rights.

[1047] Janet Hope, *Biobazaar: The Open Soure Revolution and Biotechnology* (Harvard University Press 2008) 319.

[1048] *MS v Sweden [1997] ECHR No 20837/92.*

In the thesis I propose that the solution to ensure the right balance between individual rights and biobanks' need to share collected information is the use of a broad informed consent. Open consent can be used in the biobank's activities to ensure that the tissues are not left unutilised and that such form of consent can assure the maximum value of the collected biological tissues. If collected samples are not restricted to the one-time or one-research use, we can expect that other studies are performed on the same samples and more scientific information is presented.

What I am proposing further is the unification of biobanks' consent templates. Common templates would reduce the administrative costs and advance the sharing of biological samples and data. Creating templates will have to take on the challenges to generalise consent forms and provide templates that are comprehensive to the extent that different research purposes and legal unpredictabilities are taken into account. They also would need to ensure that the current intended use of the samples or data is covered by the scope of the consent under the relevant legal regimes. The conception of broad consent for medical research has a lot of advantages, so this kind of templates would assist in making future use of biosamples and data possible.

The acceptability by research participants of open consent was shown by several analytical studies.[1049] People are keen to protect their rights and their privacy, their body integrity. But they are also willing to participate in socially positive activities: donate blood, bone marrows, be organ donors after death. If a person sees, that his participation has a favorable effect to the life of others, and that he can assist by donating this body samples, a person will not doubt to participate. What is important, is to create a transparent links and close bonds between the biobank's and donor. Explaining and educating population about the positive influence the biobanks have or might have to the human health would increase the number of participants and also, collections of samples.

It is a long way the biobanks must go to show that they are useful establishments. The cooperation and common goals must lead biobanks to work together and share their knowledge. Created intangible barriers does not give any good to the biobanks themselves or to the public. The legislation does not always rightly reflect the social needs and can unwillingly unbalance the social relationships. Biobanks are very new

[1049] Yann Joly and others, 'Fair Shares and Sharing Fairly: A Survey of Public Views on Open Science, Informed Consent and Participatory Research in Biobanking' (2015) 10 PLoS ONE; Saskia C Sanderson and others, 'Public Attitudes toward Consent and Data Sharing in Biobank Research: A Large Multi-Site Experimental Survey in the US' (2017) 100 American Journal of Human Genetics 414.

institutions in the world. And even if there are already quite a number of bio repositories, there are still no international legal instrument regulating biobanks activities. The establishment and functioning of the biobanks are mostly regulated by national laws, secondary acts or biobank's internal rules.

Some countries have national laws governing the role and working methods of the biobanks. For example, Spain, Estonia, Finland, Iceland, Sweden, Norway, all these countries have specific laws on the establishment of biobanks and the use of human samples in research studies. However, the biggest majority of counties, including the US, UK, Germany or France, does not have specific legal rules regulating biobanks. Therefore, it is quite important for the biobanks to enter into beneficial bilateral or multilateral co-operational agreements and concur on the sample and data sharing policies.

The biobanks' umbrella organizations are already established and working towards the goal to unite biobanks and their resources. The NIH and BBRMI-ERIC projects has created international freely available databases where scientist can access information about the samples or find some research results from different repositories. Understanding the common wealth of the work biobanks are doing, states and European Union are investing great funds to lift biobanks activities.

And last but not least, the scientist also supports the idea of open knowledge. From 1996, when at the summit in Bermuda, the leaders of the HGP agreed that all human genomic sequence information generated by centers funded for large-scale human sequencing should be made freely available and published in the public domain within 24 hours after generation, the idea to share scientific information freely is growing and expanding. The answers to my questionnaire, which is presented in the Annex I of the thesis, shows, that researchers support open sharing and are not willing to monopolize the research result by the IPR. Some answer examples to the question "*Do you think open access is important for researchers in biotechnology field?*" are:

"The more people can obtain information the most effective their research will be."

"Yes, important, not in the least to prevent repetitive collections and work. For example, population controls samples should be open access."

"Open access speeds up development of better (public) health care."

"Very important for critical analysis, for new discovery and validation, and for meta-research."

What is expected from the biobanks is to be a source of knowledge and to lead, or at least start, the medical revolution, which centres the individual medicine, and has a goal to establish the wellness of the patient not just to cure a disease. If our goal is truly to help to eliminate human suffering, then we should spend more time thinking about alternative and supplementary ways of encouraging pharmaceutical innovation beyond the way to protect all the innovations with the intellectual property rights.

RESUMEN

Esta tesis se emprendió con el desafío de responder la pregunta de si los derechos de propiedad intelectual creados por las actividades de los biobancos pueden ser manejados de una manera más abierta para asegurar la distribución equitativa del conocimiento y las mejoras en la investigación médica. Los biobancos, siendo depósitos de muestras genéticas humanas, tienen como tarea principal proveer a la comunidad científica de suficientes datos científicos y recursos genéticos como para poder avanzar en el desarrollo de la investigación médica. Si aceptamos que la investigación genética puede ayudar a curar enfermedades y tratar a las personas, los biorepositorios humanos, que almacenan cientos y miles de muestras de tejidos, juegan un papel muy importante. Por lo tanto, las restricciones creadas por los derechos de propiedad intelectual pueden ser inadecuadas y evitar que los biobancos realicen su objetivo principal. Compartir los descubrimientos de los científicos es crucial para los biobancos y el trabajo repetitivo naturalmente retrasa el avance científico.

Durante mi investigación he indagado en qué tipos de derechos de propiedad intelectual están estableciendo y pueden poseer los biobancos. También se debatió sobre el uso de los derechos de propiedad intelectual en los biobancos y se presentaron propuestas para las posibles alternativas sobre cómo los DPI pueden ayudar a avanzar en la distribución de los resultados de la investigación genética.

Limitaciones

En mi investigación, he descubierto que una de las primeras limitaciones para compartir los recursos biológicos son los derechos de autor y los derechos de protección de las bases de datos. Incluso si el gen humano, como tal, no puede ser protegido mediante derechos de autor, la recogida de bases de datos de biobancos puede serlo, y todos los datos recopilados por los biobancos están automáticamente protegidos por los derechos “sui generis” en Europa. El derecho de las bases de datos está siendo muy cuestionado por los académicos legales y los agentes económicos no parecen estar muy interesados en tales derechos. Los estudios han demostrado que la implementación de la protección de bases de datos en Europa no ha aumentado la creación de bases de datos, lo cual era el objetivo principal de la Directiva. Más allá cualquier protección de base de

datos legislativa, el crecimiento y la cantidad de bases de datos en EE. UU es mucho mayor que en la UE. Entre 2002 y 2004, la participación europea en las bases de datos disminuyó del 33% al 24%[1050].

Además, no se encontraron evidencias de que los biobancos alguna vez hayan usado los derechos de bases de datos para proteger sus recursos genéticos. Pero independientemente de estos hechos, mientras los derechos de la base de datos estén vigentes, los recursos del biobanco están protegidos automáticamente por los derechos "sui generis" y su protección puede reclamarse de acuerdo con los términos de la Directiva de Bases de Datos. Hasta ahora, no existe mejor manera de ceder los derechos de la base de datos en los biobancos que simplemente no reclamar tales derechos o aplicar licencias abiertas a dichas bases de datos. Si los biobancos pueden establecer relaciones mutuamente beneficiosas entre sí y abrir sus bases de datos a socios mundiales, los derechos "sui generis" pueden ser orillarse en las actividades de los biobancos.

Otra limitación del DPI que es de una gran importancia para los biobancos es la patente de genes humanos y otros descubrimientos en el campo de la genética. La monopolización de las patentes de la información científica básica puede convertirse en motivo de aumento de los precios en medicamentos y de la disminución de productos útiles en el sector de la salud. Los biobancos no pueden restringir el acceso a sus usuarios o investigadores para proteger los resultados de la investigación mediante DPI. Esto no estaría generalmente aceptado si los DPI se hubiesen establecido hace más de cien años y estos derechos se hubiesen asegurado por la protección de los activos intelectuales en cualquier campo técnico, incluyendo la biotecnología.

Además, en Europa, la Directiva de biotecnología establece que los genes pueden ser patentados. Asimismo, los genes que existen en la naturaleza pueden tener protección de patente siempre y cuando se demuestre su aplicabilidad técnica. En la decisión de Myriad[1051], el Tribunal Supremo de los Estados Unidos dictaminó que "Myriad Genetics" no podía obtener la patente para la información genética codificada en los genes BRCA1 y BRCA2. Desafortunadamente, el caso no dio ninguna explicación clara sobre cuándo los genes pueden ser patentados y cuándo caen bajo el producto de la doctrina de la naturaleza. Como consecuencia, aún se otorgan patentes de genes en los Estados Unidos y en Europa.

[1050] Commission of the European Communities, DG Internal Market and Services Working Paper 'First evaluation of Directive 96/9/EC on the legal protection of databases', Brussels, 12 December 2005, 22.
[1051] Ass'N For Molecular Pathology v Myriad, 133 SCt 2107 (2013).

En esta tesis propongo la reflexión de que, para poder facilitar la transferencia de conocimientos entre biobancos, la solución puede ser abrir las licencias. Parece razonable y aceptable promocionar las licencias abiertas para patentes de genética. En la tesis se presenta el modelo de intercambio abierto y la descripción de las posibilidades de usar los DIP de manera no restrictiva. Las licencias abiertas, que se llevan usando durante décadas en software, se pueden adaptar para las investigaciones de biotecnología y las actividades de los biobancos. Las plantillas y marcos de la licencia abiertos (como las licencias Creative Commons) que están funcionando en los otros campos, pueden convertirse en una herramienta importante para compartir el conocimiento genético también.

La licencia abierta es una licencia para un trabajo protegido por DPI que se aplica a todas las personas y confirma las condiciones de la licencia. Las licencias abiertas en biobancos pueden representar un uso limitado de los términos contractuales y los derechos de propiedad para crear condiciones sociales en las que se usan los derechos de propiedad intelectual en el campo genético y se crean nuevos derechos sobre la base de un modelo de apertura. Tal licencia no necesita anular los derechos de DPI, pero permite usar tales derechos de una manera no proteccionista. La licencia abierta puede otorgar el permiso para acceder, reutilizar y redistribuir un trabajo con pocas o ninguna restricción. Lo que es más importante es que las estrategias de fuente abierta no se basan en la reforma de las leyes nacionales o internacionales. Es un contrato entre el titular de los derechos y el usuario, por lo que se gobierna por el derecho contractual y no por la ley de propiedad intelectual.

La licencia de acceso equitativo ya se ha presentado y se utiliza para compartir patentes genéticas de manera más amplia. Con una licencia de acceso equitativo, la universidad, a cambio de un pago justo de regalías, otorgaría a la otra parte (como una empresa comercial) una licencia no exclusiva para usar su tecnología patentada para producir un ítem para a la venta en países más pobres y países más ricos (sin imitaciones territoriales). A cambio, el licenciatario acordaría devolver a la universidad cualquier mejora que pudiera hacer a la tecnología y licencia cruzada de cualquier otro derecho que tenga el titular de la licencia que pueda ser utilizada para bloquear la producción de los ítems cuestionables.[1052]

No podemos esperar que la industria de la biotecnología, cuyos beneficios dependan en gran medida de los patentes y de las licencias de las tecnologías, acepte renunciar a

[1052] Hope (2008) 319.

estos derechos y divulgar toda la información al dominio público. Pero es posible que las grandes empresas acepten términos de licencia abiertos si lo ven como una solución de beneficio mutuo entre la industria y la sociedad.

El tercer inconveniente al que se enfrentan los biobancos en su trabajo diario es la protección de los datos de las personas. Este es uno de los problemas más importantes y lo que se debe tener en cuenta es cuando un biobanco quiere compartir su información y sus recursos de manera más abierta. Hoy en día, existen las decisiones de los tribunales nacionales (caso de la Corte Suprema de Islandia Nº 151/2003, Ragnhildur Guðmundsdóttir vs. El estado de Islandia) donde las personas han confirmado que un biobanco no está respetando su privacidad ni sus derechos familiares.

El requisito del consentimiento informado es muy estricto en los biobancos, y un biobanco no puede utilizar el tejido de un donante de manera más amplia de lo que la persona ha indicado implícitamente. En M.S. v. Suecia[1053], el Tribunal Europeo de Derechos Humanos descubrió que la falta de consentimiento de los datos sujetos a la divulgación de ciertos datos sensibles era un elemento clave en la constatación de una infracción del artículo 8 (el derecho a la privacidad) del Convenio Europeo sobre los derechos humanos.

En esta tesis se propone que la solución para garantizar el equilibrio correcto entre los derechos individuales y la necesidad de los biobancos de compartir información obtenida es el uso de un amplio consentimiento informado. El consentimiento abierto se puede utilizar en las actividades del biobanco para garantizar que los tejidos no pueden ser utilizados y que dicha forma de consentimiento pueda asegurar el valor máximo de los tejidos biológicos recogidos. Si las muestras recolectadas no están restringidas a un solo uso o a una sola investigación, podemos esperar que se realicen otros estudios con las mismas muestras y se presente más información científica.

Lo que propongo con mi trabajo es la unificación de las plantillas de los consentimientos de los biobancos. Las plantillas comunes reducirían los costos administrativos y avanzarían el intercambio de muestras y datos biológicos. La creación de las plantillas tendrá que asumir los desafíos para generalizar los formularios de los consentimientos y proporcionar las plantillas para que sean más completas en la medida en que se tengan en cuenta los diferentes propósitos de investigación y los imprevistos legales. También necesitarían asegurarse de que el uso previsto real de las muestras o

[1053] MS v Sweden [1997] ECHR No 20837/92.

datos estaría cubierto por el alcance del consentimiento según los regímenes legales pertinentes. La concepción de un amplio consentimiento para la investigación médica tiene muchas ventajas, por lo que este tipo de plantillas ayudarían a hacer posible el uso futuro de datos y muestras biológicas.

Varios estudios analíticos demostraron la aceptabilidad por parte de los participantes de la investigación del consentimiento abierto[1054]. La gente está interesada en proteger sus derechos, su privacidad y su integridad corporal. Pero también están dispuestos a participar en actividades socialmente positivas: donar sangre, médula ósea y ser donantes de órganos después de la muerte. Si una persona ve que su participación tiene un impacto favorable en la vida de los demás y que puede ayudar donando muestras de este cuerpo, entonces no dudará en participar. Lo más importante es crear vínculos transparentes y estrechos entre los biobancos y el donante. Explicando y educando a la población sobre la influencia positiva que los biobancos tienen o podría tener para la salud humana aumentaría el número de los participantes y también, recolección de muestras.

Es un largo camino que los biobancos deben recorrer para demostrar que son organismos útiles. La cooperación y los objetivos comunes deben llevar a los biobancos a trabajar conjuntamente y compartir sus conocimientos. Las barreras intangibles creadas no dan ningún bienestarni a los biobancos mismos ni al público. La legislación no siempre refleja correctamente las necesidades sociales y puede desequilibrar involuntariamente las relaciones sociales. Los biobancos son instituciones muy nuevas en el mundo. Incluso si hoy en día existen bastantes repositorios biológicos, todavía no existe un instrumento legal internacional que regule las actividades de los biobancos. El establecimiento y el funcionamiento de los biobancos están regulados principalmente por las leyes nacionales, actos secundarios o normas internas del banco biológico.

Algunos países tienen leyes nacionales que gobiernan el papel y los métodos de trabajo de los biobancos. Por ejemplo, España, Estonia, Finlandia, Islandia, Suecia, Noruega, todos estos países tienen leyes específicas sobre el establecimiento de biobancos y el uso de muestras humanas en los estudios de investigación. Sin embargo, la mayoría de los mencionados, incluyendo los EE. UU., El Reino Unido, Alemania y Francia, no cuentan con normas legales específicas que regulen los biobancos. Por lo tanto, es muy

[1054] Yann Joly and others, 'Fair Shares and Sharing Fairly: A Survey of Public Views on Open Science, Informed Consent and Participatory Research in Biobanking' (2015) 10 PLoS ONE 1; Saskia C Sanderson and others, 'Public Attitudes toward Consent and Data Sharing in Biobank Research: A Large Multi-Site Experimental Survey in the US' (2017) 100 American Journal of Human Genetics 414.

importante que los biobancos participen en los acuerdos de cooperación bilateral o multilateral beneficiosos y se pongan de acuerdo sobre las políticas de muestreo e intercambio de los datos.

Las organizaciones “paraguas” de los biobancos ya están establecidas y trabajan para lograr el objetivo de unir los biobancos y sus recursos. Los proyectos de NIH y BBRMI-ERIC han creado bases de datos internacionales libremente disponibles, donde los científicos pueden acceder a información sobre muestras o encontrar resultados de investigaciones de diferentes repositorios. Al entender la riqueza común del trabajo que hacen los biobancos, los estados y la Unión Europea están invirtiendo grandes fondos para elevar las actividades de los biobancos.

Y, por lo último, pero no menos importante, el mundo científico también apoya la idea del conocimiento abierto. Desde el año del 1996, cuando en la cumbre de Bermuda los líderes del HGP acordaron que toda la información de la secuencia genómica humana generada por los centros financiados para la secuenciación humana a gran escala debería estar disponible libremente y publicarse en el dominio público dentro de las 24 horas posteriores a la generación, idea de compartir información científica libremente está creciendo y expandiéndose. Las respuestas a mi cuestionario, que se presenta en el Anexo I de la tesis, muestran que los investigadores apoyan el intercambio abierto y no están dispuestos a monopolizar el resultado de la investigación mediante el IPR. Algunos ejemplos de respuestas a la pregunta "¿Cree usted que el acceso abierto es importante para los investigadores en el campo de la biotecnología?" Son:

"Cuantas más personas puedan obtener información, más efectiva será su investigación".

"Sí, es importante, para evitar las recolecciones y el trabajo repetitivo. Por ejemplo, las muestras de controles de población deben ser de acceso abierto".

"El acceso abierto acelera el desarrollo de una mejor asistencia sanitaria (pública)".

"Muy importante para el análisis crítico, para los nuevos descubrimientos, validaciones y para la meta-investigación".

Lo que se espera de los biobancos es ser una fuente de conocimiento y liderar, o al menos comenzar, la revolución médica, que se centrara en la medicina individual con elobjetivo de establecer el bienestar del paciente no solamente para curar una enfermedad. Si nuestro objetivo es verdaderamente ayudar a eliminar el sufrimiento humano, entonces deberíamos dedicar más tiempo a pensar en formas alternativas y complementarias de

fomentar la innovación farmacéutica más allá del camino para proteger todas las innovaciones con los derechos de propiedad intelectual.

ANNEX 1

Survey on intellectual property rights in biobanks

During my research, I have prepared a questionnaire for scientists and researchers, as well as biobanks' personnel about IPR in biobanks. The target audience of this questionnaire was scientists and researchers, as well as biobanks' personnel, who is working with genetic information or whose research is related to the analysis of biological substances.

The questionnaire was sent by email to 465 representatives from EU biobanks. The email addresses were acquired from BBMRI-ERIC Directory 4.0, which brings together biobank collections and biobank networks. In the Directory 4.0, the biobanks describe the institutional aspects of biobanks and their collections of samples. The collections allow biobanks to describe in more detail what sample sets and data sets are available, to better meet the needs of users browsing and searching the Directory. Furthermore, the Directory can now capture how biobanks are organised into biobank networks, indicating what properties they share and which institutional biobanks host collections for multiple biobank networks.

There were 13 multiple choice or open questions in this questionnaire. Some of the questions were closed-ended questions, where the respondents were given a list of predetermined responses from which to choose their answer. Other questions were open-ended questions, were survey respondents were asked to answer each question in their own words. In total there was 31 answers to the questionnaire. In the diagrams, I present the answers to closed-ended questions. The open-ended questions are presented by showing all the answers given.

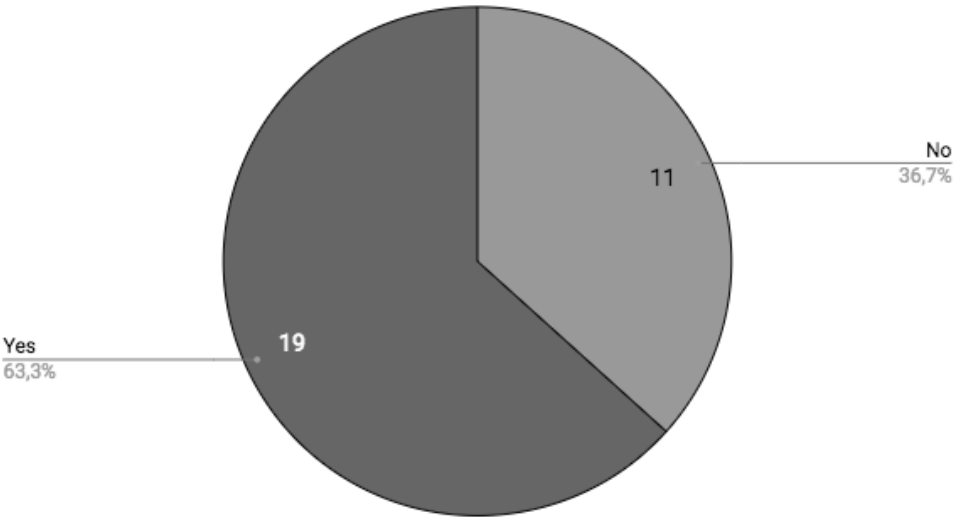
Some conclusions can be made based on the answers:

1. Most respondents were from public institutions (80,6%).
2. Half of the respondents do not encounter real problems to access biological samples (48,4%). Others (38,7%) indicate several restrictions to access the samples: long waiting time for the approval of research and delivery of samples/data; juridical, administrative and ethical restrictions; strict evaluation of the research, ethical rules of the Ethical Boards; high fees.

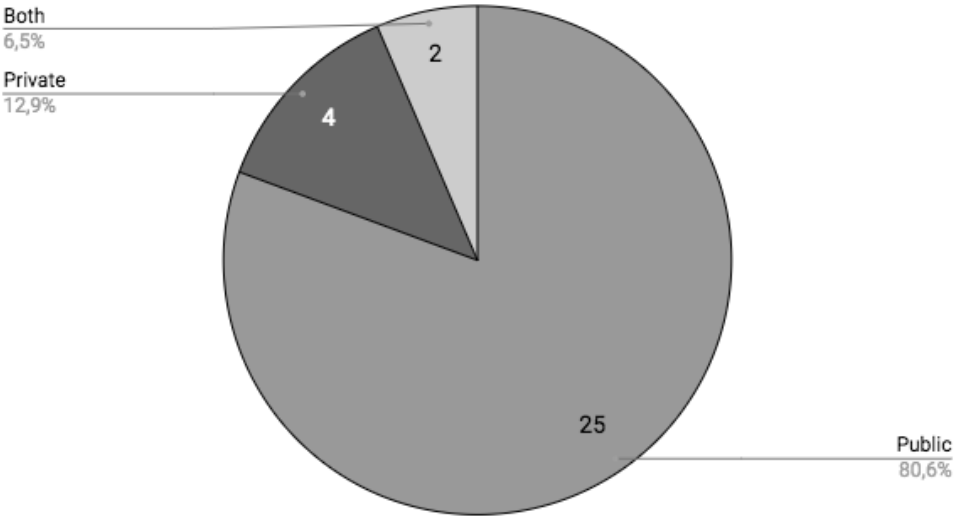
3. 93,3% of respondents have never been restricted to use any information/knowledge/genetic sequence code or other, because it was protected by patents or other intellectual property rights. However, two respondents have replied affirmative. One has mentioned NIPT test for Down syndrome screening.
4. Patenting does not seem to be one of the main objectives of participants. 86,6% of respondents have never considered patenting and have never applied for a patent, for the research results (for revealed genetic information, gene sequence, methods of analyzing information…). 13,3% replied positively, that they already are authors of patent or have applied for patent protection.
5. In general, researchers are aware of the IPR regulation in their institution. 90,3% of respondents confirmed they are aware of the IPR regulations in their institution.
6. Majority of respondents are in opposition to gene patents. 76,5% of respondents believe gene patents should not be allowed. 6,7% reply that they believe gene patent should be allowed. 16,8% have no opinion or the answer does not disclose the definite opinion of the respondent.
7. Open biotechnology is not yet so much known and applied by researchers. 26 responses were given to the question about open biotechnology. 14 respondents replied that they have not heard and is not using open source technologies. 12 respondents replied that they know about open biotechnology and has named several open sources they are using.
8. Survey showed that open data is very important to the researchers in the biobanks. From 28 responses, 26 respondents replied why they think open access is essential for researchers in biotechnology field and that it helps to reach better results when the information is available for free to anyone. 1 answer to this question was negative and one respondent expressed doubts.
9. Withdrawal of participants can be a problem to continue research. Participants withdraw from research have caused 4 researchers (12,9%) problems to continue their investigation. 77,4% (24 answers) of respondents, however, has never been restricted to use samples because of withdrawal. Two more researchers replied, that they have faced the withdrawal, but it has not caused negative consequences for ongoing research.

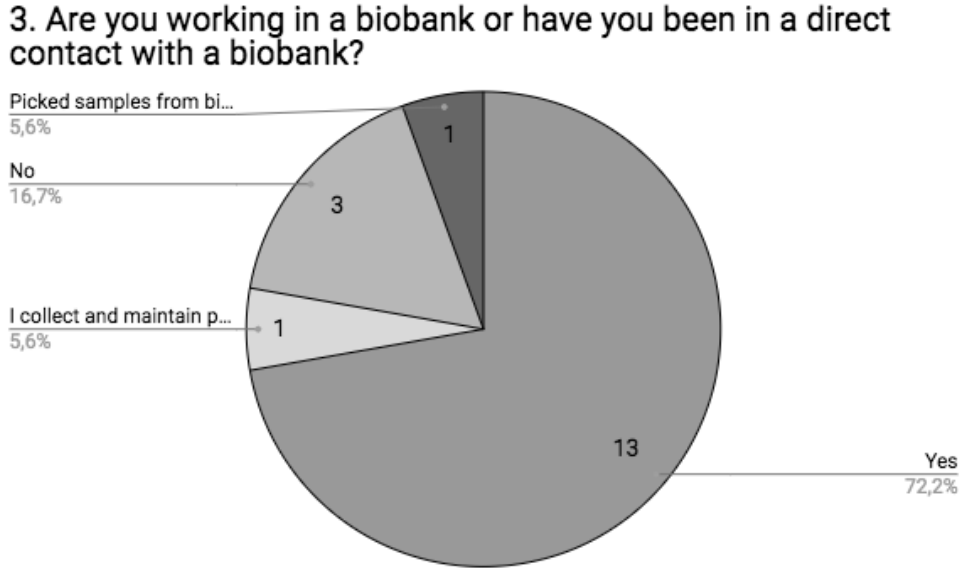
The charts and answers to all the questions are represented below.

1. Are you a researcher in biotechnology field?



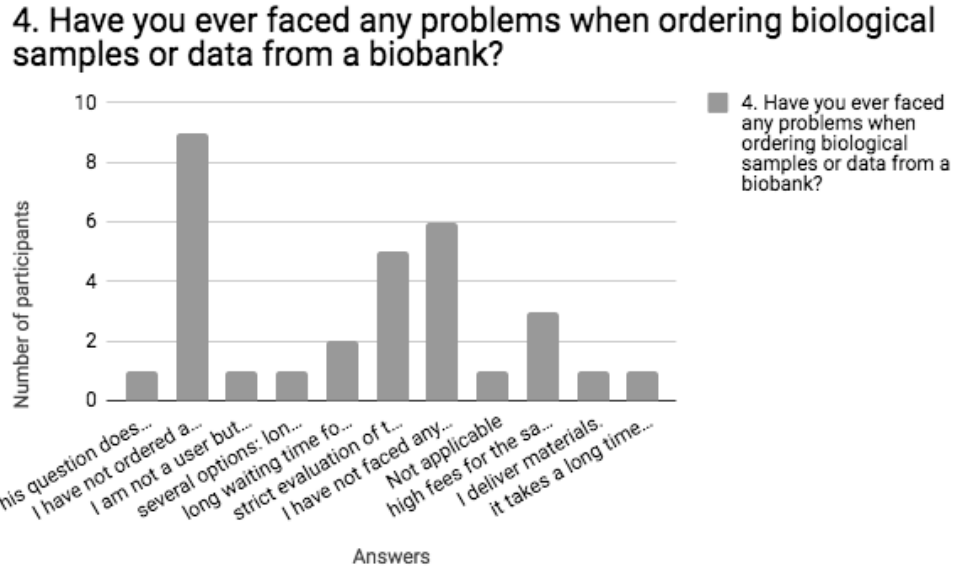
2. Do you represent public or private institution?





ANSWERS:

- Picked samples from biobank
- I collect and maintain patient cohorts, including clinical data and DNA samples



ANSWERS:

- This question does not apply as i work for a biobank
- I have not ordered any information yet
- I am not a user but a provider of samples
- several options: long time , juridical administrative, ethical: all are useless
- long waiting time for the approval of research and delivery of samples/data
- strict evaluation of the research, ethical rules of the Ethical Boards

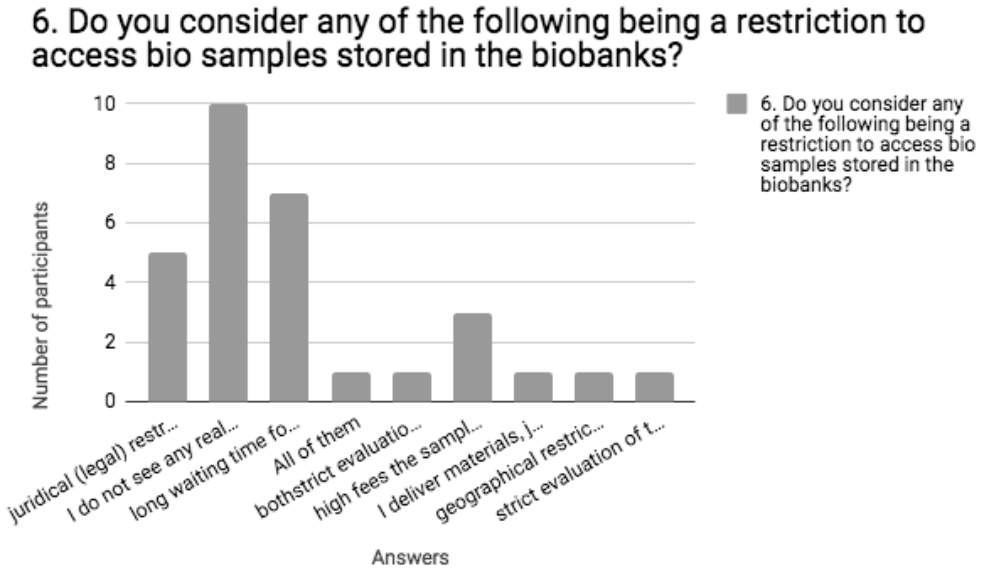
- I have not faced any problems
- N/A
- high fees for the samples/shipping
- juridical (legal) restrictions (including intellectual property rights: valid patents, database protection, other)

5. If you have faced any problems when accessing biological samples/data stored in biobanks, can you describe the situation shortly?

15 responses

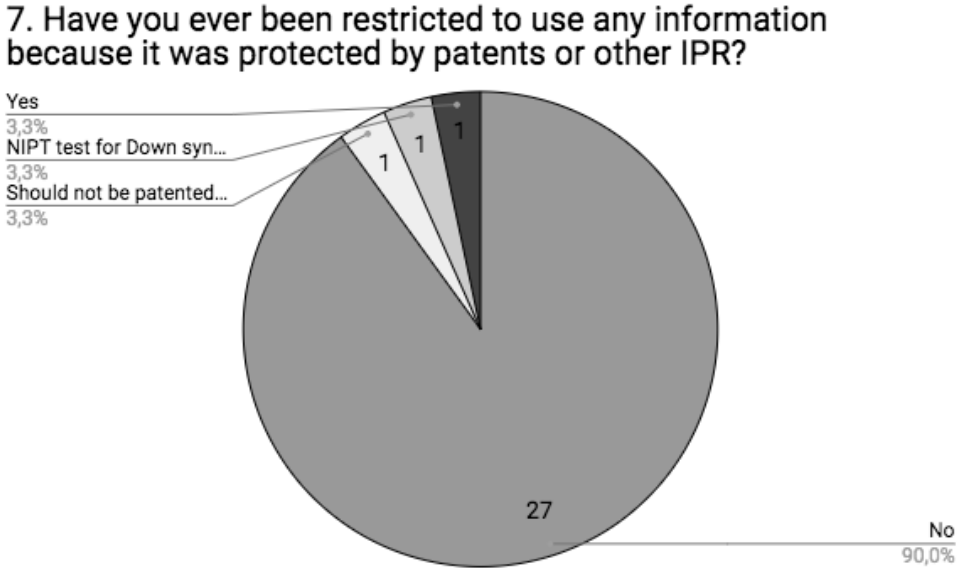
- not applicable (2)
- We didn't request samples so far, we're sending them.
- Under ethical or legal considerations, there is an administrative or juridic lobby which hampers clinical research and access to the material. This is very frustrating. When discussing with patients association, they all consider positively the need of research but there are too many Even informed and signed consent is unrealistic as the patient at the illness time is not considering the need for research as a priority and has to sign too many papers. In fact, a legal agreement should be generalized with information to the patients (without the need of signed consent) but then there should be a national website in European countries to declare the opposition and to disagree which would be much more efficient for the very rare subgroup of patients which refuse.
- Demandes refusées officiellement pour conflit d'intérêts ou notoirement retardée pour examen juridique concernant la propriété intellectuelle
- Lack of accurate clinical data
- We haven’t yet access to other biobank samples/data
- Actually, I did not face problems that were not included in the items of the MTA developed by our Legal Officers. Thus, at least for me, possible problems are already familiar within our Institute organization.
- As a biobanker we provide the samples and the data
- Within the Parelsnoer Institute (PSI) we have a strict protocol for issuances from our collections. This includes, for every delivery, permission of the scientific access committee and approval of all local ERB's of the eight participating university hospitals. This may be considered prohibitive for investigators approaching the PSI collections.

- The main problem is the relative high cost that are associated to asking for data or samples in several biobanks. In general, the evaluation of the research takes some time, but is less restrictive. When it comes to sending samples outside the EU, I am currently struggling, because our university lawyers require me to inform patients of privacy issues that cannot be guaranteed.
- a lot of bureaucracy
- see above
- Too high fees
- Samples are restricted to research which the patients were informed about



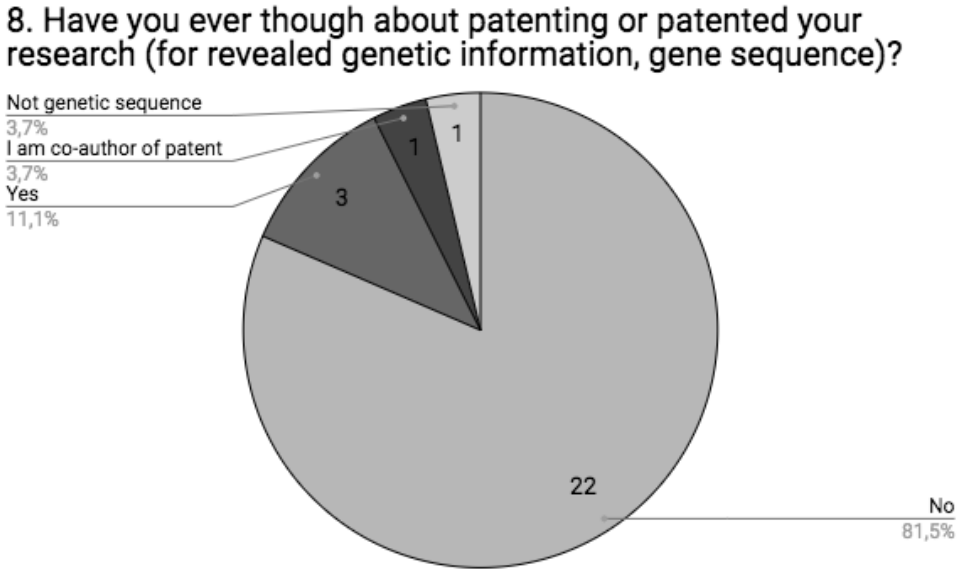
ANSWERS:

- juridical (legal) restrictions (including intellectual property rights: valid patents, database protection, other)
- I do not see any real restrictions to access biobank's samples
- long waiting time for the approval of research and delivery of samples/data
- high fees the samples/shipping
- geographical restrictions of the shipping of the samples (do not send to all countries)
- strict evaluation of the research, ethical rules of the Ethical Boards



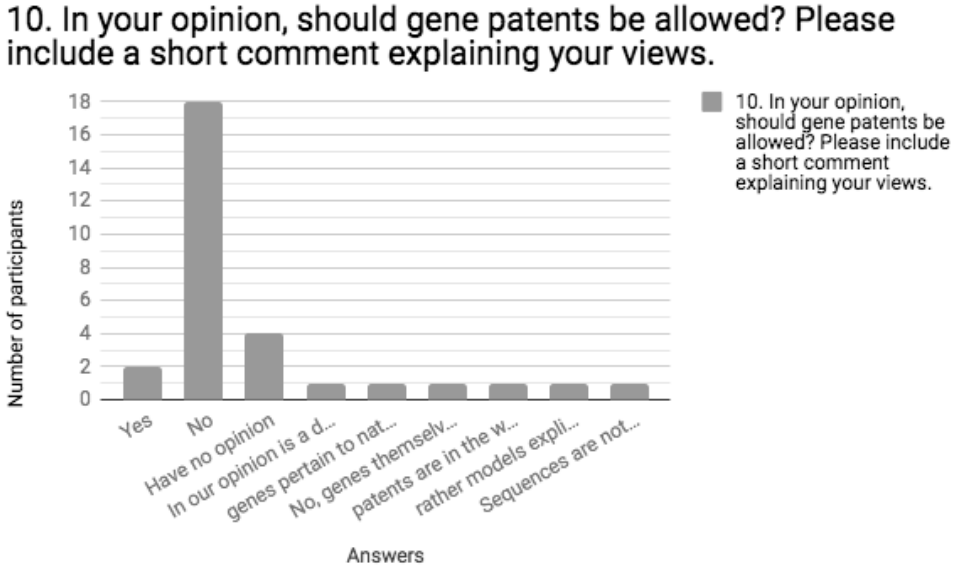
ANSWERS:

- Should not be patented as the genome should be public
- NIPT test for Down syndrome screening



ANSWERS:

- I am aware of authorship regulations in my institution and I know that I cannot claim any property or economic rights over my invention (35,5%)
- I am aware of authorship regulations in my institution and I know that I can claim certain property or economic rights over my invention (54,8%)
- I am not aware of any regulations of this kind and I do not know to whom such rights belong. I believe that rights over my discovery entirely belong to a researcher (to me) (3,2%)
- we are working mainly on diagnosis and we haven't yet encurred in intellectual property issues (3,2%)
- I am not the 'owner' (3,2%)



ANSWERS:

- In our opinion is a delicate topic, that must be evaluated more in details. Our biobank is based on human samples.
- genes pertain to nature not to single researchers or institutions
- No, genes themselves do not represent commercial value nowadays.
- patents are in the way of public health
- rather models explined some feature based on genes
- Sequences are not a designed product that could be patented

11. Have you heard about the use of the Open Source technologies or use of other open licenses in biotechnology? If yes, can you name open access databases or tools that you are using for your research?

26 responses: No (14 answers)

Yes (12 answers):

- Yes, but currently I don't use, except pubmed, Ensemble, geneCards.
- Open Access,
- dbSNP, 1000 Genome, EVS, gnomAD
- PSI collections are included in the BBMRI-NL and BBMRI-ERIC catalogue. To these an Open Source policy is applicable.
- Yes, among other DBgap
- Open Genetic databases like ClinVar Exac, others

- Yes. I deposit data, including genetic data, in several open databases including NatGEO and openfmri.
- GNOMAD
- various sequence tools and database platforms

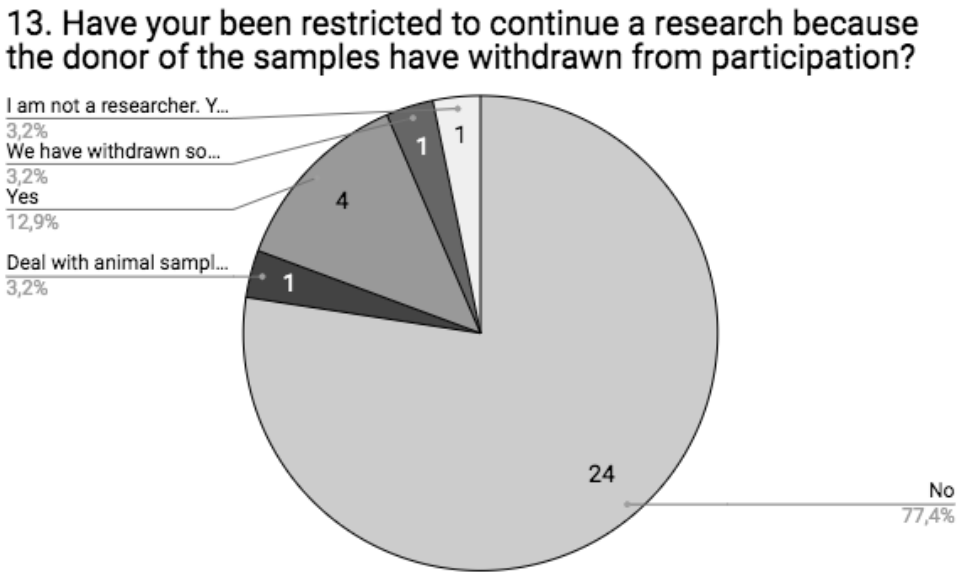
12. Do you think open access is important for researchers in biotechnology field? Do you believe it helps to reach better results when the information is available for free to anyone? Please include a short comment explaining your views.

28 responses: No (1 answer); Not sure (1 answer)

Yes (26 answers):

- yes - open access is important for researchers in biotechnology. With information being free it helps progress research faster, especially if the work has already been done by someone else.
- Yes, information should be accessible for the public because majority was funded by public money.
- Yes, I even think of it as an ethical issue: if research is funded publically, e.g. by tax money or charity money, the output should be available for free to everyone.
- Yes, but this should be sponsored with transparency rules
- en théorie oui mais du fait de la restriction des fonds publics pour la recherche, il ne faut pas supprimer la possibilité pour les chercheurs de breveter certains de leurs résultats. Comme toujours c'est un problème d'équilibre.
- Yes, I am in favor of open source policies in biotechnology
- Yes. Sharing and exchange of information are the basis of reaserch
- Yes, I am absolutely in favour of open access, for reaching RAPIDLY better results. Indeed, the quality of the open access data should be warranted!
- Yes, I do believe this is important.
- I think that we should try to be as open as possible but also need to be aware that some limitations are needed, for example to protect donors
- I agree with both sentences. The most people can obtain information the most effective their research will be.
- Open access is necessary for biobanks in the public domain. This means not restricted access for all bona fide investigators, provided they have a decent research proposal.

- Yes, important, not in the least to prevent repetitive collections and work. For example, population controls samples should be open access.
- I think that reasonable pay for generating knowledge is necessary but that open access speeds up development of better (public) health care
- In general, one would prefer that information is available as wide as possible.
- Very important for critical analysis, for new discovery and validation, and for meta-research
- Open access is important, but for human samples and data, consent and privacy may mean only managed access is possible
- Yes, need to be available but well protected so that they are only used for those with permission to do so. But this shouldn't cost much if anything.



ANSWERS:

We have withdrawn some samples of our biobank because of consent issues but this was a very small amount (only 1 or 2 cases)

I am not a researcher. Yes, we have encountered withdrawal of material but to my knowledge never with such consequences.

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