

Outstanding legal and ethical issues on biobanks

An overview on the regulations of member states of the EuroBioBank project



Ministerio de Sanidad y Consumo



<http://www.eurobiobank.org/>

**OUTSTANDING LEGAL
AND ETHICAL ISSUES ON BIOBANKS**

**AN OVERVIEW ON THE REGULATIONS
OF MEMBER STATES OF THE EUROBIOBANK
PROJECT**

This work has been funded by:

EUROBIOBANK (Network of DNA, Cell and Tissue Banks for Rare Diseases).
Funded by the European Union V Framework Research (QLRI-CT-2002-02769).

REPIER (Rare Diseases Epidemiological Research Network)
Network funded by the Instituto de Salud Carlos III. File N.º G03/123.



Edita: Instituto de Salud Carlos III
Ministerio de Sanidad y Consumo

NIPO: 354-05-003-7
Depósito Legal: M-46889-2005

Imprime: Rumagraf, S.A.
Avda. Pedro Díez, 25. 28019 Madrid

AUTHORS

Amelia Martín Uranga

PhD in Law, Lecturer in Law at the UNED (National University of Distance Education)

Scientific Adviser for the BBVA Foundation-Provincial Government of Biscay, Interuniversity Chair of Law and Human Genome, University of Deusto.

M.^a Concepción Martín-Arribas

Nurse Researcher, PhD in Epidemiology and Public Health.

Institute of Research in Rare Diseases.

Instituto de Salud Carlos III (ISCIII).

Madrid, Spain.

Jeanne-Hélène di Donato

PhD in biology.

Director of banks and collection Department of AFM-Généthon, Evry.

Biological Resources Centres consultant.

Manuel Posada de la Paz

PhD in Medicine, Head of the Toxic Oil Syndrome Unit.

Institute of Research in Rare Diseases.

Instituto de Salud Carlos III (ISCIII).

Madrid, Spain.

EUROBIOBANK PARTNERS

Corrado Angelini, University of Padova, Italy.

Fabrizia Bignani, EURORDIS, France.

Anne-Mary Bodin, EURORDIS, France.

Olivier Cohen, University Joseph Fourier, France.

Alexander. E. Felice, Molecular Genetics Laboratory, University of Malta.

Dorita Galea, Laboratory of Molecular Genetics, University of Malta.

Christophe Guitart-Arnaud, Teamlog, France.

Cécile Jaeger, Association Française contre les Myopathies (AFM), France.

Veronika Karcagi, National Center for Public Health (NCPH), Budapest, Hungary.

Hanns Lochmüller, Muscle Tissue Culture Collection (MTCC), Friedrich-Baur-Institute, Ludwig-Maximilians-University, Munich, Germany.

Marija Meznaric-Petrusa, University of Ljubljana, Medical Faculty, Slovenia.

Maurizio Moggio, Ospedale Maggiore Policlinico (IRCCS), University of Milano, Italy.

Marina Mora, Istituto Nazionale Neurologico Carlo Besta (INNCB), Italy.

Luisa Politano, Second University of Naples (SUN), Italy.

Safa Saker, Généthon, France.

Françoise Salama, EURORDIS, France.

Monica Sciacco, Ospedale Maggiore Policlinico, University of Milan, Italy .

Christine Verellen-Dumoulin, Université Catholique de Louvain, Belgium.

Sandrine Villaeys, Teamlog, France.

TABLE OF CONTENTS

PREFACE	5
FOREWORD	7
I. INTRODUCTION	9
1.1. Biological samples: necessary for biomedical research	9
1.2. Relevant legal framework on the subject-matter (bank and collection)	11
2. PRELIMINARY CONSIDERATIONS ON THE SAMPLE AND THE SOURCE SUBJECT OF THE SAMPLE	17
2.1. Legal Nature	17
2.1.1. Personal rights	18
2.1.2. Ownership rights	18
2.1.3. Position taking	19
2.2. Concepts and general principles	20
2.2.1. Sample	20
2.2.2. Tissue	21
2.2.3. Tissue establishment	22
2.2.4. Biobank	22
2.2.4.1. Definition	22
2.2.4.2. Data preservation period	23
2.2.4.3. Security measures	23
2.2.5. Classification of the data subject to legal protection	24
2.2.5.1. Personal and sensitive data	24
2.2.5.2. Anonymous data	25

2.2.5.3.	Unlinked data	26
2.2.5.4.	Health data	27
2.2.6.	The right not to know	28
2.2.7.	Information to provide to third parties	30
2.2.8.	Unexpected findings	31
2.3.	Source subject	32
2.3.1.	Sample subject and data subject	32
2.3.2.	Rights of the person concerned: consent and information	33
2.3.2.1.	The importance of the consent	33
2.3.2.2.	Consent to data collection	34
2.3.2.3.	Consent to take part on a research	35
2.3.2.4.	Contents of the data to provide to the subject ..	39
2.3.3.	Particular cases	43
2.3.3.1.	Minors and incapacitates	43
2.3.3.2.	Foetuses and embryos tissues	46
2.3.3.3.	Tissue samples of deceased persons	47
3.	LEGAL DIFFERENCES BETWEEN RESEARCH AND DIAGNOSIS SAMPLES	49
3.1.	Introduction	49
3.2.	Donation or transfer of the samples for research by the subject ..	50
3.3.	Donation or transfer of sample for research not attributable to the subject	51
3.4.	Donation or transfer of sample for diagnosis attributable to the subject	51
3.5.	Donation or transfer of sample for diagnosis not attributable to the subject	52
4.	THE SAMPLE AND ITS FUTURE USE	53
4.1.	The relationship with the patient	53
4.1.1.	Legal framework	53
4.1.2.	Can a product derived from a biological sample be patented?	56

TABLE OF CONTENTS

4.1.3.	The question of consent as a requirement for patentability	59
4.1.4.	Ownership of the product patent derived from the sample	61
4.1.5.	Commercialisation of samples	62
4.1.6.	A real case: comments on the case Moore v. Regents of the University of California	65
5.	CONCLUSIONS AND RECOMMENDATIONS	69
6.	APPENDIX	75
6.1.	Regulation	75
6.1.1.	International regulation	75
6.1.2.	European regulation	75
6.1.2.1.	European regulation	75
6.1.2.2.	Regulation of the European Union	76
6.1.2.3.	Regulation of the Member States	76
	— Estonia	76
	— France	76
	— Germany	77
	— Hungary	77
	— Italy	77
	— Malta	78
	— Slovenia	78
	— Spain	78
	— Sweden	79
	— United Kingdom	79
6.1.2.4.	Regulation of the Non Member States	79
	— Island	79
	— Norway	79
6.2.	Case-law	79
6.3.	Other documentation: opinions and guidelines	80
6.4.	Bibliography	81

PREFACE

The publication of this book is both the result of a significant task developed within the framework of collaboration in a European project called EUROBIOBANK and the activity of one of the Spanish networks on Rare Diseases called Epidemiological Research Network on Rare Diseases (REpIER), coordinated by the Institute of Health Carlos III, which has participated in both actions but, above all, on the management and coordination of works which have resulted in this review on legal and ethical aspects of Rare Diseases biobanks throughout Europe.

The standardization work of the activities related to management and maintenance of the biobanks, has exclusively been focused on Rare Diseases and has clearly made of this work a pioneer in its kind. Consequently, this review is called to become a focal point in Europe during the next years.

Within this context, the book we are now presenting, provides updated information on all the legal and ethical problems that must be taken into account for the storage, care and handling of biological samples from patients affected with Rare Diseases. The review of the State of the Art of all the subjects dealt with, as well as, the wide geographical spectrum on which this review is based, (8 member states in the European project) confers to this work both an indubitable interest and a high-level of application.

Research on Rare Diseases is currently a priority within the framework of the Health and Consumer Affairs General Directorates in the European Community, as well as in most Member States and associates. This is why actions such as those carried out by participants in the EUROBIOBANK project, under the superb leadership of those in charge of the Rare Diseases European Organization

(EURORDIS), are an example of the appropriateness in which funds invested by research funding agencies have been used, thus leading to clearing the way in anticipation of a better future for Rare Diseases.

In Spain, the Institute of Health Carlos III, is promoting action policies that may help to launch research on Rare Diseases, by funding a Rare Diseases Research Programme including in its tasks issues such as: research projects, training programmes, implementation of research networks and group associations established as Biomedicine Network Research Centres (CIBER). In addition, and through the Spanish Genome Foundation, which funds the DNA National Bank, it is our intention to centralize all the samples collected from the different Rare Diseases banks and from other existing Cooperative Research Networks , in order to improve biomedical research. Finally, the Spanish Government is preparing a new law on Biomedicine Research that, for the first time, will regulate the creation and functioning of biobanks in Spain.

I am sure, that the readers of this book, will find in it a place to handle more safely and with a wider legal and ethical covering the samples from patients with the only purpose of making research on these diseases more profitable respecting, at the same time, the citizens rights.

DR. D. FRANCISCO GRACIA NAVARRO
Director
Instituto de Salud Carlos III

FOREWORD

EuroBioBank (www.eurobiobank.org) is a European network of biological banks established in 2001 whose main objective is to boost research on rare diseases by facilitating access to quality human biological resources and their associated data (DNA, cells and tissues) from patients with rare diseases. From 2003-2005, the EBB network was further developed thanks to the funds received from the European Commission, under the European Union's Fifth Framework Programme «*Quality of Life and Management of Living Resources*». The consortium started with 16 partners from 8 European countries with a patients' organisation, Eurordis (European Organisation for Rare Diseases) coordinating the project. A total of approximately 155 000 documented human biological samples are available via the 12 banks of the consortium. In 2004, approximately 6 800 samples have been distributed by Eurobiobank partners throughout Europe for research purposes.

Already at the initiation of Eurobiobank it became evident that legal and ethical issues with respect to the collection, distribution and use of human biological materials require particular attention. These issues touch upon rights of patients, families, care-givers, scientists and the society. Legislation in Europe and the member states involved is not harmonized, in parts incomplete or controversial. Therefore, it is of great value to identify the current status and inherent problems of legal and ethical issues related to rare, human biomaterials in Europe, and Eurobiobank is very grateful to the authors of this publication to have taken this on. Indeed, this should be regarded as a first, important step toward harmonization of legal and ethical matters and requires further action.

In summary, I wish to emphasize the penultimate objective of biobanking in

rare disorders: to aid research towards a better understanding and improved therapy of frequently disabling or life-threatening disorders with an anticipated benefit for our patients.

HANNS LOCHMÜLLER, MD
Professor of Neurology and Molecular Neurogenetics
Scientific Coordinator of Eurobiobank

1. INTRODUCTION

1.1. BIOLOGICAL SAMPLES: NECESSARY FOR BIOMEDICAL RESEARCH

Medical research has many expectations on the discoveries that may arise from the knowledge of our molecular biological basis. In this context, biobanks will play an important role not only in the identification of the causes of diseases in an individual or a group of individuals; but also in the development of diagnosis, and in the application of therapeutic and preventive methods. Biobanks can become useful tools for researching common and low prevalence or rare diseases. In addition, biobanks can help us to study the basis for the development of «medicine-à-la-carte» —farmacogenetic and farmacogenomic¹—. Now, the creation of biobanks for specific biological materials related to diseases which are going to be researched has become a common practice². But at the same time, biobanks are considered to be a source of potential worry from the point of view of data protection; there are questions such as future treatment and use, period of preservation and security measures, in which nobody has think of while collecting the biological data. In fact, the subject-matter of study has interesting perspectives,

¹ Same opinion, C.M. ROMEO CASABONA, «La utilización de muestras biológicas con fines de investigación biomédica» (Use of biological samples with biomedical research purposes), Instituto de Investigaciones Jurídicas (Legal Research Institute), Universidad Autónoma de México (Autonomous University of Mexico), 2004, in press.

² A National DNA Bank has been created in Spain in 2004 to promote biomedical research, there is hope in making progress in the discovery of new treatments, more specific and with less side effects. The aim is that the projects of the National DNA Bank are integrated in international initiatives, such as the public population project on genomics, where several nations take part e.g. the United Kingdom (BioBank UK), Canada, Island (Iceland: Health Sector Database) or Estonia (Estonian Genome Project). *Diario Médico* (Spanish Health Journal) of 16 March 2004.

and at the same time it exceeds the legislation in force, highlighting the legal loophole which we meet when dealing with this issue.

The collection and storage of organs, tissues, cells and products (DNA, proteins, etc.) for therapy, diagnosis and research³, is not a new practice, it has been carried out for many years in laboratories and hospitals. Useful biological samples of human beings come from different sources, but a significant amount of them come from ordinary health assistance acts: material from surgery and other activities, such as wastes from samples obtained for diagnosis tests: blood and other fluids collection, cytology, biopsies; birth products (placenta and umbilical cord); abortion and decesses; donation of gametes or embryos for assisted reproduction techniques. Additionally, large-scale population-related biobanks are being set up in some countries and will allow approaches to a wide range of health-related issues, such as in Estonia. We have to bear in mind that the materials that we have mentioned can be donated for biological research, or that they have been donated with a specific consent to their use in biological research, and it seems that both practices will increase in the future.

Now most of the countries in Europe have been subject legal regulations with the purpose of granting the protection of human health, and that is the reason why we pay specific attention to donation and therapy activities. In fact, the biological material collected with specific purposes will be settled by a specific law (regulation on organs and tissues transplants, on assisted reproduction techniques, on research with embryos and human foetuses)⁴.

³ The number of samples stored is estimated to be over 282 millions in the United States of America in 1999 and that number increases 20 million each year, National Bioethics Advisory Commission, *Research involving human biological materials: ethical issues and policy guidance*, vol. I (Report and Recommendations). See a detailed description on the origin of the samples stored in the USA in National Bioethics Advisory Commission, *Research involving human biological materials: ethical issues and policy guidance*, vol. I, p. 14, most of them are samples stored in institutes of anatomic pathologies, but the most spectacular increase in the number of samples is to be found in the field of new born screening.

See J. GALBE SÁNCHEZ-VENTURA «Cribado neonatal de metabolopatías congénitas» (New born screening of congenital metabolism deformities), pp. 35-43. The author analyses the scope of the issue, the diagnosis method and other questions such as the new born screening of congenital hyperthyroidism, phenylketonuria, mucoviscidosis, through the blood samples of a high number of new born children.

Three million of samples are stored each year in laboratories of anatomic pathologies of the United Kingdom, Peter FURNESS, «Consent to using human tissue», p. 759.

⁴ We have to highlight the following regulations from different national systems of law:

— France: Law relating to the protection of the people who lend themselves to biomedical research. Law n° 88-1138 (20 december 1988) modified by the law n° 94-630. And Bioethical law. Law n° 94-653 and 94-654 (29 July 1994) modified by the law n° 2004-800 (6 August 2004).

1.2. RELEVANT LEGAL FRAMEWORK ON THE SUBJECT-MATTER (BANK AND COLLECTION)

The legal framework on the subject-matter is quite poor, as it has been dealt with on monographic works and in general terms. However, there are several issues related to the main subject-matter of our study, and we can find laws on those other issues. In this section we will make reference to the legislation on biobanks, leaving the rest of the legislation to be considered in the corresponding section.

On an international level we have to mention the Recommendation No (92) 1 of the Council of Europe, *on the use of DNA analysis on the framework of criminal justice system*⁵, and R (92) 3, *on Genetic Testing and Screening for Health Care Purposes*⁶, both consider the biological samples and bodily tissues as *data carriers* (principle 8), and that they have to be treated the same way as medical data processed automatically. In other words, biological samples are not personal data, but they bear this kind of information, and they can be «collected» through the appropriated analysis. However, scientific researchers have opted to include biological samples in the legal scope of the rules on the protection of personal data⁷. And there are legal principles in Europe allowing so, e.g. the collection of biological material is included in the right of protection of clinical trial data⁸. The United States of America has followed this criterion in some

— Spain: the banks of tissues collected for donation and research regulated in the Royal Decree 411/1996, of 1 March; the blood banks for hemodonation, in the Royal Decree 1854/1993 of 22 October; the banks of embryos and gametes, in the Act 35/88 on assisted reproduction techniques; the Act 42/88 of 28 December, on donation and use of human embryos and fetuses or of their cells, tissues or organs; and finally the Royal Decree 412/1996.

— Slovenia: The removal and transplantation of human body parts for the purposes of medical treatment act de 27 January 2000. *Zakon o odvzemu in presaditvi delov cloveškega telesa zaradi zdravljenja* (ZOPDCT).

⁵ Adopted by the Committee of Ministers on 10 February 1992 at the 470th Meeting of Ministers' Deputies.

⁶ Adopted by the Committee of Ministers on 10 February 1992 at the 470th Meeting of Ministers' Deputies.

⁷ Australia Law Reform Commission, *Essentially yours: the protection of human genetic information in Australia*, p. 477.

International Bioethics committee: collection, treatment, storage and use of genetic data (session of september 2001).

⁸ Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medical products for human use (OJEC, No. L121 of 1/5/2001, pp. 34-44).

initiatives⁹, such as in the *Genetic Privacy Act*, where it is understood that the *identifiable* biological samples have to be in the scope of the aforementioned Act¹⁰.

The International Declaration on human genetic data elaborated by the UNESCO, and adopted the 16 October 2003¹¹, is the first international legal instrument that settles a number of rules about biological samples and on the personal data which may be collected from those samples. This legal instrument establishes that the genetic data may contain information of unknown relevance in the moment of the collection of the biological samples and, that the genetic data may be culturally important for individuals or groups of people. It also states the requirements which have to be met to use biological samples preserved when genetic data are to be collected: previous, free, informed and express consent from the concerned person is required. However, the national law can establish exceptions to this requirement when the data is important for medical and scientific research, or for the public health. We have to take into account that this document has a great importance because it sets up some principles that will be the basis for future national regulations on the matter.

On an international level we have to mention the Proposal for an instrument on the use of archived human biological materials in biomedical research, of the Steering Committee on Bioethics of the Council of Europe of 2002¹². This document deals with some very important aspects such as the procedure of information and consent, the use of biological material *post mortem*, the participation on the financial gains, etc. It is expected to be adopted in the next months.

In the European Union, there is a great interest on the subject of biobanks¹³ and for the last years there are several research projects and working meetings which have been taking place. Even though, there is a legal loophole on the subject-matter, there are some regulations on some aspects related to biobanks.

⁹ See the regulations of the United States <http://www.ncsl.org/programs/health/Genetics/prt.htm>

¹⁰ George ANNAS/Leonard H. GLANTZ/Patricia A. ROCHE, *The Genetic Privacy Act and commentary*, pp. 53 and 54.

¹¹ Adopted unanimously and by acclamation on 16 October 2003 by the 32nd session of the General Conference of UNESCO.

¹² Proposal for an instrument on the use of archived human biological materials in biomedical research. Steering Committee on Bioethics, CDBI/INF (2002)5. Strasbourg, 17 October 2002.

¹³ Biobanks is one of the main areas to promote from the EU—together with other matters such as stem cells research, xenotransplants, genetic trials and essays on animals—, as it is laid down in the Commission Communication on Life Sciences and Biotechnology's Strategy for Europe. Art. 16 Com (202) 27 final of 23 January 2002.

The Directive 2001/20/EC, on clinical trials, establishes on article 8 that the Commission will settle detailed guidance on the application format and documentation to be submitted in an application, in particular for the protection of personal data. This guidance was published in April 2003 and establishes that the security measures of the right to personal data protection from subjects under clinical trial will respect the provisions of the directive 95/46/EC which includes the protection of the collected biological material.

The 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 data¹⁴, is remarkable relating to personal data. The importance of this Directive relating the use of biological samples relies on the possibility of rendering them and the personal data of the patient anonymous which may be a requirement to research, as we will further explain in this paper¹⁵. In any case, and as we will further explain, the regulation on data protection—which exists in most of the seven States taking part in the EuroBiobank project¹⁶—is not applicable in all its scope to the biological sample.

¹⁴ OJEC, No. L 281 of 23 November 1995, pp. 31 and ff.

¹⁵ See section 2.2.5.2. on anonymous data in this report.

¹⁶ The regulations adopted on the matter in these countries follow the aims and the spirit of the Directive 95/46/EC. The regulations on the matter in the Member States of the Eurobiobank Project are the following:

Germany: Federal Data Protection Act of 1 January 2003. Bundesdatenschutzgesetz (BDSG).

Slovenia: Decree on the promulgation of the Personal Data Protection Act (ZVOP-1). Adopted by National Assembly of the Republic of Slovenia in its session of 15 July 2004.

Spain: Organic Law 15/1999 of 13 December on personal data protection. BOE (Spanish Official Journal) No. 298, 14 December, 1999.

France: Law No. 78-17 (6 January 1978) relative à l'informatique, aux fichiers et aux libertés; Law No. 94-548 (1 July 1994) relative aux traitements des données nominatives ayant pour fin la recherche dans le domaine de la santé; Law No. 2004-801 (6 août 2004) relative à la protection des personnes physiques à l'égard des traitements des données à caractère personnel.

Hungary: Act No. XLVIII of 2003 (modifies the Act LXIII of 1992) on personal data protection. 2003. évi XLVIII. Törvény a személyes adatok védelméről és a közérdekű adatok nyilvánosságáról szóló 1992. évi LXIII. törvény módosításáról.

Italy: Legge del 06/10/1998 n. 344, differimento del termine per l'esercizio della delega prevista dalla legge 31 dicembre 1996, n. 676, in materia di trattamento dei dati personali

Malta: Data Protection Act as Chapter 440 of the Laws of Malta. In force since 15 July 2003.

According to the criteria of Copenhagen, all the countries who joined the EU in May 2004 committed themselves to transpose the Directive 95/46/EC before the accession. Currently all these countries have adopted legislation on the matter, including most of the key elements of the Directive. See the I Report on the Application of the Directive on data protection, (COM/2003/0265 final).

But this biological sample carries information that has to be protected as a potential source of genetic personal data, what is more, the *whole* genetic personal data. The loophole of control of the source subject¹⁷ (the person from whom the sample is collected), is a serious danger for his right of personal data protection.

The last regulation from the EU on the subject has been recently adopted, it is 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 cells¹⁸. This Directive lays down the standards of quality and safety for human tissues and cells intended for human applications, in order to ensure a high level of protection of human health (article 1 and explanatory statements). This Directive was adopted because the graft of cells and human tissues is a branch of healthcare which is experimenting an important development and gives key opportunities for the treatment of diseases which have been incurable until now. To this end the quality and safety of these substances have to be guaranteed to avoid the transmission of diseases.

In the field of comparative Law, it is important to highlight the Biobanks Act of Sweden¹⁹ issued 23 May 2002, because it gives a legal definition of biobank, and at the same time it lays down the main features of this body, such as: the foundation and terms of foundation of biobanks, information and consent, use and transfer of the samples, etc.

Island has a specific Act on biobanks for population with healthcare purposes from 1998²⁰, followed by Estonia²¹ and Slovenia²² (which is one of the States Member of the EuroBiobank project). On the other hand, the United Kingdom has created a health data bank with a broad sample of the population²³ —which may increase over the years— and since the 15 November 2004 the Human Tissue Act²⁴

¹⁷ It is preferably to use «source subject» instead of «donor», because strictly speaking the source does not always become a donor.

¹⁸ OJEC, No. L 102 of 07/04/2004, pp. 48-58.

¹⁹ Biobanks [Health Care] Act (2002:297) Lag (2002:297) om biobanker i hälso- och sjukvården m.m.

²⁰ Act on a Health Sector Database of 1998.

²¹ Human Genes Research Act of 2000.

²² Healthcare Databases Act of 11 July 2000. Zakon o zbirkah podatkov s področja zdravstvenega varstva (ZZPPZ).

²³ <http://www.ukbiobank.ac.uk>

²⁴ <http://www.hms.gov.uk/acts/acts2004/20040030.htm>

is in force, with a whole chapter on consent, emphasising the relevance of the concept.

In the Spanish system of Law, there is not a specific regulation applicable to the collection, access and use of biological samples for scientific research stored at health care centres, universities or industrial centres strictly speaking. There is a regulation on human tissue banks, the Royal Decree 411/1996 (*Real Decreto* 411/1996), for those cases where the tissues are going to be grafted to patients whose treatment has been medically recommended. The aforementioned legal text deals with aspects related to granting the quality of the foresaid materials with the aim of protecting the health of the recipient.

The provisions issued on the matter in the reports by Ethical Committees are important because of the guidelines that they offer, even though they do not have legal value. For example, the Reports from the European Group on Ethics of human tissues²⁵ and on umbilical cord banking, which were recently issued²⁶. The Opinion on Biobanks for the research from the Council on National Ethics of Germany²⁷ that carries out a thorough study on the question in its country and ends with a joint Declaration on the subject issued by the fore mentioned authority and the National Advisory Committee for Life and Health Sciences of France, concluding in the need of regulating the matter. And finally the guidelines from the Nuffield Council on Bioethics²⁸ and the Medical Research Council Ethics Series, on the use of human tissues and biological samples for research²⁹, and by other authorities from the Netherlands³⁰ are also interesting documents.

²⁵ Opinion about «Ethical aspects of human tissue banking» of the European Group on Ethics in Science and New Technologies to the European Commission, No. 11, 21 July 1998.

²⁶ Opinion about «Ethical aspects of umbilical cord blood banking» of the European Group on Ethics in Science and New Technologies to the European Commission, No. 19, 16 March 2004.

²⁷ «Biobanks for research», German National Ethics Council, Berlin, 2004.

²⁸ Nuffield Council on Bioethics, *Human tissue. Ethical and legal issues*, London, 1995.

²⁹ Medical Research Council Ethics Series, «Human tissue and biological samples for use in research. Operational and ethical guidelines», London, 2001.

³⁰ Dutch Federation of Medical Scientific Societies, «Code for proper secondary use of human tissue in the Netherlands», Rotterdam, 2003.

2. PRELIMINARY CONSIDERATIONS ON THE SAMPLE AND THE SOURCE SUBJECT OF THE SAMPLE

2.1. LEGAL NATURE

The DNA banks emerge leads us to think about the question of «commercialisation of the sample» (with which we will deal further in this report), but before we are going to try to determine its legal nature (personal or ownership), and then we will try to answer to the question of commercialisation. It is important to solve the question on whether the sample arises personal or ownership right, as it determines how researchers relate to donors. It is advisable to consider this question as it determines any claim by any person on the commercial products resulting from the sample. The current trend towards a more informed and detailed consent undermines the debate on «personal right against ownership rights» relating to human material banks, as the consent can derive from the application of any of both approaches³¹.

The legal nature of the biological material is different to the one of the data that it carries, and if they are collected, the data should be used respecting the principles of ownership of personal genetic data. Nevertheless, we will have to consider the double nature of the samples on the configuration of the protection system, as the biological material is a part of the human body that has been separated from it and it has a different protection to the one granted to the potentially inferred data³².

³¹ B.M. KNOPPERS/M. HIRTLE, «Banking of human materials, intellectual property rights and ownership issues: emerging trends in the literature international policy positions (I)», *Law and the Human Genome Review*, No. 5, 1996, p. 96.

³² P. NICOLÁS JIMÉNEZ, *La protección jurídica de los datos genéticos de carácter personal* (Legal protection of genetic data of personal nature), Ed. Comares, 2005, in the press.

The terms «personal rights» and «ownership rights» show two different philosophical approaches to the relation between a person and the elements or parts of his body once they have been collected.

2.1.1. Personal rights

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 a good which can be subject to private property rights.

According to this principle of personal rights, the right to personal integrity includes respect to anatomic pieces once removed from the human body and *while the identification of the source is possible*. The informed consent is the instrument used to grant the respect and the protection of the integrity of the person and his bodily material. The control of the person over his anatomic pieces is granted demanding the informed consent from the owner of the material and offering legal resources to face any damages derived from the breach of any of the fore mentioned rules. By doing so, the right to self-determination of the person covers the grant of the right to dignity of the human body and of the pieces removed from it. This right involves the right to control the destiny of the removed tissues and cells, which is completely different and independent from the ownership rights³³.

In France the regulations on bioethics adopted on July 1994³⁴ followed the basis of the National Advisory Committee for Life and Health Sciences³⁵, establishing the non-ownership nature of the human genome or of any part of the person. This regulation was the one which adopted an approach in favour of the personal rights most clearly.

2.1.2. Ownership rights

It is held that a framework of ownership rights will be the perfect way to protect the rights of the patients and the subjects under research, given the fact that

³³ B.M. KNOPPERS/M. HIRTLE, «Banking of human materials, intellectual property rights and ownership issues: emerging trends in the literature international policy positions (I)», *ob. cit.*, pp. 98-99.

³⁴ Act No 94-653, 29 July 1994, on the respect of the human body and the Act 94-654, 29 July 1994, on donation and use of elements and products of the human body, on assisted reproduction techniques and on prenatal diagnosis.

³⁵ Avis sur l'application des tests génétiques aux études individuelles, études familiales e études de population. Statement of 24 June 1991, «The genome of a person, as it is referred to a «being» instead of a «having», cannot be commercialised, neither the rest of the physical elements of his body».

the ownership rights offer mechanisms of control that allow individuals to control what happens with their anatomic pieces³⁶. In this way, property rights give a valid answer to grant the principles of equity and justice, and prevent unfair enrichment. In any case, we have to state that assuming that the elements of the human body are property goods does not mean that they are completely transferable, as it is perfectly plausible to impose restrictions to their transfer³⁷.

2.1.3. Position taking

It is convenient to clarify this matter in order to solve the questions which may arise in the future, such as what happens once the tissue has been collected from the human body, who is the owner of the rights if there are any, and who is the owner of the patent rights: the source subject, the researcher, the authority or company, or all of them.

We can maintain that the sample as a biological substance separated from the body, is neither a personal element, nor is it the subject of fundamental rights, because most of the regulations that we are studying allow us to dispose of human wastes and deceased body samples. In this sense we assume that a biological sample is a thing³⁸, subject to private property and that the owner is the source subject. This approach is also held in the *Genetic Privacy Act*³⁹. In contrast, the National Advisory Committee for Life and Health Sciences of France holds that new scientific interest on the parts separated from the body may not lead to determine a right to dispose of them because of the risk of arising commercial

³⁶ To have a perspective on the Common Law systems of Law in favour of ownership rights, see R. HARDIMAN, «Toward the right to commerciality: Recognizing property rights in the commercial value of human tissue», *UCLA Law Review*, Vol. 34, 1986, p. 207.

³⁷ Same opinion, B.M. KNOPPERS/M. HIRTLE, «Banking of human materials, intellectual property rights and ownership issues: emerging trends in the literature international policy positions (I)», *ob. cit.*, p. 101.

³⁸ Same opinion, V. ANGOITIA, *Extracción y trasplante de órganos y tejidos humanos. Problemática jurídica* (Removal and transplant of human tissues and organs. Legal controversies), Ed. Marcial Pons, Madrid, 1996, p. 158; M. CÁRCABA FERNÁNDEZ, *Los problemas jurídicos planteados por las nuevas técnicas de reproducción humana* (Legal problems arising from the new techniques of human reproduction), Ed. Bosch, Barcelona, 1995, p. 71; P. NICOLÁS JIMÉNEZ, «Los derechos del paciente sobre su muestra biológica: distintas opiniones jurisprudenciales» (The patient rights on his biological sample: different case-law opinions), *Law and the Human Genome Review*, No. 19, 2003, p. 212.

³⁹ Section 104 (a) «An individually identifiable DNA sample is the property of the sample source». Final Report of a project by G. ANNAS et al, Health Law Department, Boston University School of Public Health, 1995, section 104.

interests⁴⁰. The hypothesis held in the present document is the opposite to this last criterion, because we establish that the sample is a thing, which is in accordance with the right of each person to dispose the donation parts of his body, and the law recognises that the subject can decide on the destiny of his blood, organs, tissues and gametes, and their removal is not considered to be an abandonment but a «donation». According to this line of thinking, it is held that the British system of Law has opted for recognising a right of ownership on the parts separated from the body⁴¹. And as we will see further on this paper, the recognition of this right of property does not involve the free commercialisation of the sample; in fact, there can be settled limitations depending on the human origin and the difference between some parts of the body and other. These limitations are clearly laid down on article 5 of the Italian Civil Code according to which the acts of possession of the body are legal as long as they are not contrary to the Law, the public policy or morality.

2.2. CONCEPTS AND GENERAL PRINCIPLES

We should clarify from the beginning that the Directive 2004/23/EC will not apply to tissues and cells used as an autologous graft⁴² within the same surgical procedure; nor to the blood or blood products, because they have their own regulation⁴³; nor to the organs or part of organs, if their function is to be used in the human body with the same purpose as the entire organ (Article 2). In other words, the Directive does not cover the research using human tissues and cells when they are used with purposes other than their application in the human body, such as when used for in vitro research or in animal varieties.

2.2.1. Sample

As it is established on the aforementioned International Declaration on Human Genetic Data adopted by the UNESCO, the biological sample is «any

⁴⁰ Consultatif Nacional d'Éthique pour les Sciences de la Vie et de la Santé, *Problèmes éthiques posés par les collections de matériel biologique et les données d'information associées: biobanques, bibliothèques*, Avis, núm. 77 of 20 March 2003, p. 28.

⁴¹ P. MARTIN/J. KAYE, *The use of biological sample collections and personal medical information in human genetics research*, The Wellcome Trust, London, 1999, p. 38.

⁴² An autologous graft are tissues removed and transplanted back to the same individual (Recital 8 of the Directive 2004/23/EC).

⁴³ They are currently regulated by the Directive 2001/83/EC, the Directive 2000/70/EC, the Recommendation 98/463/EC and the Directive 2002/98/EC.

sample of biological material (for example blood, skin and bone cells or blood plasma) in which nucleic acids are present and which contains the characteristic genetic make-up of an individual (article 2. iv). The Declaration applies to samples before and after analyzing⁴⁴. The sample has a double nature, on one hand it is a biological sample, and on the other it is a source of information.

There is no regulation establishing the rights over biological samples. But, as we will see further on, the possibility of donating substances and tissues is recognised in most regulations of the Member States of the project.

The biological sample is not subject to the regulation of the law on data protection, nor can it be considered a file to this extent. However, data collected from analyzing the biological sample will be in the scope of this regulation. In this sense, there is case law comparing the right to access to the clinical record with the right to access to data of the sample⁴⁵. The principles for personal data protection shall govern both the processing and the transfer of samples⁴⁶.

2.2.2. Tissue

Tissue means all constituent parts of the human body formed by cells⁴⁷. In addition, cell means individual human cells or a collection of human cells when not bound by any form of connective tissue⁴⁸.

⁴⁴ P. NICOLÁS JIMÉNEZ, *La protección jurídica de los datos genéticos de carácter personal* (Legal protection of genetic data of personal nature), *ob. cit.*

⁴⁵ Judicial Decision of the High Court of Justice of Cantabria, Spain, of 16 May 2001 and of the Provincial Court of Vizcaya, Spain, of 21 June 2000. A commentary on them by P. NICOLÁS JIMÉNEZ, «Los derechos del paciente sobre su muestra biológica: distintas opiniones jurisprudenciales» (The rights of the patient on his biological sample: different case-law opinions), *ob. cit.*, pp. 207 and ff.

⁴⁶ Established in Germany in the Gesetz zur Änderung des Bundesdatenschutzgesetzes und anderer Gesetze Vom 18. Mai 2001 BGBl. 2001 Teil I Nr. 23, 22/05/2001, Seite 904. In Estonia in the Decree on the promulgation of the Personal Data Protection Act (ZVOP-1). Adopted by the National Assembly of the Republic of Slovenia in its session of 15 July 2004. In Spain in the Organic Law 15/1999, of 13 December, on personal data protection, BOE n° 298, 14-Dic-1999). Hungary: Act No. XLVIII of 2003 (modifying the LXIII of 1992) on personal data protection. 2003. évi XLVIII. Törvény a személyes adatok védelméről és a közérdekű adatok nyilvánosságáról szóló 1992. évi LXIII. törvény módosításáról. In Italy the Legge del 06/10/1998 n. 344, differimento del termine per l'esercizio della delega prevista dalla legge 31 dicembre 1996, n. 676, in materia di trattamento dei dati personali. Also, in Malta Data Protection Act (Chapter 440) of 15 July 2003. And in France: Law No. 2004-801(6 août 2004) relative à la protection des personnes physiques à l'égard des traitements des données à caractère personnel

⁴⁷ Article 3.1 b) of Directive 2004/23/EC.

⁴⁸ Article 3.1 a) of Directive 2004/23/EC.

2.2.3. Tissue establishment

Tissue establishment means 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 cells⁴⁹.

2.2.4. Biobank

2.2.4.1. Definition

A legal definition on this concept is to be found in the Swedish Biobanks Act, defining this concept as «biological material from one or several human beings collected and stored indefinitely for a specified time and whose origin can be traced to the human or humans from whom it originates» (section 2). This act uses contradictory terms such as «stored indefinitely for a specified period of time» and it does not specify if it is a private or a public body who stores the material.

Additionally, the definition given by the German National Ethics Council on its opinion on Biobanks does not make reference to the period of time and defines biobanks in general terms as «collections of specimens of human bodily substances associated or associable, with personal data and information on their donors»⁵⁰.

According to the joint paper by the French and German National Ethics Councils of 2 October 2003⁵¹, biobanks are «privately or publicly maintained bodies for the long-term storage of human bodily substances and for the storage of personal data and information on the donors of these substances». They establish that the bodily substances such as the cells, tissues and blood, as well as DNA, are the physical medium of genetic data.

The Danish government created a working group to evaluate the need of non-government bills on the issue of biobanks. This group defined biobanks as an organized structure of human biological material accessible with some criteria, and where the information contained in the biological material can be related to people.

All these definitions make reference to the possibility of relating the data with the concerned person. In fact, it seems that it will be useful to give to the researcher the power to relate the data with the source, e.g. to evaluate the evolution of a

⁴⁹ Article 3.1 o) of Directive 2004/23/EC.

⁵⁰ GERMAN NATIONAL ETHICS COUNCIL, *Opinion Biobanks for research*, Berlin, 2004, p. 21.

⁵¹ Published by the GERMAN NATIONAL ETHICS COUNCIL, *Opinion Biobanks for research*, Berlin, 2004, p. 97.

disease, the reaction to a treatment, etc., and this power should be specified in the regulations of each Member State. Further, we do know that it is possible to relate stored DNA with a particular person, if we have some complementary information; even if the DNA register does not have personal nature. In this sense, the issue of anonymisation can be questioned.

2.2.4.2. *Data preservation period*

The issue on the preservation period of the data is related to the viability of anonymisation process.

The Dutch authority on data protection has faced situations in which the anonymisation or suppression of data contained in biobanks could decrease the value and function of these data bases, in the sense that data cannot be related to identifiable people. For example, in data bases for longitudinal research related to several generations, such as the register of cancer cases. In these situations, it is necessary to consider some favourable arguments for the preservation of data for a longer period of time.

In general, identifiable features can be eliminated from research data bases after some years, so the data is rendered anonymous again and it cannot be related to an identifiable person anymore.

2.2.4.3. *Security measures*

Analysing the question about security measures for the protection the data processed on medical and scientific research is also imperative. Regarding biobanks, it is advisable to implement significant safety measures, on organizational and technical scales, with the aim of protecting data according to article 17 of Directive 95/46/EC⁵². As the working party in data protection

⁵² It establishes that:

1. Member States shall provide that the controller must implement appropriate technical and organizational measures to protect personal data against accidental or unlawful destruction or accidental loss, alteration, unauthorized disclosure or access, in particular where the processing involves the transmission of data over a network, and against all other unlawful forms of processing.

Having regard to the state of the art and the cost of their implementation, such measures shall ensure a level of security appropriate to the risks represented by the processing and the nature of the data to be protected.

2. The Member States shall provide that the controller must, where processing is carried out on his behalf, choose a processor providing sufficient guarantees in respect of the technical security

accurately points out, the controller of the data can be asked to carry out study the risks, to apply security measures, to inform and form the personnel permanently, to limit the access, to avoid unauthorised access, etc.

2.2.5. Classification of the data subject to legal protection

To succeed on this kind of research it is usual to have different personal data, such as data related to the health of specific people, as well as genetic data which may be related to their health and both shall be identifiable. But generally, it is proposed some procedure allowing to join research purposes with the protection of individuals whose data could be used on research, reaching some kind of balance between both purposes. The data *anonymisation* through techniques of personal data codification to avoid the identification of the source subject is among these procedures; also the *pseudoanonymisation* (reversible dissociation procedure) disaggregating or separating the identifiable data of the source from the other data of medical-scientific interest. But still, the last procedure grants a limited protection of the data⁵³.

2.2.5.1. Personal and sensitive data

The regulations on data protection do not give a concept in broad and uniform terms of data of personal nature, so the Spanish legislation defines it as «any

measures and organizational measures governing the processing to be carried out, and must ensure compliance with those measures.

3. The carrying out of processing by way of a processor must be governed by a contract or legal act binding the processor to the controller and stipulating in particular that:

- the processor shall act only on instructions from the controller,
- the obligations set out in paragraph 1, as defined by the law of the Member State in which the processor is established, shall also be incumbent on the processor.

4. For the purposes of keeping proof, the parts of the contract or the legal act relating to data protection and the requirements relating to the measures referred to in paragraph 1 shall be in writing or in another equivalent form.

⁵³ Relating to the sample, we have to consider the possibility of identifying the subject of an anonymous sample through the comparison between stored samples. This possibility has to be considered to qualify the anonymisation process as reversible or irreversible. See Human Genetics Commission, *Inside information. Balancing interests in the use of personal genetic data*, p. 91. there has been some reserves on the possibility of really rendering samples anonymous because of the increase of banks and of the possibility of comparing them Paul MARTIN and Jane KAYE, *The use of biological sample collections and personal medical information in human genetics research, ob. cit.*, p. 52.

information related to identified or identifiable people»⁵⁴. In this sense, the regulations of Slovenia refer to it as «any data which links to an individual, regardless of how it is expressed»⁵⁵. The collection, use, cession, storage, etc, have to respect the principles laid down on the national regulations of the EuroBiobank project Member States.

The Malta Data Protection Act⁵⁶ (Article 2) and the Law on Liberty and Informatic in France⁵⁷ (article 2) distinguishes between personal data from sensitive personal data. The first one is defined as any information relating to an identified or identifiable natural person; an identifiable person is one who can be identified, directly or indirectly, in particular by reference to an identification number or to one or more specific factors of his physical, physiological, mental, economic, cultural or social identity. The sensitive personal data means personal data that reveals race or ethnic origin, political opinions, religious or philosophical beliefs, and membership of a trade union, health, or sex life. The German Data Protection Act refers to these data in the special categories of personal data (article 3.9).

2.2.5.2. Anonymous data

The anonymisation is a process by which it is impossible to reasonably find any link between data and the subject to which it is referred to. So, anonymous data are considered to be those where the identity of the person to whom they are referred to is unknown and its identification is impossible, because these data was collected like this, or because even if they were collected together with the identification of the person, they have been rendered anonymous afterwards.

This category of data is outside the scope of Directive 95/46/EC, as we can infer from recital 26 establishing that «whereas the principles of protection must apply to any information concerning an identified or identifiable person; whereas, to determine whether a person is identifiable, account should be taken of all the means likely reasonably to be used either by the controller or by any other person to identify the said person; whereas the principles of protection shall not apply to

⁵⁴ Article 3 a) of the Spanish Act of data protection. This definition is taken from the article 2 a) of the Directive 95/46/EC which adds that «an identifiable person is one who can be identified, directly or indirectly, in particular by reference to an identification number or to one or more factors specific to his physical, physiological, mental, economic, cultural or social identity».

⁵⁵ Article 6.1. of the Personal Data Protection Act (ZVOP-1), of 15 July 2004.

⁵⁶ Malta Data Protection Act (Chapter 440) of 15th July 2003.

⁵⁷ Law No. 2004-801 of 6th August 2004

data rendered anonymous in such a way that the data subject is no longer identifiable; whereas codes of conduct according to article 27 may be a useful instrument for providing guidance as to the ways in which data may be rendered anonymous and retained in a form in which identification of the data subject is no longer possible». Certainly, Directive 94/46/EC does not give a definition about the meaning of anonymisation, but what the Directive determines is that the principles of protection will not apply to those data rendered anonymous and where the person concerned cannot be identified.

The Federal Data Protection Law of Germany is more satisfactory defining the depersonalisation of the data as «the modification of personal data so that the information concerning personal or material circumstances can no longer or only with a disproportionate amount of time, expense and labour be attributed to an identified or identifiable individual» (Article 3.6.)⁵⁸.

2.2.5.3. *Unlinked data*

It is important to specify the difference between data unlinked to an identifiable person (rendered anonymous) and data irretrievably unlinked to an identifiable person. Data unlinked to an identifiable person, which is data that are not linked to an identifiable person, through the replacement of, or separation from, all identifying information about that person by use of a code⁵⁹. It can be applied to a biological sample. And Data irretrievably unlinked to an identifiable person: is data that cannot be linked to an identifiable person, through destruction of the link to any identifying information about the person who provided the sample⁶⁰. It can also be applied to a biological sample. So, it is fundamental to distinguish between data rendered anonymous and unlinked data, as the last one is reversible on its own nature, allowing the identification, and the anonymisation does not allow that «reasonably»⁶¹ (only under exceptional circumstances, as the Federal Data Protection Act establishes).

⁵⁸ Federal Data Protection Law of 1 January 2003.

⁵⁹ Definition taken of the UNESCO Declaration Article 2. x.

⁶⁰ Definition taken of the UNESCO Declaration Article 2. xi.

⁶¹ According to the Directive 95/46/EC on data protection, «*Unlinked data*» are those which are not possible to link with the identity of the subject with *reasonable effort* —to determine whether a person is identifiable, account should be taken of all the means likely reasonably to be used either by the controller or by any other person to identify the said person (recital 26)— directly or indirectly, in particular by reference to an identification number or to one or more factors specific to his physical, physiological, mental, economic, cultural or social identity. Second statement of article 2 a) of the Directive 95/46/EC.

2.2.5.4. *Health data*

According to the WHO, health is a state of complete physical, mental and social well-being and not merely the absence of diseases or infirmity⁶². If we add to this concept the definitions by the Council of Europe on the Convention on Biomedicine⁶³ that establishes that health data are «data related to physical and mental health in the past, present and future of an individual. It can be data of a healthy, ill or deceased individual. These data shall include information on alcohol abuse or drugs consumption»⁶⁴ and Recommendation (97) 5 of the Council of Europe on the protection of medical data the expression «medical data refers to all personal data concerning the health of an individual. It refers also to data which have a clear and close link with health as well as to genetic data» (Principle 1), resulting that health data are any data concerning the past, present or future physical or mental well-being of a living or deceased human being, medical data are also those which have a close relation with the described situation, particularly information related to the abuse of alcohol, drugs consumption and genetic data are to be included.

In fact, the concept of health is very broad and it will include, for example, the genetic data⁶⁵. According to article 8.1. of the Directive 95/46/EC, categories of personal data whose sensitivity requires a higher level of protection includes «health related data». Genetic data may provide to an extent a detailed picture of a person's physical disposition and health condition and therefore could be

⁶² Definition adopted in the I Health Conference, held in New York and signed on 22 July 1946.

⁶³ State of signature and ratification of the Convention on Biomedicine of the Member States of the EuroBiobank Project:

- **Germany:** has neither signed nor ratified.
- **Spain:** Signed on 4 April 1997, ratified on 1 September 1999 and came into force on 1 January 2000.
- **Slovenia:** Signed on 4 April 1997, ratified on 5 November 1998 and came into force on 1 December 1999.
- **France:** Signed on 4 April 1997, has not ratified it.
- **Hungary:** Signed on 4 April 1997, ratified on 9 January 2002 and came into force on 1 May 2002.
- **Italy:** neither signed nor ratified.
- **Malta:** neither signed nor ratified.

⁶⁴ Explanatory report, paragraph 45.

⁶⁵ Recommendation No. R (97) 5 of the Council of Europe establishes that «genetic data refers to all data, of whatever type, concerning the hereditary characteristics of an individual or concerning the pattern of inheritance of such characteristics within a related group of individuals».

considered as «health related data»⁶⁶. Considering the extremely particularity of the genetic data and their relation with the information able of revealing the health condition or the ethnical origin, they have to be treated and essentially sensitive data according to the mentioned article 8.1 of the Directive and, in this sense, they have to be subject to reinforced protection as laid down in the Directive and in the national transposition laws, abovementioned.

If in some Member States the legislation on data protection explicitly grants a sensitive character to genetic data, with all the corresponding protections and restrictions, in most of the Member States the treatment of genetic data is not regulated by any specific law. However, some Member States (as France) do settle complementary dispositions on the treatment of genetic data.

2.2.6. The right not to know

The participants of the research have the right to know the results of the investigation which concern their interests. We can state that there is an unanimous opinion recognising that the right to know has to be followed by the right not to know, particularly in those cases where the previous knowledge of the disease only carries suffering and does not have any advantage from a therapeutic point of view⁶⁷. In fact, the current trend holds that it was not appropriate to inform systematically the family of patients carrying a gene of an incurable disease creating a permanent anxiety without a possible direct benefit for the members of the family, as no useful treatment would be available to them in the near future⁶⁸.

The Convention on Biomedicine of the Council of Europe recognises that «everyone is entitled to know any information collected about his health. However, the wishes of individuals not to be informed shall be observed» (article 10); and the Spanish Act 41/2002 establishes that «patients have the right to be

⁶⁶ Opinion held by the working party established according to article 29 of the Directive 95/46/EC. Working Document on Genetic Data, adopted on 17 March 2004.

⁶⁷ Italian National Committee on Bioethics, *Bioethical guidelines for genetic testing* of 19 November 1999.

French law No. 2002-303 (4 march 2002) relative aux droits des malades et à la qualité du système de santé.

⁶⁸ Opinion of the National Commission on Informatics and Liberties, stated by the working party established according to article 29 of the Directive 95/46/EC. Working Document on Genetic Data, adopted on 17 March 2004, p. 10.

informed about all the information available on any activity in the healthcare sector (...). Further, any natural person has the right to not to be informed» (article 5), «the refusal of the patient to receive information is limited by the interest of the patient's health, of third parties, of the community or of therapeutic demands. When the patient expressly states his desire of ignorance, his wish will be respected stating it on paper (...)» (article 9). The regulation of the right not to know is new in the Spanish legislation since the Act 42/2002, where it was regulated in a restrictive way: the exercise of this right is subject to the interest of third parties and the community's health, this makes sense if we consider the required evaluation of common interests, but also the health of the patient himself and the therapeutic demands of the case. The literal interpretation of this precept leads the right not to know to a practical ineffectiveness, contrary to the spirit of the legislator. A teleological interpretation is required to offer correctional mechanisms for the execution of this right in a limited extension⁶⁹. In the same way in France, the right to not know exists except when thirds are exposed at the risk of transmission⁷⁰. Nevertheless, in the German legislation the right not to know is not expressly regulated, despite of the voices in favour of its legalisation⁷¹; nonetheless there are initiatives to adopt a new law on genetic test regulating this matter among others⁷². However, the right not to know is a legal right of the individual based on the fundamental rights, especially on the right of unrestricted development of personality (§ 1 and 2 GG).

In any case, the exercise of the patient's right not to know of any feature about their health cannot represent a limitation to the validity of their consent to an intervention; for example, the patient can consent the extirpation of a cyst without being willing to know its nature⁷³.

When biological samples are collected for medical and scientific research purposes, the information provided at the time of consent should indicate that the person concerned has the right to decide whether or not to be informed of the

⁶⁹ P. NICOLÁS JIMÉNEZ, *La protección jurídica de los datos genéticos de carácter personal* (Legal protection of genetic data of personal nature), *ob. cit.*

⁷⁰ Article L 111-2 of public health code introduced by the law No. 2002-303, 4 march 2002

⁷¹ German Organization of Professional Doctors (1999) and in the Conference on Data Protection (2000). <http://www.dhgp.de/ethics/index.html>

⁷² Coalition contract (2002-2006) of SPD and Bündnis 90/Die Grünen. For further information visit <http://www.dhgp.de/ethics/index.html>

⁷³ J. SÁNCHEZ CARO, *Diario Médico* (Spanish Health Journal) of 31 May 2000.

results of the research⁷⁴. It seems difficult to extend the scope of right not to know to the case where the result could considerably benefit his health, in this case the person should be informed of the result.

2.2.7. Information to provide to third parties

Should this information be provided to the family? In any case, and as we have explained, the genetic data obtained from a patient, from a legal point of view, is personal information. So it is subject to the protection that the Law grants to the right of information of the patient's health. The doctor is subject to the duty of medical secrecy and breaching this duty can lead to criminal punishments⁷⁵. However, there are legal mechanisms that link this general principle with other interests: the state of need or the fulfilment of duties are circumstances that justify the breach of medical secrecy. These circumstances can take place when a doctor discovers the genetic data of a patient and faces the dilemma of whether to inform or not his family. In these cases, acting on a state of need means that informing about the genetic data of the family avoids such a bad situation that it justifies breaching the right of privacy of the patient. Act fulfilling a legal duty means that informing the patient the doctor fulfils the legal duty of aiding the patient.

In any case, if the omission of the genetic data results in a damage or danger for the integrity or the life of the family members we are facing a situation of limiting the rights of the subject established by the presence of other people, from a constitutional point of view. From a criminal point of view, we could be facing the possibility to identify a state of need or even duty higher than confidentiality to the health professional, what may justify the breach of the secret. Particularly, this omission could be compared to the omission of aid duty⁷⁶, which is considered to be a tort; however, in very specific cases where the family member manifests serious symptoms of the disease, he or she will not have the proper medical aid because of a lack of diagnosis and it is considered to be the hereditary mechanism of the disease.

Furthermore, from the civil point of view, there is a damage resulting from the omission of the duty of information between married couples and descendants

⁷⁴ Art. 10 of the UNESCO International Declaration on Human Genetic Data. Same opinion: Medical Research Council Ethics. *Human tissue and biological samples for use in research. Operational and ethical guidelines*, London, 2001, p. 4.

⁷⁵ For example article 199 on the Spanish Criminal Code.

⁷⁶ Article 195 of Spanish Criminal Code. Article 223-6 of French Penal Code and article 9 of Medical Deontologic French Code.

(including non-marital descendants), which may entail liabilities. It is even more difficult to determine the duty of descendants with their parents, between brothers, biological relatives whose links are not legally recognised, and between partners. It is interesting to highlight that the French Act on Bioethics of 6 August 2004 expressly points out that there is no liability resulting from the lack of transmission of genetic data from an individual to its relatives, what is an exception to the rule that may apply if this specification was not laid down.

On the Convention on Biomedicine of the Council of Europe and on the Universal Declaration on the Human Genome of the UNESCO, the concept of protection of privacy seems to be based on an individualistic concept. Given the sensitiveness of the issue, we should find a balance between the right of the affected person not to inform on its genetic data and the main implications or consequences which may arise from the disclosure and use of this data to the biological relatives. In this context we can consider if genetic data are only and exclusively property of the source person from which they have been collected, and if the family members have the right to access to these data without the consent of the source subject. A case on the topic raised in Italy in 1999, through the decision adopted by the Garante per la protezione dei dati personali (Authority for the Protection of Personal Data), that allowed a woman to access the genetic data from her father without his consent. The application was accepted because the right of the parent to confidentiality could not prevail against the right of health of the woman (in other words, «her mental and physical well-being»)⁷⁷. In any case, the general authorisation n° 2198 (point 5) from the Italian Authority to the protection of personal data excludes the communication of genetic data to the family of the affected person.

2.2.8. Unexpected findings

The provided information should also consider the possibility of unexpected findings. On the informed consent we can know the position of the subject regarding the communication of these findings. Recommendation (97) 5 of the Council of Europe on the protection of medical data, deals with the issue of unexpected findings («discoveries») as follows «The person subjected to genetic analysis should be informed of unexpected findings if the following conditions are

⁷⁷ This decision was published on the *Boletín del Garante, Ciudadanos e sociedades dell'informazione*, No. 8, 1999, pp. 13-15.

met: *a)* Domestic Law does not prohibit the giving of such information; *b)* The person himself has asked for this information; *c)* The information is not likely to cause serious harm: *i).* To his/her health; or *ii).* To his/her consanguine or uterine kin, to a member of his/her social family, or to a person who has a direct link with his/her genetic line, unless domestic law provides other appropriate safeguards. Subject to sub-paragraph *a)*, the person should also be informed if this information is of direct importance to him/her for treatment or prevention» (principle 8.4). The problem is that we are facing a legal gap on how to act when these findings seriously affect health.

In fact, Domestic Laws do not regulate the issue of unexpected findings⁷⁸, and the question could be solved considering that the patient has the right to know all the data about his/her health (e.g. article 5 of the Spanish Act 41/2002). We could interpret that it covers all kind of information, including unexpected findings, with the limits established by the law, such as the therapeutic exception —possibility of omission of the information by medical decision based on the damage on the health of the patient— mentioned in the Convention on Biomedicine of the Council of Europe, letting this matter on the will of each domestic legislation (regulated in the Spanish Act 41/2002, Article 5.4)⁷⁹. However, it seems reasonable that the unexpected finding shall be related to health, the individual should not be informed about other kind of data which does not affect his/her health.

2.3. SOURCE SUBJECT

2.3.1. Sample subject and data subject

The legislation on data protection of the Member States of the EuroBiobank project seems to be quite unanimous establishing that the rights to dispose of the sample and data belongs to the source subject (article 3 of the Spanish Act on data protection, article 1 of the Federal Act on Data Protection and article 3 of the Slovenian Act on the matter).

⁷⁸ In fact, this matter is not regulated in the Italian system of law, but it is in the Italian Code of Good Practice for Medicine (article 30).

⁷⁹ Article 5.4.: «The right to access health data of patients is limited to the accreditation of a therapeutic demand. Therapeutic demand is the faculty of a doctor to act professionally without previously informing the patient, when objectively the knowledge of his own situation can seriously damage his health. In that case, the doctor will reasonably state the circumstances in the case story and communicate his decision to the family or legal relatives of the patient».

2.3.2. Rights of the person concerned: consent and information

2.3.2.1. *The importance of the consent*

The consent is one of the main issues when considering legal and ethical regulations on biobanks, because the consent has two interests which are legitimate and opposite at the same time: the right of the source subject to protect his/her personal data and the interests of the scientific community. Actually, scientists sometimes may want to compare data and samples to donors with the purpose of relating results to real cases, mainly on observational research. We have to bear in mind that in some epidemiological researches the observation period is long, it takes generally some decades; as a result, it is difficult to determine which kind of test would be necessary to carry out in the moment of collecting the sample. Should it be necessary to ask for a new consent each time that a test is carried out? It can happen that after thirty or forty years the donor has died. These facts manifest that sometimes it is not recommended or necessary to have the consent of the person concerned. In France, research is possible if the donor gave «beforehand» its consent or if an ethics committee delivered a positive opinion⁸⁰. In the Dutch system of Law it is established that the consent has to be adequately probed and justified granting that the privacy of the person concerned is not going to cause a disproportional damage; that the research is of general interest; that it is not possible to carry out the research without the nominative data; that the affected person did not present any previous opposition or that the mentioned opposition could not be predictable (in case of decease)⁸¹. It seems logical that in epidemiological researches there has to be certain flexibility when dealing with the consent, always protecting the rights and guarantees of the source subject. In addition, it is advisable that the ethical committees which are going to evaluate this kind of research should handle the question trying to reach the most suitable solution.

The consent is defined as «any freely given specific and informed indication of the wishes of the data subject by which he signifies his agreement to personal data relating to him being processed» in the Malta Data Protection Act⁸²; also defined in these terms in the Article 6.14 of the Slovenian Data Protection Act.

⁸⁰ Article L1211-2 of French public health code introduced by the Law No. 2004-800, 6 august 2004.

⁸¹ H.J.J. LEENEN, «Genetics, confidentiality and research», *European Journal of Health Law*, Vol. 7, 2000.

⁸² Art. 2 of the Malta Data Protection Act (Chapter 440) of 15 July 2003.

Directive 2004/23/EC and the Spanish law have the same provisions relating to the donation principles (anonymous and free) and the rights of the subject (information, consent, data protection and confidentiality). Particularly, we highlight that regarding the consent of the subject, the Directive delegates on the domestic legislation the specific system of requirements; article 6 of the Slovenian Act on organs transplants⁸³ establishes the need of a free and written consent, and in the Spanish law, articles 7 and 8 of the Royal Decree 411/1996 establish the duty of giving an express consent in the case of a living donor and the presumption of consent in the case of deceased donors.

The British Human Tissue Act regulates all the matter on collection, storage and use of samples and tissues under the principle of «appropriate consent» (Section 3) which is the consent granted by the living person—in the case of deceased people, it is a written consent—. If any of these activities were carried out without the appropriate consent, they shall be punished.

2.3.2.2. *Consent to data collection*

It is advisable to differentiate between the consent to data collection and the consent to participate in a research. The first is governed by the regulations on data protection, while for the second there is no general provision, but sector regulations, e.g. for clinical trials.

For the collection of personal data on health, shall be granted an express consent (articles 3.h and 7 of the Spanish Act on Data Protection and articles 6.14 and 8.1 of the Slovenian Act on the subject-matter, and article 8-1 of the French Law on Personal Data Protection⁸⁴).

The granted consent allows the use of data with similar purposes to the ones which justified their collection. Future processing with historical, statistical or scientific purposes will not be considered incompatible. article 16 of the Spanish Act 41/2002, on the «use of clinical record» refers to the Spanish Act on Data Protection, and advises that when accessing to the clinical record with epidemiological, public health, research or teaching purposes the identification of the patient's data shall remain separated from the clinical data to ensure

⁸³ The removal and transplantation of human body parts for the purposes of medical treatment act of 27 January 2000. Zakon o odvzemu in presaditvi delov cloveškega telesa zaradi zdravljenja (ZOPDCT).

⁸⁴ Law No. 2004-801, 6 august 2004.

anonymity⁸⁵. In other words, the use of samples with different purposes to those that the subject expressly consented requires dissociation or express consent. There is a general consent to collect data with research purposes. However, when these data are donated by the responsible of the treatment of a third party—a situation similar to the transfer of samples—a specific consent is required from the owner for each cession.

In the German legislation, there is a principle by which any action affecting the integrity of the individual requires an informed consent on the purposes, nature, meaning and implications of the sample collection. Any damage is punished by criminal law (article 223ff of the Penal Code) and by civil legislation (article 823.1 of the Civil Code).

2.3.2.3. *Consent to take part on a research*

The consent to take part on a research has to be obtained. The first text which fixes this rule is the French law in 1988 on protection of the people who lend themselves to research⁸⁶.

The Directive 2001/20/EC on clinical trial⁸⁷ can be applied, and there are some similarities between concepts, even though the subject-matter is not exactly the clinical trial because there is no subject on the process but his bodily parts. It is essential that the subject gives his informed consent—defined as a decision which must be written, dated and signed, freely taken after being duly informed of its

⁸⁵ «The access to the case store with legal, epidemiological, public health, research or academic purposes is regulated on the Spanish Organic Law 15/1999, on Personal Data Protection, and the Act 14/1986, on Health, and other dispositions. The access to the case story with these purposes binds to preserve the identifiable personal data of the patient unlinked from those of clinical-assistance nature, in order to keep the patient anonymous, except if the patient has given his consent not to unlink them. The cases of investigations of the legal authority are an exception, and in these cases judges and courts will determine how to proceed. The access to documents and data from the case story is strictly limited to the specific purposes of each case».

⁸⁶ Law No. 88-1138, 20 december 1988.

⁸⁷ Directive 2001/20/EC of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. *OJEC*, No. L 121 of 1 May 2001, pp. 34 and ff.

Transposed to the Spanish regulation through the Spanish Royal Decree 223/2004, of 6 February, which regulates the clinical essays with drugs, *BOE* (Spanish Official Journal), No. 33 of 7 February 2004. This Royal Decree substitutes the regulation in force on the matter, particularly the Spanish Royal Decree 561/1993.

nature, significance, implications and risks— (article 2. j of the mentioned Directive). This consent has to be explicit, which means related to a specific research, to a specific trial (Directive 2001/20/EC). However, the requirement of explicit consent makes reference to in vitro interventions, which it is not the case of samples research.

Secondly, the Spanish act Royal Decree 411/1996 establishes that the collection of human tissues from a living donor of age has to be previously informed on the consequences of his decision and the donor has to give an express, free, conscious and disinterested consent⁸⁸. In addition, the *Agencia Española de Protección de Datos* (Spanish Agency for Data Protection) does not require an explicit consent to obtain health data on a specific research; so, we can say that the collecting health data for research can be consented in general terms.

However, the general consent to use the sample means that specific data known by the owner is being used, as well as potentially having the complete genetic information. This issue has been dealt with in Anglo-Saxon documentation, as well as the question of blanket consent⁸⁹. This last possibility is supported by scientific research and its demands⁹⁰, and because the application for a new consent can entail a probably undesired intrusion in the life of the original case trial⁹¹. There are people in favour of applying for a specific consent to analyse data when the original disease is not involved⁹², or a renewal of consent in case of important changes in the original protocol of research⁹³ (for example, a change of purposes or of the methodology). Maybe the best solution is the intermediate one which links the rights of the subject and the interests of the research called «substitution formula», according to which there shall be an «application for mediation» which keeps the identification codes of unlinked samples; these samples could be used in

⁸⁸ Spanish Royal Decree 411/1996, of 1 March, which regulated the activities relating the use of human tissues.

⁸⁹ P. NICOLÁS JIMÉNEZ, *La protección jurídica de los datos genéticos de carácter personal* (Legal protection of genetic data of personal nature), *ob. cit.*

⁹⁰ Nina T. HOLLAND et al., «Biological sample collection and processing for molecular epidemiological studies», p. 219.

Also in Nuffield Council on bioethics, *Pharmacogenetics. Ethical Issues*, paragraph 3.38.

⁹¹ Royal College of Physicians Committee on Ethical Issues in Medicine, «Research based on archived information samples», p. 264.

⁹² Advisory Committee on Genetic Testing, Advice to Research Ethics Committees, p. 7. Nuffield Council of Bioethics, Human tissue and biological samples for use in research, p. 20. Medical Research Council, Human tissue and biological samples for use in research, p. 15.

⁹³ See Le Réseau de médecine génétique appliquée (RMGA), *Énoncé de principes sur la conduite éthique de la recherche en génétique humaine concernant des populations*, third recommendation.

any research and, if the subject consents it, he would be able to know which tests are being carried out with the samples consulting the mentioned application; additionally, this body will be in charge of applying for a new consent if required⁹⁴.

It is argued that the blanket consent does not fulfil the duty of being previously informed⁹⁵ which is a requirement for research and as a result it does not fulfil the functions of the informed consent, so it is nothing but a symbolic expression instrument. The blanket consent does not represent a manifestation of the individual wish and its effectiveness to protect biological samples from potential damages surged in the processing is uncertain, but this will not predetermine its invalidity⁹⁶. This objection has been argued saying that in these cases it is impossible to apply this requirement of informed consent *on its full extension and for any case*, because there is no danger of physical damage to the subject⁹⁷, and that more important than the requirement of *broad* previous information (which is impossible) is the *genuine* consent⁹⁸. And further, the aim of informing previously to the consent is to avoid an unavoidable error, and it cannot be said that the blanket consent is invalid in this sense⁹⁹.

Certainly, if the consent is granted to obtain from the sample any genetic data in any scientific research (potentially all subject's data), there is a huge loss of control on personal data¹⁰⁰. But, there can be settled procedures to grant the subject's powers on his/her data: firstly, confidentiality and guaranties to the right not to know; secondly, the duty to inform the competent body about the researches

⁹⁴ Comité Consultatif National d'Étique pour les Sciences de la Vie et de la Santé, Avis n° 77, *Problèmes éthiques posés par les collections de matériel biologique et les données d'information associées: biobanques, biothèques*, p. 5.

⁹⁵ This was the objection to this possibility by Morgan Capron in the National Bioethics Advisory Commission *Research involving human biological materials: ethical issues and policy guidance*, vol. I (Report and Recommendations), p. 65.

⁹⁶ Allen BUCHANAN, «An ethical framework for biological samples policy», p. B-18.

The Nuffield Council of Bioethics is also against the blanket consent as the one issued in terms of «any biological or medical research», *Human tissue and biological samples for use in research*, p. 15.

⁹⁷ National Bioethics Advisory Commission, *Research involving human biological materials: ethical issues and policy guidance*, vol. II (Report and Recommendations), 6.

⁹⁸ The ethically significant requirement of consent is not that it be complete, but that it be genuine on the potential risks, since achieving fully informed consent is not possible, Nuffield Council on bioethics, *Pharmacogenetics. Ethical Issues*, paragraph 3.29.

⁹⁹ P. NICOLÁS JIMÉNEZ, *La protección jurídica de los datos genéticos de carácter personal* (Legal protection of genetic data of personal nature), *ob. cit.*

¹⁰⁰ P. NICOLÁS JIMÉNEZ, *La protección jurídica de los datos genéticos de carácter personal* (Legal protection of genetic data of personal nature), *ob. cit.*

which are being carried out with the samples¹⁰¹. This last requirement represents the right of the subject to withdraw the consent and the subsequent destruction of the sample, and the right to be informed about the circumstances in which researches are being carried out. However, it is advisable to join the blanket consent with a specific consent for certain types of researches depending on the criteria of the Commission in charge of revising these researches¹⁰², for example, those researches which could arise any ethical controversy, such as the ones that study different features and behaviours of a specific ethnic group¹⁰³.

Consequently, the blanket consent has to be preceded by the corresponding information that grants the powers of the subject, which become more important than in the case of granting a specific consent¹⁰⁴. In the case of the blanket consent, the subject shall be informed about the fact that the consent to the collection of the sample is voluntary; that the consent to the analysis is voluntary; provide information about the data that can reasonably be expected to be obtained from the genetic analysis; about the use that the sample source will be able to make of the data derived from the genetic analysis; of the right to inspect records that contain information derived from the genetic analysis; of the right to the confidentiality of the results of the analysis; the right to render anonymous the sample; of the right to consent cessions; the subject shall also be warned on the importance of the results of the analysis to the source's relatives; and of the availability of genetic counselling¹⁰⁵.

¹⁰¹ Comité Consultatif National d'Étique pour les Sciences de la Vie et de la Santé, Avis n° 77, *Problèmes éthiques posés par les collections de matériel biologique et les données d'information associées: biobanques, biothèques*, p. 5 y 25, deals with the convenience of an «institution of mediation» undertaking these competences.

¹⁰² Allen BUCHANAN, «An ethical framework for biological samples policy», p. B-20.

¹⁰³ Human Genetics Commission, *Inside information. Balancing interests in the use of personal genetic data*, 96 and in the Nuffield Council of Bioethics, *Human tissue and biological samples for use in research*, p. 16. They point out that a specific consent is required to carry out some genetic researches, such as those related to personality, behaviour, sexual orientation or intelligence. The Medical Research Council, in the report *Human tissue and biological samples for use in research*, p. 16, advises that the specific consent is particularly important to carry out genetic researches in some fields, such as behaviour, personality, sexual orientation or intelligence.

¹⁰⁴ P. NICOLÁS JIMÉNEZ, *La protección jurídica de los datos genéticos de carácter personal* (Legal protection of genetic data of personal nature), *ob. cit.*

¹⁰⁵ Most of them established on section 101 of the Genetic Privacy Act, George ANNAS / Leonard H. GLANTZ / Patricia A. ROCHE, *The genetic privacy act and commentary*. The authors propose that the sample shall be destroyed if the subjects demands so, an option that we do not share given the fact that he is not the owner anymore.

Actually, it is sensible to establish several options relating to consent, including the general consent for research, and others such as consenting research for a specific study, consenting research for a specific study with the possibility of granting future consent to further projects, consenting the research with a unlinked sample for any study, or consenting the research with the sample not rendered anonymous for any research¹⁰⁶.

In short, there is no need to have a specific consent to obtain health data on a specific research according to regulations on research or on personal data protection. But, if there is a cession, in this case the subject has to give his/her consent to this operation.

The features which have been exposed on consent are essential if the sample is not anonymous —take into account that the source subject shall give consent for the transfer of the sample when it is identifiable—, if the sample was rendered anonymous, as we defined before, the criteria herein mentioned will not be applicable¹⁰⁷. However, it is not only important the question of consent, but also questions such as providing information on the destiny of the data and providing access to the records derived from them.

2.3.2.4. *Contents of the data to provide to the subject*

The Proposal for an instrument on the use of archived human biological materials in biomedical research of the Council of Europe of 2002, establishes the contents of the information provided to the subject distinguishing between general information (article 15.1) and specific information (article 15.2). On the first category, the information shall include:

- The potential for their materials and data to be stored for research purposes.
- The arrangements to ensure respect for private life and ensure the confidentiality of personal data.

Secondly, it has been held that if the samples are stored in an identifiable way, it has to be determined which kind of diseases can be studied in the future and the consequences for the source subject. Medical Research Council, *Human Tissue and Biological samples for use in research. Operational and Ethical Guidelines*, p. 15.

¹⁰⁶ National Bioethics Advisory Commission, *Research involving human biological materials: ethical issues and policy guidance*, vol. I (Report and Recommendations). Recommendation number 9.

¹⁰⁷ Same opinion, GERMAN NATIONAL ETHICS COUNCIL, *Opinion Biobanks for research*, *ob. cit.*, p. 46.

- The right of the individual to give or withhold consent to storage and research uses of such materials or data.
- The right of the individual to express his/her wishes regarding consent procedures for future research use.

And on the second category, the specific information shall include:

- The right to give or withhold consent for the project.
- The right to withdraw consent at any time.
- Any arrangements for disposal of the materials and erasure or anonymisation of the data.
- The arrangements for feedback to the individual of information generated during the research that is relevant to their health, healthcare, and counselling.
- The arrangements for making available to the individual research results that do not have a direct bearing on their health, healthcare, and counselling.
- Any foreseeable commercial uses of the materials and data, including the research results.

The German National Ethics Council also deals with the matter and establishes as information to be supplied to the subject before the consent is granted the following: the voluntary nature of participation, the purposes, nature, scope and duration of the proposed use, including proposed genetic analyses; the extent and conditions of a possible transfer of samples and data, in particular if exported; the possibility or otherwise of the communication of research results to the donor; advice on the possible implications of the communication of the results of genetic analyses for the donor and his/her relatives, including any possible duty to divulge (e.g. to insurance companies); anonymization or pseudonymization of samples and data; the right of access; the donor's right to rectify or withdraw; the fate of samples and data if the biobank is closed down; and issues of the payment of expenses, or benefit sharing if the donor has the right to take part in the benefits derived from the commercialisation of the product or the process where the sample or data has been used¹⁰⁸. Undoubtedly, the information shall be supplied individually and in accordance with the nature of each research.

¹⁰⁸ GERMAN NATIONAL ETHICS COUNCIL, *Opinion Biobanks for research, ob. cit.*, pp. 56-57.

In addition to the information that has to be provided to the subject before having his/her consent, we have to consider the regulation on personal data protection and the requirements of the regulations on research:

1. Before collecting personal data, the subject shall be informed expressly and precisely of the following elements:

- a) The existence of a file or processor containing his/her medical data and the type of data collected or to be collected, the purpose or purposes for which they are or will be processed and to whom they may be communicated.
- b) The compulsory or facultative nature of answering questions.
- c) The implications of allowing or refusing data collection.
- d) The possibility, if any, for the data subject to refuse his/her consent, to withdraw it and the consequences of such withdrawal.
- e) The identity of the controller and of his/her representative, if any, as well as the conditions under which the rights of access and of rectification may be exercised.

When data are donated, or the sample is transferred, the subject shall receive the information relating to the grantee.

2. To take part on a research, the legislation on clinical trial established the information on a given trial. We have discussed that the consent to use a sample on a research shall be general. But if the consent is not general, it is advisable to follow the dispositions settled by law—in Spain the Royal Decree 223/2004 on clinical trial with drugs and in France law on protection of the people who lend themselves to research biomedical—and inform on the requirements laid down in this regulation. These regulations require that the subject has to be informed on: the purpose, the methodology, the expected benefits for him or for the society, constraints and risks derived from the study (number of visits, additional tests...), the voluntary nature of the participation, the donor's right to withdraw, people who will have access to the data and the way in which confidentiality will be held, the researcher responsible for the clinical trial and how to contact him if necessary.

If we consider the legislation in force on the topic, particularly the Swedish Act on Biobanks, this Act clearly defines the principle of informed consent establishing that tissue samples may not be collected and stored in a biobank without the donor being informed about the aim and purposes for which the biobank may use them and thereafter giving his or her consent (chapter 3, section 1). Further, the Act says that tissue samples stored in a biobank must not be used

for other purposes than the ones previously informed about and consented to. They cannot be used without the consenting human being informed about the new purpose and consented to this (chapter 3, section 5). Finally, the human being consenting to the use of a tissue sample may at any time withdraw his or her consent (chapter 3, section 6).

Detailed guidance on the application format and documentation to be submitted in an application for an Ethics Committee opinion on the clinical trial on medicinal products for human use, establishes that in case of the collection of samples the subject shall be informed on to whom the data and samples are accessible, the location and duration of retention, the person who will be responsible for keeping the samples and the results, plans to anonymise or destroy samples after analysis¹⁰⁹. In clinical trials where genetic testing is included, this should be clearly explained to the subject. The information should give the background and purpose of the genetic tests, the planned analyses and whether the samples will be kept to make future analyses possible in conjunction with the planned project (7.5.2).

Generally the source subject has the right to be informed on the destiny of the sample, if it differs from the original (e.g. a diagnosis procedure or its destruction) and, the subject will have to give his/her consent in this case, even if there was an original refusal to any other use. However, it is important to know the purpose of such consent, as most samples of this kind do not have any utility for the patient once the diagnosis and pathologic analysis are done, and traditionally, health centres got rid of the samples following the appropriate procedures.

There is no doubt, as the joint paper by the French and German National Ethics Councils¹¹⁰ establishes, that the information to be furnished at the time of entry into the bank and before samples or data are used for any research, the project must be particularly precise and must take account of a wide range of possible subsequent activities. For this reason there can be no single binding model for consent. Instead, the regulations to be drawn up must be flexible enough to suit the needs of the entire spectrum of possible research projects.

An informed consent unduly taken can lead us to embarrassing situations such as the one which took place in Texas. At the Tech Texas University, in the state of

¹⁰⁹ Detailed guidance on the application format and documentation to be submitted in an application for an Ethics Committee opinion on the clinical trial on medicinal products for human use. April 2003. Brussels, ENTR/F2/BL D(2003).

¹¹⁰ Published by the GERMAN NATIONAL ETHICS COUNCIL, *Opinion Biobanks for research*, p. 101.

Spanish Regulation: article. 7.2 of the aforementioned Royal Decree 411/1996, of the 1 March.

Texas, samples of DNA and brain tissues collected to study Alzheimer disease¹¹¹, were about to be destroyed because a considerable number of samples were taken without legal informed consent. The use of samples without a written consent breaches the federal law on human tests. However, the district court of this state considered the collective demand —by the affected relatives— arguing that samples are irreplaceable and that destroying a single DNA sample could unable the research with all the other samples from the relatives. So, the University could not destroy them because of the usefulness that they represented for the research against Alzheimer, even if there was not an informed consent.

2.3.3. Particular cases

2.3.3.1. *Minors and incapacitated*

There is no impeachment on the donation of tissues or samples from incapacitated or minors for diagnosis, if it is carried out having the previous authorisation from the parents or tutors¹¹². The problem arises when carrying out an intervention to a minor or an incapacitated to collect a biological sample for research. In these cases it is advisable not to accept the biological sample, because of the implications, unless the need of researching is strictly justified and the minor or incapacitated had a special interest in doing so. In this case, as well as in the case of diagnosis, the legal representatives have to give an informed consent on the aforementioned aspects¹¹³. The German National Ethics Council¹¹⁴ shares these criteria, and the British Human Tissue Act which requires in these cases «appropriate consent» from the person who has parental responsibility of the minor¹¹⁵.

The Swedish on Biobanks also establishes that tissue samples from minors shall not be collected and stored in a biobank without providing information to the guardian about the aim and purpose or purposes for which the biobank may be used

¹¹¹ The DNA data bank for research this disease had a collection of samples from 2,200 families to try to identify the genes responsible of the disease. The bank has more than 10,000 blood samples, 150 tissues and 600 complete case histories of patients with a confirmed diagnosis.

¹¹² Spanish Regulation: article. 7.2 of the aforementioned Royal Decree 411/1996, of the 1 March. French regulation, public health code, articles L 1121-7, L1121-8, L1124-14, L 1122-2.

¹¹³ See section 2.3.2.4. Contents of the data to provide to the subject.

¹¹⁴ GERMAN NATIONAL ETHICS COUNCIL, *Opinion Biobanks for research*, Berlin, 2004, pp. 72-74.

¹¹⁵ Section 2 of the Human Tissue Act of 15 November 2004.

and thereafter granting his consent. This act also determines that if the minor has reached such an age and maturity he/she can take a position on the issue (chapter 3, section 2). The Slovenian Act on transplants follows this same criteria establishing that the legal representatives are those who have to give their informed consent in the case of minors and incapacitated, but if the minor or the incapacitated is able to understand the intervention they have to be considered even in case of opposition (article 6)¹¹⁶.

In cases where the consent is granted by legal representatives of minors or incompetent people, we have to take into account the national regulations on the matter. In Spain this group is regulated by the Act 41/2002, of 14 November, a basic regulation of the autonomy of the patient, and of the rights and duties of providing information and clinical documentation¹¹⁷, particularly on article 9.3 on the cases where the consent is granted by representatives and it makes reference not only to minors but also to incompetent persons¹¹⁸. According to article 9.3.c) of the Act 41/2002 the under aged patient who emotionally and intellectually is able to understand the scope of the intervention can give his/her own consent. When this is not possible, we will have «consent by representation». So, the person granting

¹¹⁶ The removal and transplantation of human body parts for the purposes of medical treatment act of 27 January 2000. Zakon o odvzemu in presaditvi delov cloveškega telesa zaradi zdravljenja (ZOPDCT).

¹¹⁷ The adoption in Spain of the Act 41/2002, of 14 November, represents an important change on the issue of consent granted by minors in the health sector because until now there was no regulation on the matter in the Spanish regulation. As a result, it was necessary to address several dispositions contained in different legal texts to establish a regime on the matter (particularly, art. 162.II.1 of the Spanish Civil Code, the art. 10 paragraphs 5 and 6. b of the *Ley General de Sanidad*, (Spanish Healthcare General Act) revoked by the Spanish Act 41/2002). The approach to the issue has changed because now it is regulated in the art. 9.3 c) of the new Act 41/2002, even if the matter is not regulated exhaustively. For a deep analysis on this new Act see S. ROMEO MALANDA, «*Minoría de edad y consentimiento Médico en la Ley 41/2002, de 14 de noviembre*» (Minors and the medical consent in the Act 41/2002), *Actualidad de Derecho Sanitario* (Health Law), No. 102, February, 2004, pp. 114 and ff.

¹¹⁸ 9.3. The consent shall be granted by the representatives in the following cases: A) When the patient is unable to decide, according to the criteria of the doctor in charge of the attendance, or if the physical or mental condition does not allow him to decide. If the patient does not have a legal representative, the consent shall be granted by family members or other relatives. B) When the patient is legally incapacitated.

If the minor is unable to understand intellectually or emotionally the scope of the intervention, the consent shall be granted by his representative after hearing the opinion of the minor if he is over 12 years old. Minors with capacity to act who are emancipated or are over 16 years old cannot grant their consent through representation. However, in case of an act of serious risk, according to the facultative criteria, the parents shall be informed and their opinion will be considered when deciding».

consent is the legal representative —as established by the Act— and not a family member or a relative as established on the revoked article 10.6.b) of the *Ley General de Sanidad* (Spanish General Act on Health).

The doctor attending the under aged patient will determine in each particular case who shall decide if he/she has the mature conditions required, or if in contrast he/she will need the consent from a legal representative¹¹⁹. So, according to article 9.3.a) the capacity of a person to make decisions depends on the criterion of the doctor in charge of attending the patient. On any case, in the case of non-emancipated or patients under 16 years old, and because of the practical difficulties to determine the capacity of the under aged to grant their consent, it is advisable that the doctor consults the legal representatives before treatment for safe reasons¹²⁰, especially when dealing with medical acts which involve serious risks. Doing so, the doctor can make his mind about the maturity of the minor to understand the risks of the intervention, helping the doctor to determine whether the party is valid or not to decide whether or not to undergo the intervention¹²¹.

According to the Italian System of Law the capacity to decide of a minor on genetic tests, is addressed by the dispositions of article 2 of the legal decree number 282 of 30 June 1999 on «Dispositions to guarantee the privacy of the personal information in the health field»¹²², that has incorporated the article 23 of the Act 675/1996¹²³. The first impression is that it excludes any capacity of decision of the minor, as the under aged are considered to be legally incapacitated. However, the scope of the mentioned Act shall be limited by doing a systematic interpretation of the rule where the minor is included in a general context that allows him/her to take existential decisions and where the minor is considered to have legal capacity to do so. Consequently, minors cannot be submitted to the paternal authority; and as a

¹¹⁹ M.J. SANTOS MORÓN, «Sobre la capacidad del menor para el ejercicio de sus derechos fundamentales. Comentarios a la TCS 154/2002 de 18 de julio» (On the minor's capacity to execute his fundamental rights. Commentary to the TSC 154/2002 of 18 July), *La Ley*, 12 December 2002, p. 4.

¹²⁰ C.M. ROMEO CASABONA, *El médico y el Derecho penal, La actividad curativa (licitud y responsabilidad penal)* (*The doctor and criminal law 1, the healing activity (legality and criminal liability)*), Ed. Bosch, Barcelona, 1981, p. 318.

¹²¹ S. ROMEO MALANDA, «*Minoría de edad y consentimiento Médico en la Ley 41/2002, de 14 de noviembre*» (Minors and the medical consent in the Act 41/2002), *ob. cit.*, p. 116.

¹²² Decreto legislativo. N° 282 de 30 julio de 1999 *Disposizioni per garantire la riservatezza dei dati personali in ambito sanitario*.

¹²³ Ley 675/1996 de 31 de diciembre sobre la tutela delle persone e di altri soggetti rispetto al trattamento dei dati personali.

result other subjects will have the power to give their consent for the treatment only when the minor, due to his/her age or other reasons is physically or mentally incapacitated to express his/her wishes¹²⁴.

The French Act on bioethics of August 2004 expressly allows the removal of haematopoietic cells from the bone marrow of a minor, if it is the only therapeutic remedy (only for therapeutic purpose) and it is carried out for the benefit of his/her siblings. In any case, the removal cannot be carried out without the consent of each one of the legal representatives, and the doctor who has proposed the graft or by any other appointed doctor shall provide information on the risks and the eventual consequences of the removal. The consent is manifested before the French High Court (*Tribunaux de Grand Instance*) or the appointed Magistrate, which grants that the consent is free and clear. In case of vital emergency, the consent is accepted by the Prosecutor of the French Republic in any means, and this consent can be withdrawn at any time. However, the authorisation to carry out the extraction is appointed by the Committee of Experts which previously grants that all means to find an older donor compatible with the receptor have been tried without success and that the minor has been informed about the removal in order to obtain his/her wish, in case the minor is suitable for donation. In this case, the withdrawal of the minor is an obstacle for the extraction (article 1241-3).

2.3.3.2. *Foetuses and embryos tissues*

According to the Spanish Act 42/1998, of 28 December, on donation and use of human embryos and foetuses as well as their cells, tissues and organs, if they are clinically not viable or dead (article 2.b). The act to dispose of these materials has to be preceded by sufficient information and an express, conscious, written and free consent. Donors are parents, who can be minors or incapacitated. Additionally, the legal representatives have to give their consent if they are not emancipated minors or incapacitated. In France, the collection, conservation and use of foetus tissues are possible for research purpose if the woman give her consent after having taken its decision of termination of pregnancy; but if donor is minor it is not possible to collect foetus tissues except in case of research the causes of the termination of pregnancy¹²⁵.

¹²⁴ Established by the National Bioethics Committee of Italy. Bioethical guidelines for genetic testing, of 19 November 1999.

¹²⁵ French law No. 2004-800; article L 1241-5 of Public Health Code.

Moreover, cell lines from preimplantatory embryos can be collected if they are not viable or dead, according to the dispositions of article 16.2 of the *Ley 35/1998 sobre Técnicas de Reproducción Asistida* (Spanish Act 35/1998 on Assisted Reproduction Techniques). The living viable embryos are regulated by the dispositions of the Spanish Act 45/2003, of 21 November, which modifies Act 35/1998, of 22 November on Assisted Reproduction Techniques. According to the Act 45/2003 the only body with the capacity to collect cell lines and distribute them is the *Centro Nacional de Trasplantes y Medicina Regenerativa* (Spanish National Centre for Transplants and Regenerative Medicine)¹²⁶.

In France, the use of stem cell from embryo is regulated and submitted to specific autorizations from the authorities¹²⁷.

The Swedish act on biobanks devotes chapter 3, section 3 to this issue and establishes that tissue samples from a foetus shall not be collected and stored in a biobank without having the informed consent of the pregnant woman about the aim and purpose or purposes for which the biobank has been created. If the woman has deceased, the same procedure is applicable on her closest relative.

2.3.3.3. Tissue samples of deceased persons

The French Act on Bioethics of 2004 only allows the removal of tissues and cells, or the collection of human bodily products of a person whose death has been stated only if he/she not opposed before his/her death (article 1241.6).

In the Spanish Royal Decree 411/1996, the consent is presumed for the removal of human tissues of people who deceased without leaving an explicit opposition (article 8)¹²⁸. In the Spanish Royal Decree 2070/1999, of 30 December, on the activities of collection and clinical use of human organs, the consent is only presumed if the removal is carried out with therapeutic purposes¹²⁹.

In the British Human Tissue Act appropriate consent means that the consent was written before death; or the adult may appoint one or more persons to

¹²⁶ Spanish Act 45/2003, of 21 November, which modifies the Act 35/1988, of 22 November, on assisted reproduction techniques.

¹²⁷ Décret No. 2004-1024 du 28 septembre 2004 relatif à l'importation à des fins de recherche de cellules souches embryonnaires, aux protocoles d'études et de recherche et à la conservation de ces cellules.

¹²⁸ Spanish Royal Decree 411/1996, of 1 March, by which the activities related to the use of human tissues are regulated.

¹²⁹ Spanish Royal Decree 2070/1999, of 30 December, regulating the clinical collection and use of human organs and the territorial coordination of the donation and transplant of organs and tissues.

represent him/her after his/her death to grant his/her consent to the purposes of section 1 —removal, storage and use of tissues and organs—.

The collection of organs, tissues and other bodily parts, and in accordance to our exposition, is presumed to be granted by the subject in life, a criterion that is held by the Spanish legislation¹³⁰, but not shared by other institutions¹³¹.

¹³⁰ Article 5.2 of the Spanish Act 30/1979, of 27 October, on removal and transplant of organs: «The removal of organs or other anatomic pieces from deceased people can be carried out with therapeutic or scientific purposes, if there is no explicit opposition». Article 8 of the Royal Decree 411/1996: «The removal of human tissues from deceased people, can be carried out, if there is no explicit opposition of the deceased person, without delay and giving previous medical proof of the death».

¹³¹ Nuffield Council of Bioethics, *Human tissue and biological samples for use in research*, p. 25. It is advised not to collect samples from the deceased person with the only purpose of researching without having obtained the consent from relatives. This approach is not consistent with the fundament of donation, which is the (express or presumed) statement of the subject's will.

3. LEGAL DIFFERENCES BETWEEN RESEARCH AND DIAGNOSIS SAMPLES

3.1. INTRODUCTION

Collections of samples can have an inestimable value for the geneticist researcher¹³², because they represent the genetic diversity for the research. In addition, if they are collections of samples for diagnosis, having access to them means having human genomes of people diagnosed with a pathology and having the opportunity to compare the data to study the factors that originated the disease (e.g. let's think about on a bank of tumours removed from patients with some kind of cancer and whose samples from the biopsies have not been destroyed. The importance of having access to these samples for a researcher who is trying to find the implication of a gene on a specific cancer is clear).

The opportunity of using samples of this nature stored in the past for reasons beyond any future research is being questioned because of the continuous expansion of new lines of research. In fact, most ethical and legal controversies arise from the possibility of using these samples for different purposes to the original one.

In the case of DNA banks, sometimes the samples are donated by people for its storage or are stored as part of a research project. In these cases, people probably have given their consent to the storage of the material or they know the practices that are being carried out with the samples. However, as a matter of

¹³² As David King says, the DNA data bases are the best instrument for researches to carry out their scientific or statistical researches because of the number of registers that they contain, and the more specific the more useful the information will be. David KING, «DNA banks and the future of medical research», p. 6.

course doctors usually send samples for their storage in banks with pathology aims or for their mere preservation, as it is the case of tumour banks. Generally in these cases, there is no consent granted to use the samples for a different purpose, so, will it be possible to use them again without consent? The French Act on bioethics of August 2004 clearly establishes that the act of proceeding to the analysis of the genetic characteristics of a person with other purposes than medical or scientific research, without previous consent under the conditions settled in article 16.10 of the French Civil Code, has a fine of 15,000 € (article 226-25). In the following section we are going to study different situations.

3.2. DONATION OR TRANSFER OF THE SAMPLES FOR RESEARCH BY THE SUBJECT

The Spanish legislation establishes the possibility of removing samples of deceased people for scientific purposes¹³³, and presumes the donation in these cases¹³⁴.

In relation to the donation of a living subject, the Spanish legislation regulates the purposes of human use or assisted reproduction, and research, but we can't rule out donation for the specific purpose of research. The conditions are the following: «1. The collection of human tissues from a donor requires that the donor has been previously informed about the consequences of his/her decision and that the donor grants an express, free, conscious and uninterested consent»¹³⁵.

¹³³ «The collection of human tissues from deceased people shall be carried out with therapeutic or scientific purposes» (Article 6.2 of the Spanish Royal Decree 411/1996).

¹³⁴ «The removal of organs or other anatomic pieces from deceased people shall be carried out with therapeutic or scientific purposes, if they did not state expressly their opposition» (article 5.2 of the *Ley de Transplantes*, Spanish Act on Transplants); «1. The removal of human tissues from deceased persons, shall be carried out, if they did not state expressly their opposition, without delay and after medical verification of death. To prove the decease it is not essential to state cerebral death. 2. The opposition of the affected person to the removal of human tissues from his body, can be carried out in the from and by any of the means settled on article 8 of the Royal Decree 426/1980, of 22 February, which develops the Act 30/1979, of 27 October, on the Removal and Transplant of Organs.

¹³⁵ Human tissues cannot be collected from people who cannot grant their consent as required for mental disability, mental disease or for any other similar reason. The information shall be supplied by the doctor who is going to collect the tissues and he shall mention the somatic, physical or mental consequences and the eventual repercussions that the donation may have on his personal, family or professional life, as well as the benefits that the receptor may have after the grafting. The consent shall be written and signed by the donor and the aforementioned doctor. Under no circumstances shall the collection be carried out without the previous signature of this document. 2. The under aged can donate surgery wastes, of haematopoietic relatives and from his bone marrow. In this two cases the donation

Corresponding to the property of the sample, the Spanish legislation determines the subject's loss of ownership. The institution storing the sample has the rights on the sample, subject to the purpose or purposes of the donation.

According to the data protection Right, the consent of the subject to use the sample for research is required. A specific consent for each research is not compulsory, as it is not advisable to apply the regulation on clinical trials to this case.

In any case, the subject's consent is required to transfer his/her samples. If it is impossible to get, the samples should be rendered anonymous and transferred without identifiable data.

3.3. DONATION OR TRANSFER OF SAMPLE FOR RESEARCH NOT ATTRIBUTABLE TO THE SUBJECT

The donation and transfer are legal and there is no need to apply the principles of personal data protection, because the specific data protection act does not apply to anonymised data, as we have explained before.

3.4. DONATION OR TRANSFER OF SAMPLE FOR DIAGNOSIS ATTRIBUTABLE TO THE SUBJECT

In these cases the subjects abandons the sample and loses the ownership. The institution storing the sample owns the rights on the sample.

The new French act on bioethics is very clear on this topic and establishes that the removal of tissues or cells, or the collection of human bodily products of a living person with purposes of donation cannot be carried out unless the purposes are therapeutic, scientific, or of control of medical devices for «in vitro» diagnosis, quality control of medical tests, or in the framework of practices or technical control carried out on the mentioned materials by the French Agency of Health Security of Health Products. Additionally, this Act establishes that only the tissues

can be carried out only if there is a genetic relation between donor and receptor, and with a previous authorisation of his parents or tutors. In these cases the under aged donor has to be heard according to article 9.1. of the *Ley Orgánica 1/1996*, of 15 January, de *Protección Jurídica del Menor* (Organic Law 1/1996 on Children Legal Protection). 3. In the case where a surgery intervention is required for the collection of a tissue of a living donor, the written consent shall be formalised in the form and the conditions established in article 4 of the Royal Decree 426/1980, of 22 February. 4. The authorisation to collect human tissues will remain registered in the casa story of the donor» (article 7 of the Royal Decree 411/1996).

in a specific list —not adopted yet— can be removed for donation, or therapeutic purposes, excepting those tissues removed on the framework of a biomedical research (article 1241-1). It also establishes that the removal of tissues or cells different to haematopoietic cells collected from the bone marrow or the collection of bodily substances for donation with therapeutic purposes, or of control of medical devices for «in vitro» diagnosis, quality control of medical biology tests, or in the framework of practices or technical control carried out on the mentioned materials by the French Agency of Health Security of Health Products, according to the first paragraph of article 5311-2, cannot be carried out unless the donor, previously informed on the object of the removal, or the collection and the consequences and risks, has granted a written consent. This consent can be withdrawn at any moment, however, the conditions for granting the consent and for obtaining the authorisation established on article 1231-1 applies when the nature of the removal and the consequences for the donor justifies its application. In the case of the removal of haematopoietic cells collected from the bone marrow for donation and with therapeutic purposes cannot take place unless the donor has received previous information about the risks and the potential consequences of the removal and has granted his/her consent before the president French High Court (*Tribunaux de Grand Instance*) or the appointed Magistrate, which grants that the consent is free and clear.

3.5. DONATION OR TRANSFER OF SAMPLE FOR DIAGNOSIS NOT ATTRIBUTABLE TO THE SUBJECT

There is no controversy in this case, because the donation or transfer is legal and there is no need to apply the principles of personal data protection.

4. THE SAMPLE AND ITS FUTURE USE

4.1. THE RELATIONSHIP WITH THE PATIENT

Commercial and financial questions are also present when dealing with biobanks. In fact, the pharmaceutical and biotechnological industries which use samples for research process them afterwards to produce drugs or biotechnological products. Here we meet the question of the right of the source subject to receive financial gains from the commercialisation of the drug or product once it has been patented.

In terms of commercialisation we have two bioethical principles to consider; firstly the principle of altruism, which is in force in most legislations on organs transplant, in this sense, the source of the tissue or the organ can not receive an economic compensation because it is understood that the donor makes a «gift» to science and society. Secondly, the current system of values in our societies establishes that the human body and the parts of it should not be used for commercial transactions. This principle known as *res extracomercium* is based on the concept that the human being is an aim on itself and not a mean, this has been translated into the law of most countries prohibiting payments in exchange of blood donations, organ or tissue donations for transplant. The question which immediately arises is whether we can apply these two bioethical principles to the framework of biobanks.

4.1.1. Legal framework

The legal framework that we have to consider when studying this matter is integrated on the Directive 98/44/EC, on the legal protection of biotechnological

inventions, which has been transposed in five of the States of the EuroBiobank: Malta¹³⁶, Spain¹³⁷, Hungary¹³⁸, France¹³⁹ and recently Germany¹⁴⁰. The rest of the countries taking part on the project but which have not transposed the Directive have been denounced by the Commission before the European Union Court of Justice¹⁴¹. In fact, it is a controversial Directive which took more than ten years to adopt, and it was not warmly welcomed by all the countries of the Union. In October 1998 the Kingdom of the Netherlands filed an appeal¹⁴² (supported by Italy and Norway)¹⁴³ before the CoJEC, applying for the annulment of the mentioned Directive¹⁴⁴. Finally, and following the Advocate General¹⁴⁵ intervention, in October 2001, the CoJEC ruled out on the annulment of Directive 98/44/EC, rejecting the application of the Kingdom of the Netherlands.

We have to bear in mind article 21 of the Convention on Biomedicine of the Council of Europe which establishes that «*the human body and its parts shall not, as such, give rise to financial gain*». This article is based on the principle of human dignity. As established on the Explanatory Report, this article explains that the human body and the parts of it, as such, shall not give rise to financial gains. According to this, the organs and tissues, including the blood, shall not be bought or sold or give any kind of financial gain to the person from whom they have been

¹³⁶ The Patents and Designs Act 2000 (Chapter 417 of the Laws of Malta).

¹³⁷ Act 10/2002, of 29 April, which modifies the Act 11/1986, of 20 March, on patents, for the incorporation to the Spanish Law of the Directive 98/44/EC, of the European Parliament and of the Council, of 6 July, on the legal protection of biotechnological inventions.

¹³⁸ Act No. XXXIX. of 2002 (which modifies the Act XXXIII. of 1995) on the legal protection of biotechnological inventions. 2002. évi XXXIX. Törvény a találmányok szabadalmi oltalmáról szóló 1995. évi XXXIII. törvény módosításáról.

¹³⁹ Loi relative à la protection des inventions biotechnologiques. Loi n° 2004-1338 du 8 décembre 2004.

¹⁴⁰ Act on the protection of biotechnological inventions of 21 January 2005. Gesetz zur Umsetzung der Richtlinie über den rechtlichen Schutz biotechnologischer Erfindungen Verordnung über die Hinterlegung von biologischem Material in Patent und Gebrauchsmusterverfahren.

¹⁴¹ In fact, Italy, and by sentence pronounced by the European Community Court of Justice (Third Room), was compelled to transpose the Directive, so in this way, the appeal presented by Italy in which they claimed that it was not necessary to transpose the Directive given that to their legislation in force contemplated the regulations established in the Community text was rejected.

¹⁴² According to article 173 of the ECT (currently article 230 EC, after its amendment).

¹⁴³ The orders of the President of the Court of 3 May 1999, admitted the intervention of the Italian Republic and the Norwegian Kingdom supporting the aims of the Kingdom of the Netherlands.

¹⁴⁴ Case C-377/98, Netherlands v. Parliament and Council of the European Union, *DOCE*, No. C 378 of 5 December 1998, pp. 13-14.

collected or to a third party, a natural or legal person as, for example, a hospital or a research institute. However, technical works such as sample collection, tests, sterilisation, fragmentation, purification, storage, cultivation, transport, etc, derived from organs or tissues can give rise to a legal and reasonable financial compensation. Accordingly, this article does not ban the sell of medical or biotechnological products containing human tissues which have been processed, as long as the tissue itself is not sold. And, the article does neither ban that the person from whom the tissue has been collected receives a reasonable compensation to cover the expenses or the costs of hospitalisation, if this compensation is not a remuneration. This is what happens in the case of gametes, according to the *Comisión Española de Reproducción Asistida* (Spanish Commission for Assisted Reproduction)¹⁴⁶, the constraints of transport, loss of time, which happens when donating both sperm and oocytes, justify that the donation can and shall be compensated, in different levels, depending on the constraints and damages that may rise in each case. In fact, the report of this Commission takes into account the *Ley española de Técnicas de Reproducción Asistida* (Spanish Act on Assisted Reproduction Techniques) that defines gametes and pre-embryos donation as a «free, formal and secret contract between the donor and the authorised body», it also establishes that «donation will never have a lucrative or commercial nature»¹⁴⁷.

The Proposal for an Instrument on the use of archived human biological materials in biomedical research of the Council of Europe on its article 8¹⁴⁸ is true to the principle established on article 21 of the Convention on Biomedicine. The proposal establishes that often, biotechnological products have been developed from a biological sample, and in most cases it is difficult to determine the participation of a specific sample in the achievement of the final product, so it will

¹⁴⁵ The conclusions of the Advocate General, Sr. F.G. Jacobs, were public on 14 June 2001, relating to the mentioned action for annulment. After his legal analysis he dismisses each one of the arguments for the action putted forward by the Kingdom of the Netherlands. Opinion of advocate general, Jacobs. Case C-377/98 Kingdom of the Netherlands v European Parliament and Council of the European Union.

¹⁴⁶ COMISIÓN NACIONAL DE REPRODUCCIÓN HUMANA ASISTIDA (Spanish National Commission for Assisted Human Reproduction), *I Informe Anual* (I Annual Report), December, 1998, pp. 56 and ff.

¹⁴⁷ Art. 5, paragraph 1 and 3 of the Act 35/1988, of 22 November, on assisted reproduction techniques. BOE (Spanish Official Journal), No. 282, of 24 November 1988.

¹⁴⁸ Article 8 «Human biological materials and personal data within the scope of this instrument that are used in research shall not, as such, give rise to financial gain».

also be difficult to determine the amount which may correspond to the owner of the sample in the case of a potential commercialisation of the product. The writers of this Instrument consider that when the «profitable» cell line has been collected exclusively from an individual, some kind of compensation could be admissible. To avoid the commercialisation of the human body and other unfair situations, the only instrument to apply is a financial compensation as in the case of the donation of gametes. Further, it would be very difficult to determine if that participation has been «exclusive».

Moreover, in the EU Charter of Fundamental Rights¹⁴⁹ on article 3.2 it is expressly banned that human biological materials and personal data, as such, give rise to financial gain.

4.1.2. Can a product derived from a biological sample be patented?

The Directive 98/44/EC establishes that the human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions (Article 5.1). But for the purposes of the Directive inventions which are susceptible of industrial application shall be patentable if they concern an isolated element of the human body or produced by a technical process, even if the structure of this element is identical to that of a natural element; and the Directive assumes that the rights conferred by the patent do not extend to the human body or its elements in their natural environment. Therefore the possibility of patenting the isolated element from the human body or otherwise produced is not excluded from patentability, since it is the result of technical processes used to identify, purify, classify and reproduce it outside the human body, techniques which human beings alone are capable of carrying out and which nature is incapacitated of accomplishing by itself.

The grant of a patent on the invention derived from a biological sample shall be subject to the classical criteria of patentability, namely: novelty, inventive step and industrial application¹⁵⁰; and in these cases the Directive demands that the industrial application (utility) must be disclosed in the patent application as filed.

¹⁴⁹ OJEC, of 18 December 2000.

¹⁵⁰ A. MARTÍN URANGA, *La protección jurídica de las innovaciones biotecnológicas. Especial consideración de su protección penal* (Legal protection of biotechnological innovations. Special consideration to the criminal protection), Ed. Comares, Granada, 2003, pp. 388 and ff.

Any kind of invention shall meet not only these requirements, but it also shall be subject to other controls, known as traditional in the Right of patent, because they are classical exceptions in it: firstly, that *the publication or exploitation would not be contrary to «order public» or morality* (article 53 of the European Patent Convention) and secondly, that the *object is not* a plant or animal varieties or essentially biological processes for the production of plants or animals (article 53.b of the European Patent Convention). From an ethical-cultural point of view, the European culture has been considering the existence of limits to patentability, or the projection of the financial rights on the human body, focusing on the respect of human dignity. According to this, international¹⁵¹, European¹⁵² and national¹⁵³ regulations on patents deal with these issues establishing exclusive clauses for the «public policy», «order public», and even «morality»¹⁵⁴. The concepts of *order public* and morality are *undetermined legal concepts*, legal standards that shall be interpreted according to the common rules of each positive system of Law, which finally contain the ethical barrier among other contents¹⁵⁵. The problem is that a solid conception of these concepts may end being an obstacle for the technological

¹⁵¹ TRIPS article 27.2 allows «WTO Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect *order public* or morality (...)». This precept is also established on recital 36 of the Directive 98/44/EC.

¹⁵² Article 53 a) of the EPC «Exceptions to patentability. Europeans patents shall not be granted in respect of inventions the publication or exploitation of which would be contrary to «*order public*» or morality, provided that the exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all the Contracting States».

Article 6.1. of the Directive 98/44/EC «Inventions shall be considered unpatentable where their commercial exploitation would be contrary to *order public* or morality; however, exploitation shall not be deemed to be contrary merely because it is prohibited by law or regulation».

¹⁵³ Article 5.1.a) of the LP (Spanish Patents Act): «patents shall not be granted to inventions if its publication or exploitation would be contrary to *order public* or morality». This article lays down almost literally the disposition of article 53 of the EPC.

¹⁵⁴ A study on concepts for «*order public*» and «morality» in the U.K. patents system. E. ARMITAGE/I. DAVIS, *Patents and morality in perspective*, Common Law Institute of Intellectual Property, Londres, 1994, pp. 27 y ss.

¹⁵⁵ R.S. CRESPI, «Biotechnology patents and morality», *TIBTECH*, Vol. 15, April, 1997, pp. 123 and ff; D. BEYLEVELD/R. BROWNSWORD/M. LLEWELYN, «The morality clauses of the Directive on the legal protection of biotechnological inventions: conflict, compromise and the patent community», en R. Goldberg/J. Lonbay (Ed.), *Pharmaceutical medicine, biotechnology and European law*, Cambridge University Press, Cambridge, 2000, pp. 157 and ff; C.M. ROMEO CASABONA, «La protección jurídica del genoma humano y de las innovaciones biotecnológicas: la cuestión de su patentabilidad» (Human genome and biotechnological inventions legal protection: the question of their patentability), *ob. cit.*, pp. 80-81.

development of the nation. Moreover, regulations avoid giving a definition of these concepts. They are broad and open concepts which try to cover the different conceptions and interests of each country. We should try to reach an uniform concept for these terms and harmonise the European regulations on biotechnological inventions patentability¹⁵⁶, the risk that rises is the imposition of the concept of morality of the dominant state. However, we should explain that these concepts have to be interpreted *restrictively and not expansively*, because they are exceptions to patentability¹⁵⁷.

After the adoption of Directive 98/44/EC, it is established an orientation list of the non-patentable inventions, with the aim of providing to judges and national patent offices a guide to interpret the term *order public* and morality, however we cannot expect this list to be exhaustive. This orientation list excludes from patentability:

- Processes for cloning human beings;
- Processes for modifying the germ line genetic identity of human beings;
- Uses of human embryos for industrial or commercial purposes;
- Processes for modifying the genetic identity of animals, which are likely to cause them suffering without any substantial medical benefit to the mankind or to the animal and to the animals resulting from such processes.

So there is no mention to the prohibition of patentability of a product derived from a biological sample, as long as this sample meets the requirements of patentability and it is not contrary to the *order public* and morality, and that its object is not a plant, animal variety or essentially biological processes for the production of plants or animals. We cannot forget that there has been a decisive progress in the treatment of diseases derived from the isolation of elements of the human body and/or otherwise produced, treatments which result from technical processes for the collection of elements with a similar structure to the existing

¹⁵⁶ J.M. OTERO LASTRES, «La patentabilidad del material genético humano en el Derecho español vigente» (Patentability of human genetic material in the Spanish Law in force), *Law and the Human Genome*, Vol. II, Ed. Foundation BBV, Provincial Government of Biscay, 1994, p. 192.

¹⁵⁷ As the exception of *order public* is an extreme measure, it can neither rely on opinion polls nor on the rejection of the majority of the population, so the most advisable action is to grant the patent in case of doubt and let the legislator settle the limits and terms of use of the patent», G. PÉREZ BUSTAMANTE, «Patentes de invenciones biotecnológicas: un análisis jurídico-económico» (Patents of biotechnological inventions: a legal-financial analysis), *Law and the Human Genome Review*, No. 8, 1998, p. 173.

elements in the human body; and as a result we should promote the research for the collection and isolation of valuable elements for the production of treatment through a system of patents.

Nonetheless, the patent on inventions does not allow the owner to use the invention, the patent only allows the owner to prohibit third parties to exploit the invention with industrial or commercial purposes, and as a result the right of patentability shall not substitute or render ineffective national, European or international regulations which determine the limits and prohibitions, or organize the control of the research and the use or commercialisation of the results, particularly in terms of requirements for public health, security, environment and animal protection, preservation of genetic diversity and respect for certain ethical rules.

4.1.3. The question of consent as a requirement for patentability

Considering the regulations on biotechnological inventions legal protection, particularly Directive 98/44/EC, recital 26 deals with the need of having informed consent for patents on biological material of human origin and establishes that «where a patent application is filed, the person from whose body the material is taken must have had an opportunity of expressing free and informed consent thereto, in accordance with national Law».

Although the principle of informed consent has not been introduced in the Directive, it was present in the Plenary Session of the European Parliament in July 1997¹⁵⁸ that adopted several amendments to the Proposal of Directive on the first lecture. The only modification which the Commission¹⁵⁹ could not consider was the amendment 76, which proposed to introduce a new article 8 bis¹⁶⁰. The aim of this regulation was that the agreement or consent of the source person or legal representatives to the use of the biological material, and to the application for a

¹⁵⁸ Proposal for a Directive on the Legal Protection of Biotechnological Inventions of 16 July 1997, OJEC, No. C 286, of 22 September/July 1997, p. 87.

¹⁵⁹ Amended Proposal for a European Parliament and Council Directive on the Legal Protection of Biotechnological Inventions, introduced by the Commission, COM (97) 446 final, of 29 August 1997.

¹⁶⁰ In the second paragraph it is demanded that «when an application is made to patent human material, meanwhile, the application must contain the name and surname of the source person or his legal representative, and evidence of the use of the material and of the informed consent of the source person or legal representative to the patenting of their genetic material».

patent was a new specific patentability requirement for the invention of biological material of human origin¹⁶¹. This criterion was rejected because it was considered that the paragraph did not respect the requirements for personal data protection¹⁶². Summing up, what is left of that principle in the Directive 98/44/EC is the recital 26, where there is a direct reference to the regulation of each nation, although there is a tendency to preserve this right¹⁶³.

The recitals in the Directives have not a statutory value, but they are very useful to interpret the rules contained in the legal text. In fact, the consent could not be demanded as a patentability requirement, and the lack of consent or its lack of exactitude would not affect the validity of the patent granted, but it would be criticised¹⁶⁴, if we consider the controversy which arose in the USA in the case *Moore v. Regents University of California*, which we will further comment in this report. Neither the Directive nor the national transposition regulations 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.

In practice, the research group working with a sample ignores its origin, so these requirements shall be satisfied at the moment of collecting the sample in accordance to the regulations in force (see the abovementioned comments on informed consent). This statement cannot prevent the person object of the sample collection from asking for responsibilities to the one who has carried out the collection without consent, but it prevents the person from demanding financial gains derived from the patent on the product resulting from the sample; because the lack of consent would not be a cause of nullity of the patent.

¹⁶¹ P. SOLER MATUTES/J. SÁNCHEZ MOLERO, «La patente de genes humanos: examen especial de la propuesta de directiva comunitaria relativa a la protección jurídica de las invenciones biotecnológicas» (Human genes patents: especial examination to the proposal for an European directive on the legal protection of biotechnological inventions), *ob. cit.*, p. 8.

¹⁶² 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.

¹⁶³ J.D. FONDACARO, «Protecting patient's rights in the licensing of human cells», *Patent world*, No. 136, October 2001, pp. 18 and ff; P. SMAGLIK, «Tissue donors use their influence in deal over gene patent terms», *Nature*, No. 407, 2000, p. 821.

¹⁶⁴ See in details, A. MARTÍN URANGA, *La protección jurídica de las innovaciones biotecnológicas. Especial consideración de su protección penal* (Legal protection of biotechnological innovations. Special consideration to the criminal protection), *ob. cit.*, pp. 467 and ff. D. BEYLEVELD, «Regulating morality through patent law. Critique of the EC Directives», *Law and the Human Genome Review*, No. 12, January-June 2000, pp. 160 and ff.

Respecting the free and informed consent of the source subject involves providing specific information, particularly in the case of a patent application. This means that the subject shall know that the part of the body which has been donated, even if it contains genetic information, can be patented if all the patentability requirements are met. (novelty, inventive step and industrial application). This is a complex problem, because this means that somebody can get financial gains through the patent, which derives from the collaboration of a mainly altruistic act¹⁶⁵.

4.1.4. Ownership of the product patent derived from the sample

Formally, the owner or owners of the Patent are those who have filed the corresponding application to register the product at the Patent Office. This ownership gives all the property rights granted by the patent and the holder will generally be the applicant or applicants.

On the contrary, the inventor shall have the right, vis-à-vis the applicant for or owner of a patent, to be mentioned as such (article 62 EPC).

Any natural or legal person, and any company owned by a legal person has the right to file national or European patent applications, in accordance to the applicable law. In other words, the inventor (or co-inventor) or the assignees (in case the inventor has deceased) can file a patent application. The employer is the owner of the invention if the inventor is the employee of the company, and the invention is carried out by the inventor while his contract, work or services relation with the company is in force, and his invention is the result of a research activity which explicitly or implicitly constitutes the purpose of the contract. The employee, author of the invention, will only have right for an extraordinary compensation if the personal contribution for the invention and the importance of it for the company obviously exceeds explicitly or implicitly the content of the contract or the work relation. This principle is settled in the *Ley española de patente* (Spanish Patent Law) of 1986 (article 15), but it is a principle which has been accepted by most regulations.

¹⁶⁵ Opinion of the Group of Advisers on the Ethical Implications of Biotechnology mentioned in O. QUINTANA, «La patentabilidad de las invenciones biotecnológicas: consideraciones éticas» (Patentability of biotechnological inventions: ethical considerations), *Los retos de la genética en el siglo XXI: genética y bioética* (Challenges of genetics in the XXIst century: genetic and bioethic), M. Casado/R. González-Duarte (ed.), Ediciones Universidad de Barcelona, 1999, pp. 147-148.

If it is a worker of a public centre of research in Spain, since 2002 there is a specific regulation, Spanish Royal Decree 55/2002¹⁶⁶ which lays down the exploitation and donation conditions for the inventions carried out by the officials or by the personnel which develop research activities in some public bodies of research such as the *CSIC* (High Council of Scientific Research of Spain) and the *Instituto de Salud Carlos III* (Carlos III Health Institute of Spain), among others. In these cases, the public bodies of research are the owners of the inventions carried out by the research personnel during the development of activities included among his functions. The research personnel who may carry out any invention has to inform about it to the head or the president of the body immediately, once obtained the corresponding results. In addition, 20% of the benefits resulting from the exploitation of the aforesaid rights are to the public body of research. This distribution of profits is interesting because according to the legal text a third of the benefits are to the public body, a third for the author or authors of the invention and a third will be distributed according to the criterion established by the Board of the body, considering the importance and the transcendence of the patent, the benefits which may arise from it and the participation and collaboration of the personnel. It is a way to promote research in public bodies of research.

The right of ownership of the patent derives from the invention step. In the case of inventions containing biological samples, the act of invention corresponds to whom may collect, purify or process the sample by any means involving an inventive step, and that step gives the right to apply for the invention. Finally, the donor of the sample does not take part in the inventive step and consequently he would not have the right to be a part of the patent resulting from the sample¹⁶⁷.

4.1.5. Commercialisation of samples

Acts to dispose of the human body can obviously take place, and they can affect the integrity of it or not; in principle the donor is excluded from financial benefits, as a result of the extra-commercialisation nature of the human body and of the denial to have a real property right on it.

¹⁶⁶ Spanish Royal Decree 55/2002, of 18 January, on the exploitation and donation of inventions carried out in public research bodies, according to article 20 of the Spanish Act 11/1986, of 20 March, on Patents.

¹⁶⁷ Same opinion, Nuffield Council on Bioethics, *Human tissue. Ethical and legal issues*, pp. 94-95, London, 1995.

Our starting point is the criterion defined before: the sample is a thing, but it has to be clearly established that the recognition of the right of property does not imply the commercialisation of the sample without limits; in fact, there can be settled limits according to its human origin and to the difference between parts of the body. These limitations are duly laid down on article 5 of the Italian Civil Code according to which the acts to dispose of the human body are legal as long as they are not contrary to the law, *order public* and morality.

All Member States of the European Union follow the principle that donations of human tissues must be free, following the example of blood, and this rules out any payment to the donor. However, the donor may receive compensation for the constraints associated with tissue removal (e.g. travel expenses, loss of earnings, etc.). There are two different arguments on this matter¹⁶⁸.

1. Some parties maintain that for the sake of fairness, when the tissues become even indirectly a source of profit, donors should be paid. Furthermore, donor's remuneration might increase the supply of tissues.

The processing and conversion of tissues involve costs which may justify their commercial sale, in the same way as blood derivatives. The commercialisation of human tissues has the added advantage, according to the supporters, of encouraging the industry to invest in areas which will give a greater offer of tissues on the market. This argument could be supported in relation to «engineered» tissues which require sophisticated industrial processing techniques.

2. However, the arguments in favour of the altruistic nature of tissue donation (like organ donation) have prevailed. They are based on a regard for solidarity. Also they are inspired by the desire to avoid the human person being regarded as an object (a source of organs and tissues), as well as to avoid all risk of exploitation of the most underprivileged who might be led, in doubtful conditions of health, to donate tissue exclusively or primarily for financial reasons.

This last argument does not avoid that the good will to donate deserves some kind of recognition and support. In fact, the payment of some expenses may be

¹⁶⁸ EUROPEAN GROUP ON ETHICS IN SCIENCE AND NEW TECHNOLOGIES TO THE EUROPEAN COMMISSION, *Opinion Ethical Aspects of Human Tissue Banking*, No. 11, 21 July 1998, p. 6.

¹⁶⁹ This aspect is regulated on paragraph §10 of the Gesetz zur Regelung des Transfusionswesens (Transfusionsgesetz) of 1 July 1998 (published in the Official Journal Bundesgesetzblatt BGBI I, S. 1752).

admitted, as it is established in the German Act on blood donations¹⁶⁹ and it is settled by the Spanish National Commission of Human Assisted Reproduction. Currently, there is a broad tendency to compensate the expenses derived from donation. The payment has to be a real «compensation» and not a «remuneration» in order to execute the principle of non-commercialisation of the human body and the parts of it, and to avoid diminishing the ethical principle of solidarity. This criterion has been defined by the joint paper by the French and German National Ethics Councils of 2 October 2003¹⁷⁰. In any case, we have to avoid organizations of public or private founding turning to excessive expenses.

The solution proposed by some, such as the European Group on Ethics¹⁷¹ of establishing that tissue banking activities should be limited to public health institutions or non-profit-making organisations. In such case, this means that the delivery price of the tissues only covers the bank's expenses relating to the tissues in question. Nevertheless, given the current state of development of the sector, it is difficult to exclude tissue banking activities of pharmaceutical and biotechnological industries. These industries are very interested on this sector because of the results that they can obtain, and even public bodies can be interested in obtaining some kind of financial gain which allows them to continue with their researches and even to finance new lines of research.

It seems that according to the current state of the art on the matter and with the aim of reaching a fair balance between the source subject and third parties (pharmaceutical or biotechnological companies) the most sensible solution is the benefit sharing instead of individual remuneration. In fact, in this same line the International Declaration on Human Genetic Data of the UNESCO determines in article 19 that benefits resulting from the use of human genetic data, human proteomic data or biological samples collected for medical and scientific research should be shared with the society as a whole and the international community. Benefits resulting from the application of this principle shall take any of the following forms:

- special assistance to the persons and groups that have taken part in the research;
- access to medical care;

¹⁷⁰ GERMAN NATIONAL ETHICS COUNCIL, *Opinion Biobanks for research*, Berlin, 2004, p. 77 and 103.

¹⁷¹ EUROPEAN GROUP ON ETHICS IN SCIENCE AND NEW TECHNOLOGIES TO THE EUROPEAN COMMISSION, *Opinion Ethical Aspects of Human Tissue Banking*, *ob. cit.*, pp. 6 y 10.

- provision of new diagnostics, facilities for new treatments or drugs stemming from the research;
- support for health services;
- capacity-building facilities for research purposes;
- development and strengthening of the capacity of developing countries to collect and process human genetic data, taking into consideration their specific problems;
- any other form consistent with the principles set out in this Declaration;
- preferential access to therapies developed by virtue of their contributions to biobanks seems to be one of the criteria most commonly shared¹⁷²;
- participation in therapies as established by the HUGO Ethics Committee on its Statement of benefit-sharing of 2000¹⁷³, which recommends that profit-making entities dedicate a percentage (e.g. 1% - 3%) of their annual net profit to healthcare infrastructure and/or to humanitarian efforts.

In any case, the national regulations and the international treaties can establish limits relating these issues. Though, the refusal to the participation of the source subject on the financial gains arising from the commercialisation of the product collected from the biological sample is unanimous.

4.1.6. A real case: comments on the case Moore v. Regents of the University of California

In 1990 the Supreme Court of California had to decide on the case Moore v. Regents of the University of California¹⁷⁴. In October 1976 Mr Moore was admitted in the Medical Centre of the University of California with a rare case of

¹⁷² Joint paper by the French and German National Ethics Councils, GERMAN NATIONAL ETHICS COUNCIL, *Opinion Biobanks for research*, Berlin, 2004, p. 103.

¹⁷³ <http://www.hugo-international.org/hugo/benefit.html>

¹⁷⁴ *Moore v Regents of the University of California* [15 USPQ2d 1753] (California Supreme Court, 9th July 1990). This decision appears in I. KENNEDY/A. GRUBB, *Medical Law. Text with materials*, Second edition, Ed. Butterworths, London, 1994, pp. 1111-1128. And in *EIPR*, November 1990, p. D-223.

A commentary about this decision in J.B. PROWDA, «Moore v. the regents of the university of California: an ethical debate on informed consent and property rights in a patient's cells», *Journal of the patent and trademark office society*, Vol. 77, August, 1995, pp. 611 and ff; D. BEYLEVELD/R. BROWNSWORD, *Human dignity in bioethics and biolaw, ob. cit.*, pp. 195 and ff.

leukaemia (hairy-cell leukaemia). On the basis of this pathology, Dr Golde recommended to remove the spleen. Moore granted his consent to the operation, which was performed successfully. At the same time, Dr Golde realised that Moore's organism produced substances liberated by T lymphocyte and associated with the performance of the immunological system: lymphokines in very high levels. The hyper-production of that substance, usually scarce, enables the isolation and the artificial production of it in an industrial scale. This would represent large commercial and scientific gains. But neither Dr Golde nor his assistant Dr Quant informed Moore about the issue. Golde used the spleen cells and other substances collected from Moore to develop a cell line which he patented in 1981, jointly with Quan —MO cells¹⁷⁵—. The patent covered many methods to use Moore's cell line and to produce lymphokines. In 1982 under several agreements they granted the right for commercial exploitation to Genetics *Institute* and to *Sandoz* pharmaceutical laboratories.

In 1983 Golde asked Moore to sign an informed consent file related to the use of his cells for scientific research, introducing the file as a mere formality. The Doctor did not tell him anything about the commercial value of the biological material. Moore withdrew the consent¹⁷⁶. This is how the controversy on the ownership of Moore's biological materials started, and the following right to take part in the financial gains derived from that ownership¹⁷⁷.

But in 1990, the judgement of the Supreme Court of California put an end to the case reforming the precedent statement and refusing Moore's demand. Doing so, the Court understood that Golde had caused damages to Moore¹⁷⁸, but the court held that there was no right of ownership of biological materials because we cannot consider without limits the right of property over collected parts of the human

¹⁷⁵ US patent No. 4,438, 032.

¹⁷⁶ Mainly because he suspected something, so he contacted a lawyer who investigated the cell line patented by Golde and the financial gains arising from it.

¹⁷⁷ Moore's demand was refused at first instance, but in 1988 it was accepted by the Court of Appeals of California, which recognised Moore's right of ownership and his right to take part in the utilities. *Moore v Regents of the University of California et al.* California Appeal Court, 2 Dist., 21 July 1988.

«The Supreme Court of California granted damages to Moore against the University and against the companies which had patents on cell lines derives from tissues of this patient», F. VICENT CHULIA, *Compendio Crítico de Derecho Mercantil (Critical compendium on commercial law)*, ob. cit.

¹⁷⁸ Who breaking the relation doctor-patient, had financially exploited Moore's cells without his informed consent.

body¹⁷⁹. Thus Moore's participation in the gains was refused by the Court, not only because of the inexistence of the right of ownership, but also because a financial compensation would damage human dignity. Finally, the Court decided in favour of a personal action, which leads to the compensation for damages, instead of a property action¹⁸⁰. Even though there were dissident and relevant opinions about the case¹⁸¹.

The question is that there is no answer for one of the most controversial issues: the ownership of tissues, claimed by Mr Moore. On one hand, the Court holds that Moore does not own the materials because they are only subject to non-profit acts of autonomy. But on the other hand, there is no mention to Golden's right of ownership on the tissues, the only rights that he has are patent rights over his invention. That is the reason why the Court leaves a loophole of huge importance, not establishing who has the right of property of the biological material.

For other authors, instead of trying to solve the problem of ownership of the tissues, we should think about the question of the right to take part in the benefits arising from them, and doing so the only issue which is unquestionable in Moore's

¹⁷⁹ «The California Supreme Court, held that Moore might have a case of fiduciary breach but not of property conversion», A.M. CAPRON, «Parenthood and frozen embryos: Moore than property and privacy», *Hasting Centre Report*, Vol. 22, No. 5, 1992, p. 32.

¹⁸⁰ The High Court had two different types of actions to consider, one of *personal nature*: based on the failure to have the informed consent and on the break of the relation between doctor-patient, and the other of *patrimonial nature*, based on the rights of ownership of Mr Moore on his bodily elements.

To some authors such as DWORKIN and KENNEDY the opinion of the majority is less satisfactory than the opinion of the minority of the Court. The opinion of the majority of the Decision of the Supreme Court of California, the main decisive element was that the repartition of utilities could affect the research and the development of pharmaceutical products. There is a fear of decay of the commercial incentives for research institutions and pharmaceutical companies which is a risk for the research itself. The other decisive element was the acknowledge that the human body has a value which cannot be reduced to the market value, as such reduction will damage the dignity of the human being. G. DWORKIN/I. KENNEDY, «Human tissue: rights in the body and its parts», *ob. cit.*, p. 307.

¹⁸¹ Firstly, the opinion held by Broussard. To him in the very moment where the parts of the body are goods which flow in the market, there is no reason to deny Moore's legal interest and take advantage of that. According to Broussard the human tissues are goods, and the question is not to determine if the materials can be owned by somebody, but who should have the legal control over those goods.

The other dissident opinion by Judge Mosk, criticises the decision of the Court because it considered only the financial value of human tissues, ignoring other values related to the body.

case is the gain achieved in the pharmaceutical industry¹⁸². In this sense it has been proposed to pass an act on the grant of licenses for sharing the gains with the person that has made possible the research¹⁸³.

Summing up, considering the parts and products of the body as goods which can be objects of commerce could be regarded as a «commercialisation» of the human body and an offence to the human dignity. And it is quite unusual to find an individual with cells containing unique properties, which after their biological transformation, could develop commercially exploitable products. In those cases, if the patient does not take part in the gains he will feel exploited.

¹⁸² «The way of dealing the question is of the type «all or nothing»: if there is a right of ownership, there are financial gains; and if the ownership does not exist, we cannot even think about utilities. And there is no intermediary solution». M. TALLACCHINI, «El cuerpo y sus partes. La ubicación jurídica de los materiales biológicos humanos» (The body and its parts. The legal nature of the human biological material), *Medicina y Ética (Medicine and Ethics)*, Vol. X, No. 1, January-March, 1999, pp. 60-61.

¹⁸³ B. HOFFMASTER, «Between the sacred and the profane: bodies, property and patents in the Moore case», *Intellectual Property Journal*, Vol. 7, pp. 115-148.

5. CONCLUSIONS AND RECOMMENDATIONS

1. The collection of biological samples with purposes of biomedical research shall be carried out only with previous and express consent from the source subject. If there is no opposition from the source subject, the biological samples can be used for biomedical research even if they were collected with other purposes. In that case, the sample shall be rendered anonymous.

Samples can also be collected from minors and incapacitated with purposes of biomedical research, if the following conditions are met:

- a) that the measures required to guarantee the minimal risks are adopted;
- b) that the research shall give relevant knowledge about the disease or the situation of the research purpose, with vital importance to understand, alleviate or cure it;
- c) that these knowledge cannot be acquired by other means;
- d) that there are guarantees about the correct grant of the consent.

2. The source subject has to receive the following information before giving his consent for the processing of a biological sample with purposes of biomedical research which are not going to be rendered anonymous:

- purpose of the research to which he is granting the consent;
- expected gains;
- potential constraints, such as the need of further samples;
- identification of the responsible of the research;
- right of withdrawal of the consent and the effects of doing so (destruction or anonymisation of the sample). These effects are not extended to the data resulting from researches which already have taken place;

- period during which the sample is expected to be stored, which may be unlimited; and with mention of the conservation in a bank.
- destiny of the sample when the research concludes: dissociation, destruction or further research, in that case with consent;
- guarantee of confidentiality of the collected data. It shall be specified who will have access to personal data;
- advise on the possibility of disclosure of the information about his health condition resulting from the genetic analysis of the biological sample, as well as on the right to decide about its disclosure;
- advise on the implications of the information which may be disclosed to his relatives and the convenience of disclosing that information;
- how to contact him in case of emergency.

3. The consent shall be granted specifically for a concrete research. If a specific consent is granted for the use of the sample, this can only be used in the agreed terms, and the sample can be processed with a different methodology without the need of a new consent, if the purposes are still the same.

Secondly, there are general consents for any kind of medical research. To this end, one consent is enough to carry out any kind of research and the source subject may establish the limits that he consider appropriate.

The consent can be withdrawn at any time. The withdrawal will be translated into the destruction or anonymisation of the sample. These effects do not affect the data resulting from previous researches.

It is not advisable to grant a consent which is too broad where by any kind of genetic information can be obtained from the sample in any scientific research because it is an important loss of control over personal data for the subject. The blanket consent can be combined with the specific consent for particular types of researches according to the criteria determined by the Committee in charge of controlling these researches. And this consent shall always be preceded by adequate information on the voluntary nature of the collection of the sample, analysis, the use of the data, the right of the subject to access to the information, the right of confidentiality of the results, the unexpected discoveries and the subject's decision in that case, the right to grant donations, the exclusion from the financial gains derived from the commercialisation of the product developed from the sample, etc.

The observation period of the research may be long, so it is difficult to determine several questions at the moment of collecting the sample such as the

kind of analysis to carry out, or if it will require a new consent for a further analysis. Sometimes this may result to be very problematic, because the subject may have deceased. As a result, it seems reasonable that in the epidemiological studies there shall be some flexibility when dealing with the consent, always protecting the rights and guarantees of the source subject. Additionally, in any case it is advisable that the ethical committees evaluating a research of this nature, shall deal with it trying to reach the most reasonable solution without setting unnecessary obstacles.

4. The under aged patient who emotionally and intellectually is able to understand the scope of the intervention, as well as the purposes of the biomedical research can grant his/her own consent. When there is a lack of such capacity, the consent has to be granted by the legal representatives, but the minor's opinion has to be considered, attending to his/her personal situation, particularly when they are over 12 years old.

5. When the person does not have capacity to grant his/her consent, the consent shall be granted by his/her legal representative. This consent shall reflect the supposed wish of the subject. However, when the subject's conditions allow him/her to understand the scope of the intervention, as well as the purposes of the research, he shall grant his/her consent for the collection of the biological sample, after receiving all the required information adapted to his level of understanding.

6. The source subject has the right to access the genetic data of personal nature obtained from any research with his/her biological sample according to the regulations on personal data protection.

7. The source subject shall be informed on the genetic of personal nature obtained from any biomedical research in accordance to the terms in which he/she granted his/her consent. The right not to know of the genetic data obtained during the biomedical research, and the right not to know of the unexpected discoveries which may arise. However, he/she will be informed when the information is required to avoid causing a serious damage to the health of his/her biological relatives.

8. The personnel who access the genetic data developing their functions is subject to the duty of medical secret. Genetic data of personal nature can only be provided to third parties only with the grant of an express and written consent from the subject.

9. The subject has the right to decide about the destiny of the collected sample, no matter which was the purpose of the collection. In case it is preserved,

the subject has to be informed on the conditions of preservation. The samples can always be preserved for the purposes which justified their collection. If there is no opposition from the source subject, the samples can be preserved and used for legal purposes different to those which justified their collection. In those cases, the anonymisation is required.

10. It is legal to transfer or donate biological samples stored in a hospital to another centre with research purposes. If the sample is not rendered anonymous it is required to have the specific consent of the source subject. In cases of rare diseases, it is advisable to carry out strict processes of anonymisation. The grantee can keep the sample during the period of time required to reach the purposes of the transfer. Once the research for which the sample was transferred has concluded, the assignee shall give it back or destroy it, according to what has been agreed. The donor which recovers the sample can keep it or destroy it according to the purpose for which the consent of the subject was granted. If the consent granted a general use of the sample for research, the grantee can keep it for this purpose.

11. The transfer of samples from one country to another is only possible when in the recipient country the levels of protection are similar to those of the donor country. In addition, there is an intense global interchange in the field of cellular and histological therapies and because of that we should have global regulations. This situation demands the EU to make an effort to promote a higher level of protection with the aim of safeguarding the public health in terms of quality and security of tissues and cells.

12. According to the regulations in force it is possible to patent a product derived from a biological sample, if the product meets the three requirements of patentability and if it is not contrary to the *order public* and morality, and its object is not a plant, animal varieties or a mainly biological procedure to obtain plants or animals. And the utility or industrial application of the invention has to be expressly stated in the patent application.

13. The consent of the source of the sample is not a requirement for patentability, and the lack or inaccuracy of the consent does not affect the validity of a patent granted. This does not prevent that the person from whom the samples were collected without his/her consent can ask for liabilities to those who collected the samples without his/her consent, but not in the field of financial gains derived from the patent of the product processed from his/her sample.

14. The right of ownership over a patent derives from the act of invention. In the case of inventions containing biological samples, the act of invention is from

who collects, purifies and processes the sample by some mean which assumes the inventive step, and this intervention confers the right to apply for the invention. In other words, the source subject of the sample does not take part in the act of invention and as a result he would not have the right to take part in the patent derived from the sample, and it will be very difficult to measure his participation. This does not mean that the expenses from donation are not going to be satisfied. Further, this amount has to be an effective «compensation» and not a «remuneration» to avoid exceeding the principle of no-commercialisation of the human body and parts of it, and to avoid reducing the ethical principle of solidarity. Though, in these cases the most appropriate solution is the benefit sharing which can take one of the following forms: especial assistance to people or groups of people who have taken part in the research; access to health care, new diagnosis, facilities and services to provide new treatments or medical products derived from the research; access to therapies developed thanks to the contributions of the source subject to the biobank, etc.

15. In the case of scientific publications resulting from researches with identifiable samples, the most advisable is to render the data anonymous; if it is not possible the results can only be published with the consent of the source of the sample or if the person has not the capacity to grant his consent, an adequate authorisation shall be required. These measures are not required for the use of non identifiable samples, the opposite would be completely impossible.

As we have stated in this report, and as the commented joint paper by the French and German National Ethics Councils¹⁸⁴, the ethical and legal challenges raised by biobanks are of different nature, they claim a proper and new legal framework applicable on a national and international levels. In fact, the source subjects of samples that somehow contribute to the development of science, shall be protected by a proper regulation which avoids a bad use of personal data. At the same time, the future framework has to be flexible under any circumstances that are not an obstacle for the technical progress of biobanks and which is really important according to current data. So, it is necessary to adopt a regulation on the subject matter which considers both legal interests and which regulates the key issues that we have dealt with in this report.

¹⁸⁴ GERMAN NATIONAL ETHICS COUNCIL, *Opinion Biobanks for research, ob. cit.*, pp. 98-99.

6. APPENDIX

6.1. REGULATION

6.1.1. International Regulation

- International Declaration on Human Genetic Data. UNESCO. Adopted, the 16 October 2003.
- Universal Declaration on the Human Genome and the Human Rights. UNESCO. 11 November 1997.
- Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine. Council of Europe. 4 April 1997.
- Additional Protocol to the Convention on Human Rights and Biomedicine concerning transplantation of organs and tissues of human origin. Council of Europe. 24 January 2002.
- Recommendation (92) 1 of the Council of Europe, on the use of DNA analysis on the framework of criminal justice system,
- Recommendation (92) 3 of the Council of Europe, on Genetic Testing and Screening for Health Care Purposes
- Recommendation (97) 5 of the Council of Europe on the protection of medical data.

6.1.2. European regulation

6.1.2.1. *European regulation*

- European Patent Convention. Munich. 5 October 1973

6.1.2.2. Regulation of the European Union

- European Union Charter of Fundamental Rights. December 2000.
- 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.
- Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions.
- Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.
- 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.

6.1.2.3. Regulation of the Member State

Estonia

- Human Genes Research Act of 2000.

France

- Act No. 78-17, 6 January 1978 on informatic and liberty modified by Act No. 2004- 801, 6 August 2004 on protection of person for treatment of personal data (Protection des personnes physiques à l'égard des traitements de données à caractère personnel).
- «Huriet» Act of 20 December 1988 on clinical trials.
- Act No. 94-653, 29 July 1994, on the respect of the human body. Modified by Act No. 2004-800 on Bioethics of 6 August 2004.
- Act No. 94-654, 29 July 1994, on donation and use of elements and products of the human body, on assisted reproduction techniques and on prenatal diagnosis. Modified by Act No. 2004-800 on Bioethics of 6 August 2004.
- Act No. 2002-303, 4 March 2002 on right of the patient and quality of health system.

- Act No. 2004-800 on Bioethics of 6 August 2004.
- Act No. 2004-1338 related to legal protection of biotechnological inventions of 8 December 2004.

Germany

- Embryo Protection Act (Embryonenschutzgesetz) of 13 December 1990.
- Gesetz zur Regelung des Transfusionswesens (Transfusionsgesetz) Date: 1 July 1998 (published in the Official Journal Bundesgesetzblatt BGBI I, S. 1752).
- Stem Cell Act (Stammzellgesetz) of 28 June 2002.
- Federal Data Protection Law de 1 de enero de 2003.
- Law on legal protection of biotechnological inventions. 21 January 2005. Gesetz zur Umsetzung der Richtlinie über den rechtlichen Schutz biotechnologischer Erfindungen Verordnung über die Hinterlegung von biologischem Material in Patent und Gebrauchsmusterverfahren.

Hungary

- Act No. XLVIII of 2003 (modifying the LXIII of 1992) on personal data protection. 2003. évi XLVIII. Törvény a személyes adatok védelméről és a közérdekű adatok nyilvánosságáról szóló 1992. évi LXIII. törvény módosításáról.
- Act No. XXXIX. of 2002 (which modifies the Act XXXIII. of 1995) on the legal protection of biotechnological inventions. 2002. évi XXXIX. Törvény a találmányok szabadalmi oltalmáról szóló 1995. évi XXXIII. törvény módosításáról.
- Act No. VI. of 2002 on implementation of Biomedicine Convention of the Council of Europe. Törvény az Európa Tanácsnak az emberi lény emberi jogainak és méltóságának a biológia és az orvostudomány alkalmazására tekintettel történő védelméről szóló, Oviedóban, 1997. április 4-én kelt Egyezménye: Az emberi jogokról és a biomedicináról szóló Egyezmény, valamint az Egyezménynek az emberi lény klónozásának tilalmáról szóló, Párizsban, 1998. január 12-én kelt Kiegészítő Jegyzőkönyve kihirdetéséről.

Italy

- Legge 675/1996 de 31 de diciembre sobre la tutela delle persone e di altri soggetti rispetto al trattamento dei dati personali.

- Legal decree number 282 of 30 June 1999 on «Dispositions to guarantee the privacy of the personal information in the health field». Decreto legislativo. N° 282 de 30 julio de 1999 Disposizioni per garantire la riservatezza dei dati personali in ambito sanitario. («Disposiciones para garantizar la privacidad de información personal en el ámbito de la salud»). Decreto legislativo. N° 282 de 30 julio de 1999 Disposizioni per garantire la riservatezza dei dati personali in ambito sanitario.
- Legge del 06/10/1998 n. 344, differimento del termine per l'esercizio della delega prevista dalla legge 31 dicembre 1996, n. 676, in materia di trattamento dei dati personali.

Malta

- The Patents and Designs Act 2000 (Chapter 417 of the Laws of Malta).
- Malta Data Protection Act (Chapter 440) of 15th July 2003.

Slovenia

- Medicinal products and medical devices Act. 30 november 1999.
- The removal and transplantation of human body parts for the purposes of medical treatment act. 27 January 2000. Zakon o odvzemu in presaditvi delov cloveškega telesa zaradi zdravljenja (ZOPDCT).
- Blood Supply Act (ZPKrv). 30 May 2000.
- Healthcare Databases Act. 11 July 2000. Zakon o zbirkah podatkov s področja zdravstvenega varstva (ZZPPZ).
- Personal Data Protection Act (ZVOP-1). 15 July 2004.

Spain

- Act 11/1986 on Patents, 20 March.
- Act 35/88 on assisted reproduction techniques.
- Act 42/88 of 28 December, on donation and use of human embryos and foetuses or of their cells, tissues or organs.
- Organic Law 15/1999 of 13 December on personal data protection.
- Act 10/2002, of 29 April, which modifies the Act 11/1986, of 20 March, on patents, for the incorporation to the Spanish Law of the Directive 98/44/EC, of the European Parliament and of the Council, of 6 July, on the legal protection of biotechnological inventions.

- Act 41/2002, of 14 November, a basic regulation of the autonomy of the patient, and of the rights and duties of providing information and clinical documentation.
- Act 45/2003, of 21 November, which modifies Act 35/1998, of 22 November on Assisted Reproduction Techniques.
- Royal Decree 411/1996, of 1 March which regulated the activities relating the use of human tissues.
- Royal Decree 2070/1999, of 30 December, on the activities of collection and clinical use of human organs.
- Royal Decree 55/2002, of 18 January, on the exploitation and donation of inventions carried out in public research bodies, according to article 20 of the Spanish Act 11/1986, of 20 March, on Patents.
- Royal Decree 223/2004, of 6 February, which regulates the clinical essays with drugs.

Sweden

- Biobanks Health Care Act of 23 of May 2002 (2002:297). Lag (2002:297) om biobanker i hälso- och sjukvården m.m.)

United Kingdom

- The Human Tissue Act of 15th november 2004.

6.1.2.4. Regulation of Non Member States

Island

- Act on a Health Sector Database of 1998.

Norway

- Act on Biobanks No. 12 of 21st of February 2003.

6.2. CASE-LAW

- Judicial Decision of the Provincial Court of Vizcaya, Spain, of 21 June 2000.
- Judicial Decision of the High Court of Justice of Cantabria, Spain, of 16 May 2001.

6.3. OTHER DOCUMENTATION: OPINIONS AND GUIDELINES

Australia Law Reform Commission, *Essentially yours: the protection of human genetic information in Australia*, 2003.

Comité Consultatif National d'Éthique pour les Sciences de la Vie et de la Santé, *Avis sur l'application des tests génétiques aux études individuelles, études familiales e études de population*. Dictamen de 24 de junio de 1991.

Comité Consultatif National d'Éthique pour les sciences de la Vie et de la Santé, *Avis sur l'avant-projet de loi portant transposition, dans le code de la propriété intellectuelle de la directive 98/44/CE du Parlement européen et du Conseil, en date du 6 juillet 1998, relative à la protection juridique des inventions biotechnologiques*, Núm. 64, 8 juin 2000.

Comité Consultatif Nacional d'Éthique pour les Sciences de la Vie et de la Santé, *Problèmes éthiques posés par les collections de matériel biologique et les données d'information associées: biobanques, biothèques*, Avis, núm. 77 de 20 de marzo de 2003.

Commission of the European Communities. Communication from the Commission. Towards a strategic vision of life sciences and biotechnology: consultation document. Brussels, 4 september 2001, COM (2001) 454 final.

Commission de l'éthique de la science et de la technologie de Québec. *Les enjeux éthiques des banques d'information génétique: pour un encadrement démocratique et responsable*. Avis. 2003.

Commission of the European Communities. *Quality of life and management of living resources. Survey on opinions from national ethics committees or similar bodies, public debate and national legislation in relation to human biobanks*. Brussels. 2001.

Committee opinion on the clinical trial on medicinal products for human use, *Detailed guidance on the application format and documentation to be submitted in an application for an Ethics*. April 2003. Brussels, ENTR/F2/BL D(2003).

Danish Council of Ethics: *Genetic investigation of Health Subjects. Report on Presymptomatic Genetic Testing*, Copenhagen, 2002.

Dutch Federation of Medical Scientific Societies, *Code for proper secondary use of human tissue in the Netherlands*, Rotterdam, 2003.

European Society of Human Genetics. *Data storage and DNA banking for biomedical research: informed consent, confidentiality, quality, issues, ownership, return of benefits. A professional perspective*. Birmingham. 2000.

- European Society of Human Genetics. *Data storage and DNA banking for biomedical research: technical, social and ethical issues. Recommendations of the European Society of Human Genetics*. 2001.
- European Group on Ethics in Science and New Technologies to the European Comisión, *Ethical aspects of human tissue banking*, No, 11, 21 July 1998.
- European Group on Ethics in Science and New Technologies to the European Comisión, *Opinion about Ethical aspects of umbilical cord blood banking*, No, 19, 16 March 2004.
- German National Ethics Council, *Opinion on biobanks for research*, Berlin, 2004.
- German National Ethics Council and the National Advisory Committee for Life and Health Sciences of France, *Joint Declaration on biobanks*, 2 october 2003.
- HUGO Ethics Committee, *Statement DNA-Sampling: Control and Access*. 1997.
- HUGO Ethics Committee, *Statement on Benefit-Sharing*, April 9 2000.
- Italian National Committee on Bioethics, *Bioethical guidelines for genetic testing* of 19 November 1999.
- Medical Research Council Ethics Series, *Human tissue and biological samples for use in research. Operational and ethical guidelines*, London, 2001.
- National Bioethics Advisory Commission, *Research involving human biological materials: ethical issues and policy guidance*, vol. I (Report and Recommendations).
- Nuffield Council on Bioethics, *Human tissue. Ethical and legal issues*, London, 1995.
- Parliamentary Office of Science and Technology, *The UK Biobank*, 2002.
- Spanish National Commission of Human Assisted Reproduction. First Annual Report. Madrid. December, 1998.
- World Health Organization. *Genetic databases. Assessing the benefits and the impact on human patient rights. European partnership on patient's rights and citizen's empowerment*. 2003.
- World Medical Association, *Declaration on Ethical Considerations regarding Health Databases*, 2002.

6.4. BIBLIOGRAPHY

- ANGOITIA, V., *Extracción y trasplante de órganos y tejidos humanos. Problemática jurídica*, Ed. Marcial Pons, Madrid, 1996.
- ANNAS, G. / GLANTZ, L. H. / ROCHE, P.A., *The genetic privacy act and commentary*, Boston, 1995.

- ARMITAGE, E./DAVIS, I., *Patents and morality in perspective*, Common Law Institute of Intellectual Property, London, 1994.
- BEYLEVELD, D. / BROWNSWORD, R., *Human dignity in bioethics and biolaw*, Oxford University Press, Oxford, 2001.
- BEYLEVELD, D./BROWNSWORD, R./LLEWELYN, M., «The morality clauses of the Directive on the legal protection of biotechnological inventions: conflict, compromise and the patent community», en R. Goldberg/J. Lombay (Ed.), *Pharmaceutical medicine, biotechnology and European law*, Cambridge University Press, Cambridge, 2000.
- BEYLEVELD, D., «Regulating morality through patent law. Critique of the EC Directive», *Revista de Derecho y Genoma Humano*, Núm. 12, Enero-Junio 2000.
- BIRD & BIRD, *Medical data and data protection*, London, 2000 & 2001.
- CAPRON, A.M., «Parenthood and frozen embryos: More than property and privacy», *Hasting Center Report*, Vol. 22, Num. 5, 1992.
- CÁRCABA FERNÁNDEZ, M., *Los problemas jurídicos planteados por las nuevas técnicas de reproducción humana*, Ed. Bosch, Barcelona, 1995.
- CHADWICK, R./LEVIT, M.S.D. (Eds.), *The right to know and the right not to know*, Avebury, 1997.
- CRESPI, R.S., «Biotechnology patents and morality», *TIBTECH*, Vol. 15, April, 1997.
- DESCHENES, M./CARDINAL, G./KNOPPERS, B.M./ GLASS, K.C./, «Human genetic research, DNA banking and consent: a question of «form»?», *Clinical Genetics*, Vol. 59, 2001.
- FONDACARO, J.D., «Protecting patient's rights in the licensing of human cells», *Patent world*, Num. 136, October 2001.
- GODARD, B./RAEBURN, S./PEMBREY, M./BOBROW, M./FARNDON, P./AYMÉ, S., «Genetic information and testing in insurance and employment: technical, social and ethical issues», *European Journal of Human Genetics*, Vol. 11, Suppl. 2, 2003.
- HARDIMAN, R., «Toward the right to commerciality: Recognizing property rights in the comercial value of human tissue», *UCLA Law Review*, Vol. 34, 1986.
- KENNEDY, I./GRUBB, A., *Medical Law. Text with materials*, Second edition, Ed. Butterworths, London, 1994.
- KNOPPERS, B.M./ HIRTLE, M., «Banking of human materials, intellectual property rights and ownership issues: emerging trends in the literature internacional policy positions (I and II)», *Law and the Human Genome Review*, Num. 5 & 6, 1996 and 1997.
- LEENEN, H.J.J., «Genetics, confidentiality and research», *European Journal of Health Law*, Vol. 7, 2000.
- MARTIN, P./KAYE, J., *The use of biological simple collections and personal medical information in human genetics research*, The Wellcome Trust, London, 1999.
- MARTÍN URANGA, A., *La protección jurídica de las innovaciones biotecnológicas. Especial consideración de su protección penal*, Ed. Comares, Granada, 2003.

- NICOLÁS JIMÉNEZ, P., «Los derechos del paciente sobre su muestra biológica: distintas opiniones jurisprudenciales», *Revista de Derecho y Genoma Humano*, Núm. 19, 2003.
- NICOLÁS JIMÉNEZ, P., *La protección jurídica de los datos genéticos de carácter personal*, ed. Comares, 2005, en prensa.
- OTERO LASTRES, J.M., «La patentabilidad del material genético humano en el Derecho español vigente», *El Derecho ante el Proyecto Genoma Humano*, Vol. II, Ed. Fundación BBV, Bilbao, 1994.
- PÉREZ BUSTAMANTE, G., «Patentes de invenciones biotecnológicas: un análisis jurídico-económico», *Revista de Derecho y Genoma Humano*, Núm. 8, 1998.
- PROWDA, J.B., «Moore v. The regents of the university of California: an ethical debate on informed consent and property rights in a patient's cells», *Journal of the patent and trademark office society*, Vol. 77, August 1995.
- QUINTANA, O., «La patentabilidad de las invenciones biotecnológicas: consideraciones éticas», *Los retos de la genética en el siglo XXI: genética y bioética*, M. Casado/R. González-Duarte (ed.), Ediciones Universidad de Barcelona, 1999.
- ROMEO CASABONA, C.M., «Anonymisation and pseudonymisation: legal framework at an European level», *Medical Research and data protection across Europe*, Beyleveld et alt. (Eds.), Ashgate Publishing, Vol. 1, 2004.
- ROMEO CASABONA, C.M., *Genética y Derecho. Responsabilidad jurídica y mecanismos de control*, Ed. Astrea, Buenos Aires, 2003.
- ROMEO CASABONA, C.M., «La protección jurídica del genoma humano y de las innovaciones biotecnológicas: la cuestión de su patentabilidad», *Comunicaciones IDEI. Diez conferencias magistrales sobre nuevas tecnologías y propiedad industrial*. Núm. Extraordinario, 2001.
- ROMEO CASABONA, C.M., «La utilización de muestras biológicas con fines de investigación biomédica», Instituto de Investigaciones Jurídicas, Universidad Autónoma de Méjico, Méjico, 2004, in press.
- ROMEO CASABONA, C.M., *El médico y el Derecho penal, La actividad curativa (licitud y responsabilidad penal)*, Ed. Bosch, Barcelona, 1981.
- ROMEO MALANDA, S., «Minoría de edad y consentimiento Médico en la Ley 41/2002, de 14 de noviembre», *Actualidad de Derecho Sanitario*, Núm. 102, Febrero, 2004.
- SANTOS MORÓN, M.J., «Sobre la capacidad del menor para el ejercicio de sus derechos fundamentales. Comentarios a la TCS 154/2002 de 18 de julio», *La Ley*, 12 de diciembre de 2002.
- SMAGLIK, P. «Tissue donors use their influence in deal over gene patent terms», *Nature*, Núm. 407, 2000.
- SOLER MATUTES P./SÁNCHEZ MOLERO, J., «La patente de genes humanos: examen especial de la propuesta de directiva comunitaria relativa a la protección jurídica de las invenciones biotecnológicas», *La Ley*, Diciembre, 1998.

TALLACCHINI, M., «El cuerpo y sus partes. La ubicación jurídica de los materiales biológicos humanos», *Medicina y Ética*, Vol. X, Núm. 1, Enero-Marzo, 1999.

TAUPITZ, J., «El Derecho a no saber en la legislación alemana (I and II)», *Revista de Derecho y Genoma Humano*, Núms. 8 y 9, 1997.

