

ETHICS AND LEGAL KEYS TO BIOMEDICAL RESEARCH IN SPAIN

ANTONIO CABANILLAS SÁNCHEZ¹

JORGE ZAVALA²

Abstract: This study analyzes the Spanish regulations on Biomedical research, with special reference to the Act of July 3, 2007, inspired by the instruments adopted by the Council of Europe and the European Union as well as in the domestic laws of the United States and the United Kingdom, which are pioneers in the field. This is an advanced law which regulates basic character research and the most controversial issues, both in law and ethical spheres, especially in stem cells research, allowing, with certain limits, the use of embryos, human fetuses, ovocytes and pre-embryos. To complement this approach, the study also analyzes the legal regime applied to clinical trials for drugs and health products.

Keywords: Ethics, Spanish Law, Biomedical Research, Stem Cells, Clinical Trials.

Contents: I. INTRODUCTION; II. PRINCIPLES GUIDING HUMAN SUBJECT RESEARCH IN SPANISH LEGISLATION; III. THE BIOMEDICAL RESEARCH ACT OF JULY 3, 2007

I. INTRODUCTION

For over twenty years, Spain has been the world's leader in the donation and transplant of organs. This is because the Spanish model includes a set of legal measures to improve organ donation³, and the application has been recommended by the OMS in different regions of the world. From a future perspective, there are regulations regarding artificial insemination and biomedical research in humans, consistent with the practice in most advanced countries, where the principlism, known as the *Georgetown approach to bioethics*, is applied and is based on the work of the *National Commission for the*

¹ Professor of Civil Law. Universidad Carlos III de Madrid, Spain (antonio.cabanillas@uc3m.es).

² Associate Professor of Public International Law. Universidad Carlos III de Madrid, Spain (yojoa@der-pu.uc3m.es).

³ Ley 30/1979, de 27 de octubre, sobre extracción y trasplante de órganos (BOE n. 266 de 6/11/1979); Real Decreto 426/1980, de 22 de febrero, por el que se desarrolla la Ley 30/1979, de 27 de octubre, sobre extracción y trasplante de órganos; (BOE n. 63 de 13/3/1980); Resolución de 27 de junio de 1980, de la Secretaría de Estado para la Sanidad, sobre la organización Nacional de Trasplantes y los laboratorios de diagnóstico de histocompatibilidad (BOE núm. 158, de 2 de julio de 1980); Real Decreto 411/1996, de 1 de marzo, por el que se regulan las actividades relativas a la utilización de tejidos humanos (BOE n. 72 de 23/3/1996)

Protection of Human Subjects of Biomedical and Behavioral Research (Ainslie 2003: pp. 2099-2100).

The principlism is best used to address ethical and legal issues raised by the human experimentation method. The four basic principles in which it is inspired, respect for autonomy, which means taking into account the ability of people to make decisions, non-maleficence to avoid damages, charity as specified in the requirement to provide benefits with application of prejudice -benefit rule, and justice, which is the fairness in the distribution of benefits and risks (Beauchamp and Childress 2013: pp. 13-29; Beauchamp 1994: pp. 3-6; Ainslie 2003: p. 2100). These principles are linked to human rights (Peces-Barba 1994: pp. IX-XI) and inspire statements and codes of conduct and professional ethics, which in turn influence international instruments in biomedical research.

The laws of many states welcome these principles. Spain, for example, passed the Biomedical Research Act of July 3, 2007⁴, which is one of the first laws that was enacted by the States of the Council of Europe following the adoption of the Additional Protocol on Biomedical Research of 25 January 2005 of the Convention on Human Rights and Biomedicine of 4 April 1997⁵.

In the UK and in the U.S. the critical issue in respect to ethics and law is the research concerning pre-embryos, embryos and fetuses. To solve this problem Spain adopted a permissive approach that appears in the Biomedical Research Act, which has generated a lot of controversy, not only on ethical grounds but also on constitutional aspects.

II. PRINCIPLES GUIDING HUMAN SUBJECT RESEARCH IN SPANISH LEGISLATION

Unlike the Charter of Fundamental Rights of the European Union (Article 3),⁶ the Spanish Constitution does not specifically refer to biomedical research. Nevertheless, the Constitution is clearly in harmony with the U.S. concept of principlism, addressing the majority of the fundamental rights on which this method is based, including the dignity of the individual, the right to life and to physical and moral integrity, freedom of thought or conscience, the right to privacy, freedom from discrimination based on race or sex, and the right to protect scientific and technical inventions (Cruz Villalón 2006; Romeo Casabona 2002: pp. 1-2). All of these are present in the Belmont Report,⁷ which was highly influential not only in the United States commencing with the work of T. L. Beauchamp and J. F. Childress (2013) but also in many other countries, in the work of many NGOs and the most significant

⁴ BOE no. 159, 4 de julio de 2007.

⁵ Ratified by Spain. Official State Gazette no. 251 (20 October 1999). Spain has not ratified the Additional Protocol.

⁶ *Official Journal of the European Union* 2000/C 364/01

⁷ *The Belmont Report, Ethical Principles and Guidelines for the Protection of Human Subjects of Research*, The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, April 18, 1979.

international organizations for the protection of human rights, such as the Council of Europe and UNESCO, setting forth the ethical principles for addressing the problems that arise from biomedical research (Jonsen 1994: pp. 13-21). Principlism is universal in nature. It is inevitably applied in a diversity of cultures, religious beliefs and political systems.⁸ A common medical ethic is needed in the treatment and prevention of human diseases, where the four great principles of bioethics play an essential role (Preston 1994: pp. 23-30).

Principlism is reflected in professional codes of conduct and ethics, which in turn have influenced international instruments dealing with biomedical research, such as the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine (Convention on Human Rights and Biomedicine) of April 4, 1997⁹ and its Additional Protocol concerning Biomedical Research of January 25, 2005, as well as the Universal Declaration on Bioethics and Human Rights of October 19, 2005. The basic principles set forth in these instruments have been accurately reflected in the domestic laws of many countries. Spain's laws reflect the principlism, noting that the key issues relate to the grounds and the hierarchy of these principles. They give structure to application in biomedicine and are essential in adopting rigorous ethical decisions by the medical professionals and other health sciences (Gafo 1998: pp. 106-111; Gracia 1989: pp. 99-104; 182-197; 285-293; Castellano 1998: pp. 31-36). The law establishes the principles and guarantees that need to be respected by biomedical research on humans (Silveira 2008: p. 24). The Biomedical Research Act of July 3, 2007 is influenced by these principles¹⁰.

The principles set forth in these international instruments are present in recent Spanish legislation governing biomedical research due to the fact that they have been strongly influenced by the Convention on Human Rights and Biomedicine and its Additional Protocol concerning biomedical research, as well as by U.K. and U.S. legislation and practice. Spanish legislation in this area includes the Royal Decree of February 6, 2004 Regulating Clinical Trials with Medicines; the Medicines and Health Products (Guarantees and Rational Use) Act of July 26, 2006; the Order of the Ministry of Health and Consumer Affairs of February 5, 2007 Regulating Research on Medicines for Human Use; and the Biomedical Research Act of July 3, 2007.

The importance of research on medicines and health products explains why the first legal provisions in Spain concerning biomedical research were passed to regulate clinical trials with drugs. Royal Decree of February 6, 2004 Regulating Clinical Trials with Medicines¹¹ transposed into Spanish law Directive 2001/20/EC relating to the Implementation of Good Clinical Practice in the Conduct of Clinical Trials on

⁸ This affirmation is evidenced in the extensive work edited by R. Gillon and A. Lloyd in 1994, in which almost 100 authors from different disciplines, nationalities, religions and cultures collaborated (Gillon, R. and Lloyd, A. (1994)).

⁹ Ratified by Spain; Official State Gazette no. 251 (20 October 1999).

¹⁰ Torres Casorla and García Rico 2012: pp. 179-204; Sánchez Díaz 2012: pp. 205-221; Bonilla Sánchez 2012: pp. 223-243; Fernández-Costales Muñiz 2012: pp. 245-257; Lecuona 2011: pp. 117-122.

¹¹ Official State Gazette no. 33 (7 February 2004).

Medicinal Products for Human Use (the “Clinical Trials Directive”) within the scope of the European Union. The Royal Decree is modeled on principles governing clinical trials in human subjects set forth in the Declaration of Helsinki and the Convention on Human Rights and Biomedicine, as well as legislation protecting personal data, including the Spanish Personal Data Protection Act (Organic Law of December 13, 1999).¹²

Pursuant to the Royal Decree Regulating Clinical Trials with Medicines, a clinical trial may only be commenced when the Clinical Trials Ethics Committee and the Spanish Medicines and Health Products Agency consider that the benefits for the trial participants and society in general justify the risks. Clinical trials must be conducted according to the standards of good clinical practice published by the Ministry of Health and Consumer Affairs, which are binding upon the sponsor, monitor and investigator.¹³ Compliance with these standards is verified through inspections carried out by the Spanish Agency for Medicines and Health Products, as well as the health authorities of the Autonomous Communities within the scope of their respective powers.¹⁴ The physical and mental integrity of subjects, as well as their privacy and the confidentiality of their personal data must be guaranteed. Each clinical research participant must freely give his informed consent in writing before being included in the trial.¹⁵ The informed consent of a legal representative is required for participating minors or incapacitated adults. At any time, research subjects or their legal representatives may revoke their consent without detriment of any kind.¹⁶ As a general rule, clinical trials with investigational drugs cannot be conducted unless an insurance policy or other financial guarantee has been previously subscribed to cover damages in the event of injuries to participants that may arise as a result of the trials. If no insurance or other financial guarantee has been provided, or if they do not entirely cover the damages claimed, the sponsor of the clinical trial, the primary investigator and the hospital where the trial is conducted shall share joint and several strict liability for any impairment in the health of a trial subject, including economic loss, likewise bearing the burden of proving that they are not the consequence of the clinical trial or the therapeutic or diagnostic measures taken during the course thereof. In these circumstances, neither administrative authorization nor the favorable opinion of the Clinical Trials Ethics Committee will enable the sponsor of the clinical trial, the primary investigator and his collaborators, or the hospital or institution where the trial is conducted to disclaim liability. Unless otherwise proven, it is assumed that impairment to a subject’s health during the course of a clinical trial and for one year thereafter is the result of the trial. However, after a year the subject is required to prove the causal nexus between the clinical trial and the impairment sustained. Liability for compensation includes all expenses derived from any impairment in the clinical trial subject’s health or physical state, including any directly-derived economic loss, provided that such impairment is not inherent in the pathology under study, is not among the adverse

¹² Official State Gazette no. 298 (14 December 1999).

¹³ Articles 34-39.

¹⁴ Article 40.

¹⁵ Article 3.

¹⁶ Article 7.1-7.5.

reactions to the medication prescribed for that pathology, or is not simply part of the evolution of the illness in question as a result of the ineffectiveness of the treatment. The minimum liability guaranteed per clinical trial subject is 250,000 euros, as lump sum compensation.

Clinical Trials Ethics Committees play a fundamental role in evaluating the methodological, ethical and legal aspects of the clinical trials submitted to them and assessing any relevant changes in the trials initially authorized, as well as overseeing trials from their commencement until their final reports are submitted.¹⁷ Sponsors must likewise apply to the Director of the Spanish Medicines and Health Products Agency for authorization to conduct their clinical trials.¹⁸ The Agency may resolve to suspend or revoke a trial on its own initiative or upon a justified petition from the sponsor, if the trial contravenes the law, if the conditions under which it was authorized change, or due to noncompliance with the ethical principles designed to protect clinical trial subjects and ensure public health.¹⁹ Upon termination of the trial, the sponsor must notify the Agency and the Ethics Committees of that fact within ninety days.²⁰ Failure to comply with these obligations constitutes an administrative infraction and carries the corresponding sanctions set forth in the Medicines and Health Products (Guarantees and Rational Use) Act of July 26, 2006.²¹

The fundamental guarantees contained in the Royal Decree Regulating Clinical Trials with Medicines are likewise reflected in the Medicines and Health Products (Guarantees and Rational Use) Act of July 26, 2006. This law provides four guarantees to ensure that clinical trials are conducted satisfactorily, while protecting the fundamental rights of trial subjects. First there are guarantees of suitability, which ensure that clinical trials on investigational drugs are submitted for approval by the Spanish Medicines and Health Products Agency.²² The public health authorities have powers to inspect clinical trials,²³ ensuring compliance with standards of good clinical practice.²⁴ Trials must adhere to the content of the specific research protocol for which authorization was granted, and any subsequent changes.²⁵ All clinical trial results, whether positive or negative, must be reported to the Spanish Medicines and Health Products Agency, without prejudice to likewise notifying the authorities of the Autonomous Communities in which the research was conducted.²⁶

The second guarantee concerns ethical principles, according to which clinical trials must respect the fundamental rights of trial participants and those affecting biomedical research in human subjects, which reflect the content of the Declaration of

¹⁷ Article 10 as it relates to Articles 11-14.

¹⁸ Article 20 and ff.

¹⁹ Article 26.

²⁰ Article 27.

²¹ Official State Gazette no. 178 (27 July 2006).

²² Article 59.2.

²³ Article 59.3.

²⁴ Article 59.4.

²⁵ Article 59.7.

²⁶ Article 59.8.

Helsinki.²⁷ A third guarantee entails assumption of liability, whereby clinical trials will require an insurance policy or other financial surety to ensure coverage for any claim for damages that may derive from the research undertaken.²⁸ As was the case with the Clinical Trials Regulation, if for any reason the insurance does not totally cover the injuries caused, the sponsor of the trial, the primary investigator and the hospital or institution where the trial was conducted shall share joint and several strict liability, and shall bear the burden of proof. Neither administrative authorization of the trial nor the opinion of the Clinical Trials Ethics Committee will enable them to disclaim this liability.²⁹ Unless proven otherwise, impairment to the health of participants sustained during the trial and up to one year thereafter is deemed to be a result of the trial. However, after a year the trial subject must prove the nexus between the trial and the impairment sustained.³⁰ A fourth guarantee concerns transparency in clinical trials, which must be entered on a National Register of Clinical Trials that is public and may be freely accessed.³¹ The sponsor is likewise obliged to publish both positive and negative results. To ensure compliance with these guarantees, there is a system for inspecting and ordering provisional remedies, and health authorities carry out the necessary inspections within the scope of their powers.³² After the pertinent investigation, failure to comply with these obligations will be subject to administrative sanctions, without prejudice to any civil, criminal or other liability which the nonconforming party may incur.

The Ministry of Health Order of February 5, 2007,³³ setting forth the specific principles and directives of good clinical practice and the standards for authorizing the manufacture and import of investigational drugs for human use incorporates into Spanish law the European Union “Good Clinical Practice Directive” 2005/28/EC. As indicated in its Preamble, this Order was issued pursuant to the Second Final Provision of the Royal Decree of February 6, 2004 regulating clinical trials with medicines.

In a manner similar to the aforementioned provisions, this Order regulates the principles and directives for good clinical practice in clinical trials with investigational drugs for human use, the requisites for authorizing the manufacture and import of those medicines, detailed instructions on trial documentation and records, and the qualification of inspectors and inspection procedures.

III. THE BIOMEDICAL RESEARCH ACT OF JULY 3, 2007

The Biomedical Research Act of July 3, 2007 (Beauchamp and Childress 201; Beauchamp 1994; Ainslie 2003) incorporates into Spanish law the principles contained in the Convention on Human Rights and Biomedicine and its Additional Protocol,

²⁷ Article 60.1.

²⁸ Article 61.1.

²⁹ Article 61.2.

³⁰ Article 61.3.

³¹ Article 62.1.

³² Article 98.1.

³³ Official State Gazette no. 38 (13 February 2007).

regulating research on human subjects. Other laws, such as the Patient Autonomy (Clinical Information and Documentation Rights and Responsibilities) Act of November 14, 2002³⁴ and the Personal Data Protection Act of December 13, 1999, may be applied subsidiarily, provided that they are not in conflict with the Biomedical Research Act³⁵. This law also repealed several other provisions in this area.³⁶

This Act lends full respect to human dignity and identity rights of the individual, with respect to biomedical research, whether it be basic or clinical research³⁷, except in clinical trials with medicines and health products³⁸. Such trials are allowed during pregnancy and lactation, and in persons unable to consent because of their clinical condition³⁹. Biomedical research on embryos, fetuses, oocytes and preembryos is also supported, which has always been a contentious issue⁴⁰.

Literature in both the U.K. and the U.S. clearly distinguishes between the embryo and the human fetus. J. M. Harris, D. Morgan and M. Ford affirm that scientifically the product of conception is called “embryo” until the eighth week of gestation. From that moment, the term changes and it is referred to as a “fetus.” In practice, an embryo as the subject of research is the laboratory embryo, which is usually the result of in vitro fertilization (IVF). Moreover, within the category of embryo, a variety of terms are used: preembryo, preimplantation embryo, ex utero embryo and premature embryo (Harris, Morgan, and Ford 2003). With regard to embryo research, the fourteen-day term is essential, as was underscored in the United Kingdom in the Warnock Report of 1984. However, some authors suggest that justification for the fourteen-day limit is not convincing and propose extending the limit for research with embryos fertilized in vitro to thirty-eight days.⁴¹ One of the reports of the President’s Council on Bioethics underscores the increased capacity to intervene in the beginnings of human life, especially life outside the body, whether in the clinic or the laboratory, which has given rise to huge advances in biotechnology in recent decades. This capacity, which emerges from a confluence of work in reproductive biology, developmental biology and human genetics, has raised ethical issues involving a

³⁴ Official State Gazette no. 274 (15 November 2002).

³⁵ Second Final Provision of the Biomedical Research Act.

³⁶ Law 42/1988 of December 28 (Donation and Use of Human Embryos and Fetuses or their Cells, Tissue or Organs Act) and any provisions of any rank that are contrary to the provisions of this Law. Likewise repealed are: paragraphs 5 and 6 of Article 45 and Articles 46, 47 and 50 of Law 16/2003 of May 28 (National Health System Cohesion and Quality Act); Title VII and Chapters II and III of Title VI of Law 14/1986 of April 25 (General Health Act); the Second Additional Provision of Law 14/2006 of May 26 (Human Assisted Reproduction Techniques Act); and Articles 10 and 11 of the Bylaws of the National Center for Transplants and Regenerative Medicine passed by Royal Decree 176/2004 of 30 January (Sole Repeal Provision. Legislative Repeal).

³⁷ Article 1.1.

³⁸ Article 1.3.

³⁹ Articles 19 and 20.

⁴⁰ De Miguel Beriain, 2004: p. 358; Ruiz de la Cuesta 2012: pp. 23-39; Casonato and Penasa 2012: pp. 41-65; Ferrajoli 2011: pp. 729-744; Díaz Revorio 2011: pp. 789-826; Rivera López 2011: pp. 1065-1094; Gascón Abellán 2011: pp. 1095-1121.

⁴¹ Edwards 1989 (Cfr. Walters, L. (revised by A. Drapkin Lyerly) (2003))

number of important human goods.⁴² It is not surprising that many of the technological applications in this field are controversial. The origins of these controversies are rooted in different criteria concerning the diverse interests at stake and the weight to be given each of them: reproductive freedom, prenatal life, the status of embryos and freedom of scientific research, among many others. These interests are perceived and valued in many different ways in plural societies such as the United States. The President's Council on Bioethics has affirmed that there is profound disagreement in U.S. society concerning the degree of respect owed in vitro human embryonic life and its relation to other moral considerations such as helping infertile couples have healthy children and advancing biomedical knowledge that might lead to cures for terrible diseases.⁴³

In that regard, the United Kingdom has adopted criteria that place few limits on the application of assisted reproduction techniques and biomedical research with preembryos, implementing solutions that are more permissive than those presently existing in the United States and other countries.⁴⁴ The regulation of assisted reproduction and embryo research came to the forefront with the publicity surrounding the birth of Louise Brown. The 1984 Warnock Report recommended regulating assisted reproduction and authorizing research with embryos created in vitro for up to fourteen days after fertilization. Based on the Warnock Report, the Human Fertilisation and Embryology Act (HFEAct) was passed in 1990 to set up the necessary requisites and controls. Research protocols were initially limited to studying infertility and the causes of congenital defects, as well as to identifying abnormal genes or chromosomes in embryos (Walters (revised by A. Drapkin Lysterly) 2003: p. 925). In a statutory instrument of January 24, 2001, Parliament amended the HFEAct to permit embryo research to increase knowledge to be applied in developing treatment for serious disease. In 2003 the House of Lords further increased the scope of the HFEAct to include all types of embryos, not only those created by fertilization of eggs by sperm. Thus, the Human Fertilisation and Embryology Authority (HFEA), created in 1991, assumed the powers to authorize research with embryos created by means of nuclear transfer, as well as through fertilization with sperm (Harris, Morgan, and Ford 2003: p. 507). And on May 17, 2007 the British government authorized the creation of interspecies embryos for disease research purposes, provided that they are destroyed after fourteen days of development and are never implanted in a uterus. The authorization of this new procedure can be explained by the fact that, in contrast to the immense majority of countries, the creation of human embryos for research purposes has been permitted since 2004. The decision was the result of pressure from scientific groups faced with a severe shortage of human eggs for use in research. The HFEA must analyze each individual application, and issues its authorization only for a single line of research. An initial research project with hybrid embryos has already been conducted (Jha 2008).

⁴² *The President's Council on Bioethics, Reproduction & Responsibility. The Regulation of New Technologies*, Washington, D. C. (2004) XXXIX.

⁴³ *Id.*, 8.

⁴⁴ For an excellent analysis of historical and ideological aspects of legislative options in the United States, United Kingdom and Germany, see Belew 2003-2004: pp. 479, 486, 496, 507.

Pursuant to the NIH Revitalization Act of 1993, the United States Congress authorized the National Institutes of Health (NIH) to finance research using assisted reproduction techniques to increase the knowledge and treatment of infertility. Research authorized by Congress included the use of human embryos. Recognizing the controversies surrounding such research, the NIH decided that an analysis of ethical aspects was warranted prior to financing any of the proposed projects. For that purpose, the NIH turned to the Human Embryo Research Panel (HEPR), in charge of providing advice and recommendations in this field. The HEPR considered the moral status of embryos and the ethical standards governing research with human subjects. It affirmed that although the pre-implantation human embryo warrants serious moral consideration as a developing form of human life, it does not have the same moral status as infants or children.⁴⁵ This conclusion implies that pre-implantation embryos are not fully human beings, and thus do not warrant protection as such. Based on this determination, certain research projects that may result in the destruction of embryos have been considered acceptable for federal funding. However, the HEPR affirmed that human embryos deserve “serious moral consideration” and should be accorded treatment different from that given mere human cells or animal embryos. In that regard, the HEPR proposed restrictions on embryo research based on moral considerations. Thus, human embryos should be used in research only as a last resort, the number of embryos used should be limited and embryos should not be allowed to develop beyond the time required in the specific research protocol and never beyond the fourteen-day limit. Applying ethical standards governing research on human subjects, the HEPR invoked criteria used by Institutional Review Boards (IRBs). Egg, sperm and embryo donors must be informed of the specific purposes of the projected research, as well as its procedures and risks. Despite President Clinton’s directing the NIH not to finance the creation of embryos solely for research purposes, the majority of research involving in vitro fertilization and human embryos is federally funded. Moreover, Congress changed its previous position and prohibited the NIH from financing any project that damages or destroys human embryos. In recent years the ethical and political debate concerning research with “spare” embryos from in vitro fertilization treatments has intensified. Some authors have proposed restrictive criteria, opposing any research with embryonic stem cells resulting in the death of the embryo, which is considered a human being. The Catholic Church’s position is particularly clear in that regard. In line with the dominant position in the United Kingdom, others think that obstacles should not be placed on this type of research, considering that embryos cannot be deemed human until at least fourteen days after fertilization,⁴⁶ and that there should be no objection to the creation of embryonic stem cell banks (Ecker and O’Rourke 2007: pp. 48-50; Lott and Savulesco 2007: pp. 37-44).

⁴⁵ “Human Embryo Research Panel, National Institute of Health,” *Report of the Human Embryo Research Panel*, Vol. 1, Washington D. C. (1994) X.

⁴⁶ The debate is extraordinarily intense in the United States in which there is a confluence of scientific, ethical, religious, economic and political factors, reflected in an extremely abundant bibliography. Presently, this is perhaps the most controversial aspect of bioethics, given that biomedical research depends decisively on research with embryonic stem cells. See Steinbock 2006: pp. 26-34; DeGrazia 2006: pp. 49-57; Gómez-Lobo 2004: pp. 75-79; Johnson 2007: pp. 19-30; Fennel 2008: pp. 84-91; McLeod and Baylis 2008: pp. 467-477; Gibson 2008: pp. 370-378; Agar 2008: pp. 198-207.

The President's Council on Bioethics' Report on Reproduction and Responsibility (Washington, D.C: PCB, 2004) recommends legally prohibiting human embryo research under certain conditions, and specifically, that embryos not be maintained in vitro for more than fourteen days following fertilization. With a view to expressly respecting the status of the human embryo, research conditions have been established that are much more restrictive than those regulating research with human cells or animal embryos. For example, research must be conducted for significant scientific or medical objectives, and may only involve the use of human embryos if the research cannot be carried out by other means. As a control mechanism, ethics committees are to play a fundamental role in ensuring compliance with legal provisions governing this type of research (Douglas 2007: pp. 732-736).

In 2007, with a Democratic majority, Congress passed a law facilitating federal funding for biomedical research with surplus embryos from in vitro fertilization, with the possibility of obtaining embryonic stem cells. President Bush vetoed that legislation, considering that it threatens the life of the embryo, having constantly manifested his opposition to the unlimited use of embryonic stem cells because it results in the destruction of embryos. The intense debate in this area may be largely explained by the economic interests involved in the area of biomedical research and, in general, in medical practice, as underscored by numerous authors concerned about the "problem of commercialism in medicine."⁴⁷ In other respects, two independent teams of Japanese and American scientists have obtained pluripotent cells from skin. This research has resulted in the discovery of a technique that yields stem cells without the use of human embryos. Nevertheless, it is in the early stages and must be further developed to adequately assess its potential.

The Spanish Biomedical Research Act sets limits on in utero research with live embryos and fetuses. In utero interventions can only be conducted for diagnostic or therapeutic purposes in the interest of the embryo or fetus, without prejudice to legal provisions for the voluntary interruption of pregnancy.⁴⁸ Research on human embryos and fetuses must comply with a series of requisites to ensure that they conform to the principles on which the Biomedical Research Act is based. They must be human embryos or fetuses that have lost their capacity for biological development, and the donor or donors (or their legal representatives in the case of non-emancipated minors or incapacitated adults) must have previously given their express informed consent in writing. The project detailing the use to be made of the embryos or fetuses must be approved by the Oversight Committee for Donations and Use of Human Cells and Tissue, as well as the corresponding state or autonomous community authorities. And the team in charge of the authorized project must report the results to both the entity that authorized the project and the Oversight Committee for Donations and Use of Human Cells and Tissue.⁴⁹ Research with pregnant women may only be authorized if it entails

⁴⁷ Kassirer 2007: pp. 377-386; Rodwin 2007: pp. 387-397; Churchill 2007: pp. 407-414; Fins 2007: pp. 425-432.

⁴⁸ Article 30.

⁴⁹ Article 31.

only minimum risks for the embryo, fetus or child.⁵⁰ Research with oocytes and preembryos is authorized,⁵¹ provided that consent is obtained from their donors, which may be revoked at any time without affecting the research in question.⁵² Oocyte and preembryo donation is governed by the provisions of the Human Assisted Reproduction Techniques Act of May 26, 2006.⁵³ In any case, the creation of human preembryos and embryos for research purposes is prohibited.⁵⁴ Nevertheless, within the terms defined in the Act, any technique may be employed for obtaining human stem cells for therapeutic uses or research, as long as preembryos or embryos are not created exclusively for that purpose, including the activation of oocytes through nuclear transfer.⁵⁵ Research and experimentation are permitted with surplus oocytes and preembryos, or their biological structures, obtained from assisted reproduction treatments, for the purpose of harvesting, developing and using embryonic stem cell lines or for other purposes not related to the development and application of assisted reproduction techniques. In that regard, the conditions set forth in the Human Assisted Reproduction Techniques Act must be met, and the research must respect the ethical principles and applicable legal precepts, particularly those contained in the Biomedical Research Act and its implementing regulations, reflecting the principles of relevance, feasibility and suitability.⁵⁶ Authorization is subject to receiving approval from the management of the institution where the research is to be conducted, as well as a favorable opinion from the corresponding Research Ethics Committee. The project must indicate any relationships or common interests of any nature, if any, between the research team and the entity that conducted each of the assisted reproduction processes that produced the preembryos or that intervened in obtaining the oocytes to be used. The project must likewise contain written undertakings to provide the public authorities with data that identify and enable monitoring of the conservation of any stem cell lines that may be obtained during the research and to provide those stem cell lines free-of-charge for use by other researchers. And in the event oocytes or preembryos are used, the project must provide an indication and justification of their origin and the number used, as well as informed consent documents signed by their respective donors.⁵⁷

The preamble to the Biomedical Research Act underscores that this law governs areas that were previously unregulated or only partially covered, given changes in recent years, particularly in the areas of genetic analysis, research with human biological samples, especially embryonic ones, or biobanks. The Act explicitly prohibits the creation of human preembryos and embryos exclusively for research purposes, in accordance with the gradualist position with respect to the protection of human life set forth by the Constitutional Court in its judgments 53/1985, 212/1996 and 116/1999, but

⁵⁰ Article 19 c).

⁵¹ “Preembryo” is defined in Article 3.s), affirming that it is an embryo created in vitro, formed by a group of cells resulting from the progressive division of an oocyte from its fertilization until 14 days thereafter.

⁵² Article 32.1.

⁵³ Article 32.2.

⁵⁴ Article 33.1.

⁵⁵ Article 33.2.

⁵⁶ Article 35.1.

⁵⁷ Article 34.2.

it permits the use of any technique for obtaining human stem cells for therapeutic purposes or research, providing the preembryo or embryo is not created exclusively for that purpose and in the terms set forth in the Act. With regard to the use of surplus embryos from human assisted reproduction treatments, the legal framework is set forth in the Human Assisted Reproduction Act of May 26, 2006, which expressly prohibits so-called human reproductive cloning.

Prior to the enactment of the Biomedical Research Act, efforts were made to determine whether research with preembryos was legally admissible (Tur Ausina 2008: pp. 789-812).

Commencing with its Judgment 53/1985 of April 11 regarding Article 417 bis of the Criminal Code in relation to criminal abortion, the Constitutional Court considered the *nasciturus* not as a person and a subject of fundamental rights, but rather as a “constitutional interest” worthy of protection. The Court ruled that the arguments alleged by the appellants could not be accepted to support the thesis that the *nasciturus* also has the right to life, but rather that it is a “constitutionally-protectable interest,” and that lawmakers must not impede the natural gestation process and must adequately protect this legal interest, even with penal laws, when warranted. This case law of our Constitutional Court reflects the case law of the European Commission of Human Rights in the 1980s, which denied that the concept of person as defined in Article 2 of the Council of Europe’s Convention for the Protection of Human Rights and Fundamental Freedoms of 1950 applied to the protection of the *nasciturus*.

This Constitutional Court case law was firmly established in Judgment 212/1996 of December 19 concerning the Human Embryos and Fetuses (Donation and Use) Act 42/1988 of December 28 and in Judgment 116/1999 of June 17 on the Human Assisted Reproduction Techniques Act 35/1988 of November 22.

Constitutional Court Judgment 212/1996 of December 19 affirms that the regulation provided in the Human Embryos and Fetuses (Donation and Use) Act is based on the fundamental precept that biomedical research can only be conducted on non-viable human embryos and fetuses, case law that was reiterated in Constitutional Court Judgment 116/1999 of June 17.

Law 7/2003 of October 20⁵⁸ regulating Research in Andalusia with Human Embryos that are Non-viable for In Vitro Fertilization considers that preembryos are no longer viable after five years in cryostorage.

Law 45/2003 of November 21,⁵⁹ amending the 1998 Human Assisted Reproduction Techniques Act (Law 35/1988 of November 22) addresses the problem of surplus embryos. Any use of preembryos in cryostorage prior to the enactment of this law must be determined by the couple or woman involved, who may chose between

⁵⁸ Official State Gazette no. 279 (21 November 2003).

⁵⁹ Official State Gazette no. 280 (22 November 2003).

maintaining them in cryostorage until they are transferred, donating them for reproductive purposes, or consenting to the use of the biological structures obtained upon thawing for research purposes, within the limits set forth in the law's Final Provision. Royal Decree 2132/2004 of October 29⁶⁰ defines the requisites and procedures for research using stem cells obtained from surplus preembryos.

The new Human Assisted Reproduction Techniques Act 2006 (Law 14/2006 of May 26⁶¹) introduced essential changes in the area of biomedical research with human embryos from in vitro fertilization by authorizing research or experiments with surplus preembryos from assisted reproduction treatments.

The controversy concerning research with oocytes and preembryos involves the conflict between both the Human Assisted Reproduction Techniques Act 2006 and the Biomedical Research Act 2004 and the case law of the Constitutional Court established in Judgments 212/1996 of December 19 and 116/1999 of June 17 whereby research or experiments can only be conducted on preembryos if it does not compromise their viability, which is not the case when obtaining embryonic stem cells.

Thus the constitutionally-guaranteed protection of human life is violated when the harvesting of embryonic stem cells results in the destruction of the preembryo, implying a utilitarian concept of the embryo that ignores its status as a human being in its initial stage of gestation. The embryo is a live human being in the process of development from the moment of fertilization, since from that moment all genetic material is present. There is no preembryonic stage, since prior to the embryo the human being does not exist, there merely being two sexual cells, the egg and sperm. The term "human embryo" is not clearly defined, thus compromising legal certainty, since "preembryo" lacks scientific rigor as an autonomous category and its use is not authoritative. In effect, "preembryo" is not used in international instruments, and the Convention on Human Rights and Biomedicine and its Additional Protocol do not refer to "preembryos," but rather exclusively to "embryos." There are likewise alternatives to the use of embryonic stem cells that do not involve the destruction of embryos. These include harvesting umbilical stem cells or the possibility of creating embryonic stem cell lines without destroying an embryo, as when they are obtained from skin cells. In any event, it will be difficult to reconcile the new laws on human assisted reproduction techniques and biomedical research with the Constitutional Court's case law (Cruz Villalón 2006: pp. 25-26) unless embryonic stem cells can be obtained without the destruction of embryos.

Having thus outlined the terms of the debate, we can only await the Constitutional Court's response to a possible appeal challenging the constitutionality of research with surplus embryos from in vitro fertilization treatments, as authorized in the Biomedical Research Act. The Constitutional Court will certainly have to clarify its position concerning the protection of the *nasciturus* and the viability of human embryos.

⁶⁰ Official State Gazette no. 262 (30 October 2004).

⁶¹ Official State Gazette no. 126 (27 May 2006).

However, it should be noted that in the ample period transpired since the Act was passed, there has been no indication that any political group intends to challenge its constitutionality, most likely due to significant underlying economic interests, among others.

The draft of the Law for the Protection of Life of the Conceived and the rights of the pregnant woman amends Organic Law of November 23, 1995 of the Criminal Code, which only allows abortion when necessary to prevent a serious threat to life or physical or mental health of the pregnant woman, if practiced within the first twenty weeks of gestation, when the pregnancy is the result of an illegal act against sexual freedom or indemnity, the abortion is performed within the first twelve weeks of pregnancy and the offense must be reported previously (art. 145 *bis*). If the draft legislation finally becomes law, an ethical debate will be launched on research with preembryos in the terms allowed by Biomedical Research Law.

As a supplement to the Biomedical Research Act, Patient Autonomy (Clinical Information and Documentation Rights and Responsibilities) Act (Law 41/2002 of November 14) is applicable in any area that it does not cover.⁶² The Patient Autonomy Act does not specifically address biomedical research, although when defining interventions within the scope of medical care, it expressly refers to research. With regard to its scope of application, it should be noted that it regulates the right to medical information,⁶³ right to privacy,⁶⁴ and respect for patient autonomy, which is particularly reflected in the regulation of informed consent as a fundamental aspect of this law,⁶⁵ as well as clinical records and other documents.⁶⁶

The extraordinary importance of biomedical research in Spain in the last few years, especially with respect to the use of embryonic stem cells, has resulted in its being one of the sectors with the highest level of investments, both public and private, particularly on the part of the pharmaceutical industry, as is the case in the United States and, in general, in countries in which research in this area is conducted.⁶⁷

⁶² Second Final Provision.

⁶³ Articles 4-6.

⁶⁴ Article 7.

⁶⁵ Articles 8-13.

⁶⁶ Articles 14-23.

⁶⁷ Interministerial Committee for Science and Technology, National Plan for Scientific Research, Development and Technological Research 2008-2011.

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