

## **THE STATUS OF THE EXTRACORPOREAL EMBRYO (STEM CELLS)**

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**Keywords:** Stem Cell, Embryo, Medically Assisted Reproduction, Abortion, Law, Ethics, Ethics Committees, Belgium.

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### **Summary**

This contribution covers the ethical, legal and social issues on embryo research in one of the most permissive countries in Europe regarding new reproductive technologies. The article covers practices such as genetic diagnosis, cloning, sex selection, embryonic stem cell research, termination of pregnancy etc.

### **1. The Legal Situation**

## **1.1. The embryo in vitro**

### **1.1.1. Introduction**

Research on human embryos in vitro is covered by the Embryo Law which was adopted by the Belgian Parliament on 11 May 2003 and published in the law gazette (*Moniteur belge*) on 28 May 2003. According to article 15, the Embryo Law enters into force from the day that the Crown and the Council of Ministers, by mutual agreement, determine the administrative and financial resources attributed to the "Federal Committee for Medical and Scientific Research on Embryos in vitro" (art. 9 § 1). This Royal Decree has been taken on September 22, 2004 and has entered into force on 31 October 2004. The Federal Committee itself has recently been established by the Belgian Senate (16 March 2006).

The scope of the Belgian Embryo Law is threefold. It contains provisions governing research on supernumerary embryos (art. 3) and research on embryos created solely for research purposes (art. 4). Secondly it sums up some practices that are prohibited e.g. eugenics or medical interventions aimed at the selection or enhancement of non-pathological genetic characteristics of the human species (art. 5) and reproductive cloning (art. 6). Finally, this recent piece of law also regulates research on both the precursors and derivatives of embryos, i.e. gametes and embryonic stem cells (*ES cells*). Since the creation of embryos solely for research purposes is inextricably linked with egg cell donation, the rights and duties of gamete donors are included in this regulation as well.

### **1.1.2. History of the Embryo Law: European conformity**

The genesis of the Belgian Embryo Law has to be placed against the background of the European Convention on Human rights and Biomedicine. One of the main reasons for drafting the Convention was to discourage the establishment of "safe havens" where patients and doctors could evade restrictive laws and regulations governing their own countries.

All member states of the Council of Europe who become parties to the Convention will have to harmonize their legislation on bioethics with the principles of the Convention. Among other countries, Belgium did not yet sign nor ratify the Convention, because of article 18.2 which prohibits the creation of embryos for research purposes. The conflicting views on the ratification of the Convention were clearly expressed in the "Proposal for Resolution Regarding the Convention on Human Rights and Biomedicine of the Council of Europe". On the one hand ratification was wanted for because the Convention provided a much needed protection of human dignity, while on the other hand it was seen as a major threat to the principle of freedom of scientific research.

Implementing the Embryo Law will enable Belgium to sign and ratify the Convention, taking into account the procedure of article 36: "Any State and the European Community may, when signing this Convention or when depositing the instrument of ratification, acceptance, approval or accession, make a reservation in respect of any particular

provision of the Convention to the extent that any law then in force in its territory is not in conformity with the provision. Reservations of a general character shall not be permitted under this article.”

### **1.1.3. Definition of the extracorporeal embryo**

The Embryo Law defines an embryo as “a cell or a complex of cells with the capacity to develop into a human being” (art. 2, 1).

“An embryo created in the context of artificial reproduction, but which is not implanted in the woman’s uterus” (art. 2, 3), is called a supernumerary embryo.

The latter definition necessarily implies that the embryo has been created outside the woman’s body, i.e. *ex vivo* or *in vitro*. As a rule, if an embryo is not implanted, it will be frozen. Cryopreservation allows for the storage of embryos as long as the couple wishes to have a child. If the parents do not wish to have any further children, the embryos are truly “surplus”. The Embryo Law regulates the purposes for which supernumerary embryos may be used outside a parental project. After the end of a storage period, unused embryos may be provided for anonymous donation to other couples, experimentation or destruction.

Pre-implantation Genetic Diagnosis (*PGD*) is excluded from the Embryo Law because it is carried out on an embryo that is not considered supernumerary. There is no “research subject”, since the embryo is still within a parental project.

### **1.1.4. Research on supernumerary embryos**

Research on supernumerary embryos is primarily conditioned upon obtaining informed consent (art 8). Supernumerary embryos may only be used for purposes other than reproduction if the “concerned persons” (couple for whom the embryos were created) have given their free and informed consent. Withdrawing of consent is no longer possible once the research has been initiated.

Secondly, physicians and researchers must further comply with a certain number of rules.

Article 3 of the proposal allows research on *in vitro* embryos provided that the research project satisfies the following six conditions:

- research involving human embryos *in vitro* may only be performed if its objectives are therapeutic or if they contribute to a better knowledge of (in)fertility, tissue or organ transplantation and disease prevention or treatment;
- research must be based on the most recent scientific knowledge and comply with the requirements of sound research methodology;
- research must be carried out in a registered laboratory affiliated to an academic hospital’s care program of reproductive medicine or human genetics;
- research must be carried out under the supervision of a specialist doctor and by qualified persons;

- research is carried out using embryos up to 14 days old, excluding any cryopreservation period;
- research will only be authorized if an alternative method of research would not be as effective.

Research on in vitro embryos is controlled at both the local and the federal level. Any person commissioning or carrying out research and the head of the laboratory of human reproduction or human genetics shall draw up a joint research protocol. That research protocol requires prior positive advice of the local ethics committee of an academic hospital. The fact that research can only be carried out by a laboratory in collaboration with an academic hospital's care program of reproductive medicine or human genetics, stimulates transparency.

If the local ethics committee offers a negative advice, research will be canceled, whereas a positive recommendation shall be brought to notice of the Federal Committee for Medical and Scientific Research on Embryos in Vitro (hereafter: the Federal Committee). If a majority of the members of the Federal Committee objects to the protocol, within a period of two months after the protocol has been presented to them, embryo research cannot be executed. If the research project has been allowed, a report on the advancement of the research project must be communicated yearly (until April 30 the latest) to the Federal Committee. Failure to do so may be punished by a fine of 50 to 5000 euro.

The Federal Committee's statutory functions include (art. 10):

- maintaining a formal register of information about all research protocols, included those that have been cancelled by the local ethics committees;
- avoiding the performance of similar embryo experiments;
- evaluating the Embryo Law;
- providing relevant advice aimed at legislative initiative;
- providing relevant advice and information about the applications of the Embryo Law for the benefit of local ethics committees;
- Submitting an annual report to the House of Representatives.

The composition of the Federal Committee is regulated in article 9. It consists of 14 members specialized in the medical, scientific, legal, ethical and societal aspects related to embryo research, i.e. 4 physicians, 4 doctors of science, 2 lawyers and 4 experts in ethical issues and social sciences. Following the example of the Federal Consultative Committee on Bioethics (see: *infra*), the Federal Committee is a pluralistic body, composed of an equal number of French and Dutch speaking members. No less than one third of the members should have the same sex. One can not at the same time be a member of the Federal Committee and the Consultative Committee on Bioethics.

*Note: local ethics committees.* The composition and functioning of local ethics committees is not included in the Embryo Law. We have to refer to the Royal Decree of 12 August 1994 (*Moniteur belge* 27 september 1994). It obliges all general and psychiatric hospitals to establish a so-called 'local ethics committee'. These committees are assigned a guiding and consultative task with regard to the ethical aspects of hospital

care and a review task with regard to all protocols concerning human experimentation and reproductive human material.

The Royal Decree also governs the composition of ethics committees. According to the decree, every committee has to consist of at least 8 and at most 15 members. The membership of the committee has to represent both sexes and a majority of the members has to be associated with the hospital as a physician. It is also obligatory for every committee to contain a lawyer, a nurse and a General Practitioner who is not associated with the hospital. The law further allows for other interested parties to participate as members of the committee. Lastly, the membership of the ethics committee is not only limited in numbers but also in function. Neither the director of the health care institution, nor the chief physician, nor the chairman of the Medical Council and the chief nurse are allowed to be part of the committee.

### **1.1.5. Creation of embryos solely for research purposes**

Article 4 of the Embryo Law prohibits the creation of embryos solely for research purposes, except where the objectives of the research project cannot be achieved by research on supernumerary embryos. The Law however does not stipulate which authority is in charge of making that decision.

During the hearings in both the Senate and House of Representatives, medical specialists considered the creation of embryos justifiable, because of its importance in terms of scientific research. In general, the necessity of embryo creation solely for research purposes is demonstrated by means of three types of research that cannot be met by using supernumerary embryos. First, a genuine improvement in IVF therapy can only be achieved if scientific research is conducted with embryos specifically created for that purpose. Improvement of IVF therapy means that even more infertile couples will be able to have children. This will alleviate sorrow and distress, felt by the women involved and decrease the number of embryos necessary for a successful implantation. Secondly, in light of the promising developments in preclinical studies on the cryopreservation of human ovarian tissue, offering this technology as 'fertility insurance' to cancer patients can also be justified.

The third purpose for which scientific research with specially created embryos may be executed in the future is transplantation and regenerative medicine. Research performed with murine embryos has already demonstrated the potential for culturing tissues from ES cells. Examples of diseases caused by the loss, or loss of function, of only one or a limited number of cell types and which could benefit from human ES cell based therapies include diabetes, Parkinson's disease, stroke, arthritis, multiple sclerosis, heart failure and spinal cord lesions. To date, most embryos used for the establishment of human ES cell lines have been embryos left over from an IVF treatment. The creation of embryos by somatic cell nuclear transfer specifically for deriving ES cells has however a surplus value. So-called therapeutic cloning might substantially improve the treatment for neurodegenerative diseases, blood disorders or diabetes, since therapy for these diseases is currently limited by the availability of tissue transplants that are immunocompatible. The production of ES cells, genetically identical to the patient, for autologous transplantation may prevent tissue rejection. Since therapeutic cloning is not explicitly prohibited in the Embryo Law, it is implicitly allowed.

Contrary to the conduct of research with supernumerary embryos, oocyte donation for purposes not intended to induce a pregnancy is inextricably linked to the creation of embryos specifically for research. The provision of oocytes however requires an invasive procedure. It has to be avoided that the women, willing to donate oocytes, are put under undue pressure. If, for example, the donor knows the acceptor of the oocytes, she will be keenly aware of the distress that childlessness is causing her. As set out in the Embryo Law, ovarion stimulation therefore requires that the woman involved has attained the age of majority and has given her written consent. Here too, the local ethics committee and the Federal Commission will have to assess whether it is scientifically and ethically sound for the woman involved to provide oocytes.

### 1.1.6. Prohibitory clauses

A number of ethically unaccepted procedures are totally prohibited by law. Violating these regulates will be punished by a fine of 1000 to 10000 Euro (art. 3, 5; 4; 5 and 6). Thus it is not allowed to:

- conduct research on an embryo that has developed outside the human body for longer than fourteen days;
- implant a human embryo into an animal or to create a chimaera or hybrid;
- implant an embryo on which research has been carried out into a woman's uterus except when the aim of research is essentially therapeutic for the embryo or when research does not harm the integrity of the embryo;
- use embryos, gametes and embryonic stem cells for commercial purposes;
- conduct research or receive treatment with a eugenic purpose, i.e. selection and enhancement of non-pathological genetic characteristics;

The explanatory memorandum refers to article 13 of the Convention on Human Rights and Biomedicine. There, a distinction is made between somatic and germ-line gene therapy. The Convention allows the former and forbids the latter. Contrary to the European Convention, the Belgian Embryo Law also permits the use of germ-line gene therapy to correct pathological characteristics, not however as an enhancement technique. Therefore, Belgium will have to make a reservation on article 13 before signing and ratifying the Convention.

- utilize sex-selection techniques for non medical reasons;

This legal provision refers to both pre-conceptual and post-conceptual sex selection. The former technique rests on sperm selection whereas the latter uses PGD to choose a male or female embryo. The verbatim text of the Embryo law states that it is forbidden to “conduct research or to receive treatments aimed at sex selection, except for the prevention of sex-linked diseases” (art. 5, 5). The European Convention on Biomedicine however argues that “The use of techniques of medically assisted procreation shall not be allowed for the purpose of choosing a future child's sex, except where *serious* [italics supplied] hereditary sex-related disease is to be avoided” (art. 14). Since the Convention imposes a more rigorous condition upon sex selection (i.e. serious hereditary disease), Belgium will also have to make a reservation on article 14.

- intentionally bring about the birth of one or more individuals whose genes are identical to those of the organism from which they originate (reproductive cloning).

Apart from a fine, ignoring the ban on reproductive cloning may also lead to a prohibition to do research for a period of five years.

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### Biographical Sketches

**Herman Nys** (°1951) obtained a degree of master (1974) and doctor (1980) in law at the K.U.Leuven. He specialised in Medical Law at European universities (Nijmegen; London).

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