FPS Public Health, Food Chain Safety and Environment, DG1 Health Care Facilities Organisation, Coordination of Organs, Embryos and Bio-Ethics

Federal Commission for medical and scientific research on embryos in vitro (CFE/FCE)

ACTIVITY REPORT 2008 – 2010

CONTENTS

Preamble

As Presidents of the Federal Commission for medical and scientific research on embryos *in vitro* we have the pleasure of herewith presenting the Commission's activity report, in keeping with Article 10 § 4 of the Act of 11 May 2003.

This report covers the period from February 26th, 2008 up to and including June 30th, 2010, and follows the previous annual report for 2006-2007.

Mrs B. Jacobs, President

Prof. A. Van Steirteghem, Vice-President

Dear Madam,
Dear Sir,

In June 2008, I was elected President of the CFE/FCE, of which I have been a member since its inception in June 2006.

The present report concerns the evaluation of projects submitted to the CFE/FCE and relating to research on human embryos. In reference to the fundamental democratic principles of Belgian legislation on human embryos I can safely say that the research that is conducted in this field in Belgium is performed with the greatest earnestness.

Each research project takes the special nature of the human embryo and the necessary protection that it requires very much into account.

In the future the CFE/FCE will have to further develop its informative mission vis-à-vis specialised and non-specialised target audiences. The CFE/FCE will have to carefully monitor the sensitive questions that regularly arise in this field. We hope to report on this in our next publication.

We hope our report is read with the attention it merits.

Bénédicte Jacobs

I. Composition of the CFE/FCE

As provided for in the Embryo Act of 11 May 2003, Art. 9 §2, the Commission shall be composed of 14 effective members. The members are appointed by the Senate (Belgian Official Journal 31/03/2006, p. 18045; 5/12/08, p.124) and by law shall include four doctors of medicine, four doctors of sciences, two lawyers and four experts in ethical issues and social sciences. A substitute member with the same qualifications shall be appointed for each of the members.

The members shall represent the various ideological and philosophical movements in a balanced manner. A third of the members of the Commission shall be of the same sex and the Commission shall have the same number of Dutch- and French-speaking members. The members' mandate lasts for four years.

The Royal Decree of 22/09/2004 which sets out the administrative and financial resources that are granted to the Commission was published on 21/10/2004 (2004/22801). From that day onwards the Commission was deemed to be operational and carry out its statutory duties.

Nine new members were appointed in 2008. Their names were published in the Belgian Official Journal of 5.12.08, Ed.3 p.124.

The list of effective and substitute members who are currently officiating in the Commission can be found in Table 1. You will also find a list of attendances of the members for 2008, 2009 and 2010 in Appendix 1.

The President and Vice-President were elected during the plenary meeting of June 30th, 2008.

The Executive Bureau comprises the following members:

- President: Bénédicte Jacobs, lawyer (30/06/2008 – present)
- Vice-President: André Van Steirteghem, Professor Emeritus at Vrije Universiteit Brussel (30/06/2008 – present)

In accordance with the Embryo Act, the President and Vice-President belong to different language groups and will step down after two years.

The effective members and the substitute members are all invited to the plenary meetings and some substitute members also make a significant contribution to the meetings.

I.1. Situation until June 30th, 2010

As already mentioned, the Commission members are appointed for a four-year period. Their mandate is renewable (Article 9 § 3 of the Act of 11 May 2003 concerning research on embryos in vitro).

Given that some members were appointed in 2006 (Belgian Official Journal 31.03.2006) the Commission thus had to be reappointed at the latest in the course of 2010.

Calls for applications were published in the Belgian Official Journal on November 18th, 2009 and on March 18th, 2010.

After the second call for applications the Commission is still lacking two French-speaking doctors of medicine, one French-speaking doctor of sciences and one Dutch-speaking lawyer. No new applications were submitted following the second call. The list of candidates was submitted to the Senate but no new Commission has been appointed in the meantime.

I.2. Current situation

The composition of the Federal Commission for medical and scientific research on embryos *in vitro* and experts in ethical issues and social sciences can be found in Table 1 below:

Table 1: **Composition of the Federal Commission** (official announcements, Belgian Official Journal of 31/03/2006 and **5/12/2008)**

The Executive Bureau	
PRESIDENT	***VICE-PRESIDENT***
Bénédicte JACOBS (FR)	André VAN STEIRTEGHEM (NL)
The working groups	
Doctors of medicine	
Jean-Jacques CASSIMAN (NL)	Thomas D'HOOGHE (NL)
Gilbert COOREMAN (NL)	Paul COSYNS (NL)
Fabienne DEVREKER (FR)	**Sophie PERRIER d'HAUTERIVE (FR)**
Luc ROEGIERS (FR) – resignation on 15/06/2010 – end of mandate	Dominique CHARLIER (FR) – resignation on 06/09/2009
Doctors of Sciences	
Robert PIJNENBORG (NL) – resignation on 06/03/2009	**Björn HEINDRICKX (NL)**
Josiane VAN DER ELST (NL)	**Usha Rani PUNJABI (NL)**
Arsène BURNY (FR)	**Caroline JOUAN (FR)**
Anne VAN CAUWENBERGE (FR)	Emmanuel HERMANS (FR)

Lawyers	
Dirk VAN DER KELEN (NL) – resignation on 14/06/2010 – end of mandate Bénédicte JACOBS (President - FR)	Erik MEWISSEN (NL) **Nicole GALLUS (FR)**
Experts on ethical issues and social sciences	
Sofie BLANCQUAERT (NL) – end of mandate - 14/06/2010 André VAN STEIRTEGHEM (Vice-President - NL) **Marie-Geneviève PINSART (FR)** **Françoise CAILLEAU (FR)**	Gerry EVERS-KIEBOOMS (NL) – resignation on 14/06/2010 – end of mandate Guido PENNINGS (NL) **Laurent RAVEZ (FR)** **Henri ALEXANDRE (FR)**
The Secretariat	
Scientific Secretary	**Deputy Administrative Secretary**
Ann DEVOS (01/01/2007 - 17/12/2008) Fabrice PETERS (07/01/2008 – 31/08/2010) Didier STRAELER (01/09/2010 – 01/04/2011)	- Inge Van Mieghem (01/02/2009 - 01/06/2010) Isabelle DE MAESENEIRE (01/08/2010 - 01/10/2011)

I.3. Secretariat

As provided for in the Act of 03.10.2008 the Secretariat should consist of an A3 level Scientific Secretary and a level B Deputy Secretary.

Since the inception of the CFE/FCE the situation in the secretariat has been unstable. As a consequence the staffing changed several times. Five different employees occupied these two positions over a five-year period (see Table 1). This situation may give rise to problems stemming from a lack of knowledge of the Commission's procedures, which in turn can affect the Commission's proper functioning.

The Commission's Secretary resigned on August 31st, 2010 on which date he started his traineeship to become an established civil servant in another institution of the FPS Health, Food Chain Safety and Environment (FPS HFSE). In the interim he was replaced by an attaché of the FPS in the capacity of Scientific Secretary and by a Level B Deputy Secretary as originally provided for in the Commission's composition.

In 2010 the Secretariat consisted of a level A Secretary and a level B Deputy Secretary. These two officials have since left their positions in the FPS HFCSE during 2011. At the time of publication of this report a contractual level A1 Scientific Secretary mans the secretariat.

The CFE/FCE thus is still waiting for the appointment of a level A3 Scientific Secretary for an optimum functioning of the Secretariat.

II. The CFE/FCE in practice

II.1. CFE/FCE meetings

The CFE/FCE meets monthly, except in July and August. All meetings are held in Eurostation Block II, at 40, Place Victor Horta in 1060 Brussels. The CFE/FCE has sufficient meeting rooms there. The CFE/FCE wishes to maintain this situation in the future. Meeting attendance (2008-2010) is described in **Appendix 1**.

II.2. Financial report

The CFE/FCE's financial condition is satisfactory (see financial report in **Appendix 2**). Given the changes in the Secretariat's staffing we hitherto have not been able to organise certain activities, such as a conference.

The costs associated with the use of eComm shall also be charged in the future. Publications and official translations of reports for the CFE/FCE's own website (www.embryos.be) will also eat into the budget.

II.3 Internal communication

The e-Communities ensure that the CFE/FCE members can avail themselves of secure communication and that they can consult files, which in some cases are quite large, which block electronic mailboxes when sent by e-mail. An extension of the available IT tools could ensure that documents do not need to be printed unnecessarily.

The Secretariat uses EndNote software, which facilitates the rapid classification and layout of part of the information related to scientific monitoring.

The CFE/FCE's website is regularly updated to guarantee more transparency about its operations.

INFORMATIVE ROLE OF THE EMBRYO COMMISSION

The Commission's informative functions are:

- To inform the government, parliament, the councils of the respective communities and the general public.
- To establish a documentation and information system and keep it up to date.

The Embryo Commission's informative mission vis-à-vis the Government is reflected in this annual report.

The Secretariat deals with any questions to the Commission after consultation with the CFE/FCE.

In terms of centralising information and documentation related to research on embryos *in vitro* in Belgium it is important to provide the most complete inventory of ongoing research and even of research that has already been finalised, with a view to creating total transparency.

ADVISORY ROLE OF THE COMMISSION

III. The CFE/FCE's activities

III.1. Opinions of the Federal Commission for medical and scientific research on embryos in vitro, 2008-2010

In 2008-2010 the Commission received 14 requests for opinions, of which two did not fall within the scope of the Embryo Act.

The CFE/FCE's opinions are numbered and listed as "ADV_xxx", with xxx being the number of the opinion.

The following information has been included in the report for each opinion:

- Project title,
- Name of the researchers,
- Institution where the research is conducted,

- Project duration: start date and end date. The start date marks the date on which the project was approved,
- Project description.

1) Human embryonic stem cells as new models for the development of new therapies and exploration of mechanisms in monogenic diseases (ADV_012)

K. Sermon, I. Liebaers
Brussels University Hospital(UZ Brussel) – Centre for Medical Genetics and Reproductive Medicine

Project duration: from 06/12/2008 until 06/12/2012

Human embryonic stem cells are made from human embryos that are about six days old, whereby the embryos themselves are destroyed. These stem cells can grow for quite some time in a petri dish in the laboratory in the primitive form in which they are present in the embryo. As such they remain a source of new cells. They can grow into any tissue in the human body when given the right stimuli. That is why these cells are of great importance in medicine because they can be used, for example, for the treatment of diabetes or Parkinson's Disease. They could also be used in the pharmaceutical industry to develop and test new drugs and thus would significantly reduce the number of test animals needed in drug research.
The project envisages the creation of embryonic stem cells from PGD embryos, which cannot be used because they are affected by a genetic condition.
Such stem cells are important to understand the cause and consequences of such disorders. This could also open up possibilities for a possible treatment of these conditions.

2) (Epi)genetic stability in gametes, preimplantation embryos and human embryonic stem cells with a focus on the behaviour of dynamic mutations causing myotonic dystrophy and fragile X syndrome (ADV_013)

I. Liebaers, K. Sermon
Brussels University Hospital(UZ Brussel) – Centre for Medical Genetics and Reproductive Medicine

Project duration: from 23/05/2008 until 23/05/2012

Human embryonic stem cells (hESCs) are pluripotent cells derived from the ICM of blastocysts, which are capable of maintaining themselves in a non-differentiated state and which can differentiate into all three embryonic cell layers. As a result these cells not only hold promise in terms of future cell therapy. They also provide a research model for early human development and genetic diseases.
hESCs are immortal cell lines, which are frequently maintained in culture for a long period of time, without this seemingly affecting their pluripotency. However, mutations do take place in these cells as in every other dividing cell.

This project consists of two main lines of research:

A. The hESC's genomic stability will be examined. This is important because, should these cells ever be used in cell therapy, the recipient's safety must be guaranteed. Changes in the genome can also influence the proteome of these cells, which, in turn, may affect their capacity to differentiate into different cell types. Changes in the DNA sequence as well as epigenetic changes (methylation patterns) can have an effect on these cells.

B. The behaviour of dynamic mutations shall be examined in gametes and preimplantation embryos (as in vivo model) and in hESC (as in vitro model). hESCs carrying these mutations are interesting models, which could also reduce or even eliminate animal testing. It is important to characterise the behaviour of the mutation in this hESC before undertaking other experiments. The objective is to contribute to the elucidation of the mechanisms of instability in dynamic mutations, which is important for the development of the treatments for these patients.

3) Detection of chromosomal abnormalities in preimplantation embryos by array CGH (ADV_014)

K. Sermon, A. Mertzanidou, C. Spits, C. Staessen
Brussels University Hospital(UZ Brussel) – Centre for Medical Genetics and Reproductive Medicine

Project duration: from 05/05/2009 until 05/05/2013

Years of research on embryos obtained after in vitro fertilisation have revealed that many of them, up to half even, have abnormal chromosomes. Most of these embryos with chromosomal abnormalities will not survive after replacement in the uterus.

This project is part of the "strategic basic research (SBO)", entitled "Molecular karyotyping". The researchers shall work to create a short and efficient protocol for cell analysis by array CGH. This protocol shall be applied to human preimplantation embryos that were donated for scientific research. The results shall be used to determine the frequency of chromosomal abnormalities in embryos and the degree of mosaicism. The results will also be compared with the FISH results, to verify false-negative and false-positive rates. The researchers will also work on a protocol for the detection of unbalanced structural chromosomal abnormalities. This research may lead to the implementation of array CGH in preimplantation genetic diagnosis.

4) Genetic expression in human pre-implantation embryos and embryonic stem cells: characterisation of the human totipotent cell (ADV_015)

I. Liebaers
Brussels University Hospital(UZ Brussel) – Centre for Medical Genetics and Reproductive Medicine

Project duration: from 30/06/2008 until 30/06/2012

Our knowledge of human development during pre-implantation (i.e., the period before the embryo prepares to implant itself in the uterus) is quite limited. During this period the fertilised egg develops into a
multicellular embryo and subsequently into a blastocyst. The blastocyst is composed of the germ cells (the future foetus) and trofectoderm cells (part of the placenta). The trofectoderm is necessary for implantation in the uterus. After replacement in the uterus implantation usually occurs on day 6-7 of early development.
In order to study early development we will verify which cells in the early embryo have the capacity to develop into a complete embryo again in a laboratory setting.
To this end we shall determine the absence or presence of certain substances (proteins) in the differentiating embryonic cells with the aid of specific (molecular biology) measurement techniques and microscopy. Information about the moment when and the mechanism by which the cells of the preimplantation embryo start to differentiate is important for our knowledge of human embryology, more specifically (1) how the first differentiation (into placental tissue) and the second differentiation (into yolk sac) occur in humans and (2) what happens after cell loss during in vitro development as a result of fragmentation, biopsy for preimplantation genetic diagnosis (PGD) and damage as a result of freezing. Stem cells shall be grown from some embryos, which, in turn, shall be used for further research. This research will also contribute to our knowledge of stem cell biology, more specifically to the origin of embryonic stem cells in the embryo.

5) Optimize clinical in vitro maturation of oocytes by translational molecular research (ADV_016)

J. Smitz, P. Devroey, J. Van der Elst
Brussels University Hospital (UZ Brussel) – Centre for Medical Genetics and Reproductive Medicine

Project duration: from 05/06/2008 until 05/06/2012

IVF/ICSI is necessarily associated with a hormone treatment which is experienced as laborious and expensive by patients. This treatment causes significant overstimulation in 1 to 2% of patients stimulated for IVF/ICSI. Patients with polycystic ovary syndrome (PCOS) are especially at risk, as they may react explosively when Gonadotropins are administered. In Vitro Maturation (IVM) is an attractive alternative to IVF, avoiding heavy hormone treatments as well as serious complications. Immature oocytes are picked up from follicles in the growth phase. The current growing procedure for such immature oocytes (IVM with already commercialised culture media) however is far from perfect because the chances of implantation per embryo are only 10% (i.e., only *50%* of the rates after routine IVF or ICSI with mature oocytes). The hypothesis is that the in vitro growing procedure is not suited to most immature oocytes and that it may be possible to improve maturation in the nucleus as well as in the cytoplasm. The main objective of this study is to validate an innovative in vitro maturation protocol for part of the immature oocytes.

6) Optimization of human somatic cell nuclear transfer (ADV_017)
P. De Sutter
Infertility Centre, University Hospital Ghent

Decision: Negative opinion on 02/03/2009 for noncompliance with Article 3 2° "the research is founded on the most recent scientific findings and complies with the requirements of a correct methodology for scientific research" and Article 7 § 1 "The request for an opinion contains a detailed description of the objective, the methodology and the duration of the research".

7) Optimizing embryo culture and comparison of different sources of embryos for human embryonic stem cell line derivation (ADV_018)
P. De Sutter, B. Heindryckx, T. O'Leary, S. Lierman
Infertility Centre, University Hospital Ghent

Decision: Negative opinion on 17/06/2009 for noncompliance with Article 3 2° "the research is founded on the most recent scientific findings and complies with the requirements of a correct methodology for scientific research" and Article 7 § 1 "The request for an opinion contains a detailed description of the objective, the methodology and the duration of the research".

8) Study of the PTEN pathway during preimplantation human embryo development (ADV_019)
Y. Englert, F. Devreker, C. Hoofd
Université Libre de Bruxelles - Laboratoire de recherche en reproduction humaine

Project duration: from 21/08/2009 until 21/08/2013

Preimplantation development is characterised by a complex series of events which transforms the fertilized egg into a blastocyst that is ready to implant. This is a process of growth and of differentiation: the structures and functions become increasingly complex. One characteristic of human embryos is their high percentage of arrested development between the zygote and blastocyst stages. The arrested development is caused by perturbations at the levels of the cellular differentiation and proliferation mechanisms. These are much more complex than the mechanisms governing cell division in mature tissues.
The aim of the study is to study the expression of essential factors of murine embryonic development in humans. The study shall be conducted using advanced molecular biology methods (PCR and confocal imaging).

9) Analysis of calcium pattern in human oocytes and application of various activation stimuli (ADV_020)

P. De Sutter, B. Heindryckx, L. Leybaert
Infertility Centre, University Hospital Ghent

Project duration: from 09/07/2009 until 09/07/2013

Failed fertilisation after ICSI is mainly due to a deficiency in the oocyte activation mechanism. Our Department of Reproductive Medicine has the necessary expertise to apply assisted oocyte activation by means of ionophore during ICSI to solve this activation problem. Problems in the oocyte activation mechanism may be related to the sperm or to the egg. The sperm head contains the sperm factor which is responsible for calcium increases in the oocyte's cytoplasm. On the other hand the oocyte has to have cytoplasmic maturity to generate the Ca increases. The crucial role of the oocyte in this oocyte activation mechanism remains unclear however. The clinical application of assisted oocyte activation during ICSI is highly efficient when a sperm cell factor causes failed ICSI but less efficient when an oocyte factor is suspected. The aim of this project is to study the oocyte's role by carrying out a Ca pattern analysis on the one hand and to identify which artificial activation agents are most suited for inducing Ca increases.

10) Chromosomal abnormalities in human preimplantation embryos and embryonic stem cells: causes, mechanisms and consequences for in vitro fertilisation and regenerative medicine (ADV_021)

K. Sermon, C. Spits, A. Mertzanidou
Brussels University Hospital (UZ Brussel) – Centre for Medical Genetics and Reproductive Medicine

Project duration: from 18/12/2009 until 18/12/2013

The project studies the causes, mechanisms and consequences of chromosomal abnormalities in human preimplantation embryos and embryonic stem cells for in vitro fertilisation and regenerative medicine.

Preimplantation genetic screening (PGS) aims to promote IVF pregnancies by selecting chromosomally normal embryos. Although a high number of human embryos display chromosomal abnormalities PGS does not have the desired result. On the other hand it recently became clear that human embryonic stem cells (hESC) frequently display chromosomal abnormalities. Our hypothesis is that the cell cycle checkpoints in embryos and hESCs are not operational therefore causing these abnormalities to occur more easily. We wish to compare the key elements of the checkpoints in embryos as well as in hESCs in this project to determine whether hESC would be a good model for the study of embryos, as is often suggested. We also want to explain the great chromosomal

instability of hESC in order to improve the current culture conditions, which probably have a negative effect on the occurrence of chromosomal abnormalities. Finally we also wish to be able to explain the chromosomal abnormalities in embryos as well as the mechanisms of self-correction in order to be able to develop a new, reliable screening tool for embryos which could replace PGS.

11) Influence of embryo morphology on stem cell derivation efficiency and molecular characterisation / Identification of intermediary structures between the inner cell mass and stem cell outgrowth (ADV_022)

P. De Sutter, B. Heindryckx, T. O'Leary, S. Lierman
Infertility Centre, University Hospital Ghent

Project duration: from 02/02/2010 until 02/02/2014

The recent technique of therapeutic cloning aims to produce sex cells de novo and in vitro. This strategy consists of making embryonic stem cells (ESCs) from the inner cell mass of 5-day old nuclear transfer embryos differentiate in vitro into sex-determining cells. The aim of this project is to achieve one objective in this strategy, namely the isolation of human embryonic stem cells lines from supernumerary embryos, coupled with the three original objectives. Literature on human stem cell research has shown that the origin and quality of the used embryos is rarely described, usually because stem cell labs are not directly affiliated with an IVF lab. Bridging the gap between the embryology lab and the stem cell lab may improve the efficiency of stem cell derivation and may possibly provide an explanation for the differences in efficiency derivation between both types of labs. The project aims to examine which morphological parameter of a supernumerary embryo offers the highest chances for isolating a stem cell line. We know that the supernumerary embryos are of inferior quality compared with the embryos that are used for replacement or that are frozen. But the latter embryos are used for the patient. The supernumerary embryos thus are the largest source of embryos for stem cell research.

12) Optimizing the culture environment during the embryonic development of in vitro matured oocytes from small ovarian follicles (ADV_024)

P. De Sutter, K. Versieren, F. Dumortier
Infertility Centre, University Hospital Ghent

Project duration: from 02/02/2010 until 02/02/2014

Oocytes that are encapsulated in small ovarian follicles after hormonal stimulation have not fully completed the growth and maturation process. That is why these follicles are not punctured during the follicular puncture and these encapsulated oocytes are not used for the patient's IVF/ICSI treatment. However these oocytes may constitute an important source of study material for experimental research. Research in our centre has shown that oocytes from small ovarian follicles are easily collected during the follicular puncture. The culture systems for the in vitro maturation (IVM) of these oocytes have been

optimised in this frame. In the current project we wish to optimise the embryonic development of these IVM oocytes. Initially the embryonic development of the IVM oocytes shall be verified by ICSI with donated sperm. Then the researchers shall attempt to optimise the embryonic development of the IVM oocytes after ICSI. Reactive oxygen species (ROS) are produced during the metabolism of developing embryos. Excess production of ROS contributes to oxidative stress in embryos giving rise to various types of damage. In vivo embryos are protected against oxidative stress by various factors in the fallopian tube fluids. It is important to keep the oxidative stress during in vitro culture under control in order to increase in vitro embryo production. The aim of this study is the optimisation of the culture environment and the embryonic development of IVM oocytes from small follicles. To this end various anti-oxidants will be added to the culture medium after ICSI. In a next step we will try to improve the culture environment of the embryos by using a co-culture system after ICSI. The embryos that are formed shall be fixated. The oocytes and embryos shall thus not be replaced in patients and will be destroyed after the experiment has ended.

13) Totipotency and cell commitment during the human preimplantation development (ADV_025)

I. Liebaers, H. Van de Velde, G. Cauffman, C. De Paepe, A. Verloes, L. Petrussa
Brussels University Hospital (UZ Brussel) – Centre for Medical Genetics and Reproductive Medicine

Project duration: from 11/05/2010 until 11/05/2014

This is a continuation of the project discussed in ADV_015.

14) Vitrification of supernumerary embryos and frozen-thawed supernumerary embryos: analysis of the survival (Adv 027)

P. De Sutter, S. Lierman
Infertility Centre, University Hospital Ghent

Project duration: from 11/05/2010 until 11/05/2014

The aim of this study is to examine whether blastocysts from fresh supernumerary embryos can be efficiently frozen by vitrification. The study will also examine whether blastocysts from frozen-thawed supernumerary embryos can undergo a second freezing process.
There are several studies in literature on blastocyst vitrification from fresh embryos. These studies show that a high survival rate can be achieved after thawing. But not many studies have been conducted into the re-freezing of blastocysts from frozen-thawed embryos.

III.2 Questions submitted to the Federal Commission for medical and scientific research on embryos in vitro

In recent years the Commission also examined various questions, including several issues that were not immediately within its competences (see Appendix 3).

The Federal Embryo Commission's mission is to monitor embryo research. Nevertheless many questions that are not always related to its field of action are submitted to the Commission.

The Commission tries to respect the boundaries of its mandate as much as possible. It thus cannot answer all the questions submitted to it, especially when it does not have the necessary competences or data to do so.

MONITORING ROLE OF THE COMMISSION

IV. Scientific, legal and ethical monitoring

The Commission's Secretariat is in charge of scientific, legal and ethical monitoring, based on several sources and search engines.

The research results are regularly shared with the CFE/FCE's members during the plenaries.

SCIENTIFIC MONITORING

The PubMed and ScienceDirect databases and the EndNote programme are searched using the following search terms among others: "embryo, stem cells, Belgium".

ETHICAL MONITORING

In order to ensure that ethical subjects relating to embryos are covered as widely as possible the following sources of information are regularly monitored:

- CCB (BE)

https://portal.health.fgov.be/portal/page?_pageid=56,512676&_dad=portal&_schema=PORTAL
- PRESS OVERVIEW FPS (BE):

- SHS (INT)

http://portal.unesco.org/shs/fr/ev.php-URL_ID=1372&URL_DO=DO_TOPIC&URL_SECTION=201.html

- CDBI (EU)

http://www.coe.int/t/dg3/healthbioethic/cdbi/default_FR.asp
- EGE (EU)

http://ec.europa.eu/european_group_ethics/index_fr.htm
- *ESHRE (EU)*

http://www.eshre.eu/ESHRE/English/Specialty-Groups/SIG/Ethics-and-Law/Welcome/page.aspx/134
- *CCNE (FR)*

http://www.ccne-ethique.fr/
- *ABM (FR)*

http://www.agence-biomedecine.fr/
- *HFEA (UK)*

http://www.hfea.gov.uk/
- *Bionews (UK)*

http://www.bionews.org.uk/
- *ASRM (USA)*

http://www.asrm.org/
- *BSRM (BE)*

http://www.bsrm.be/Boardmembers.html
- *VVOG (BE)*

http://www.vvog.be/
- *GGOLFB (BE)*

http://www.ggolfb.be/public/Default.aspx?doc=3012607b-699e-4ce2-a8b0-55185eb802d9

LEGAL MONITORING

The main sources of information for legal monitoring are:
http://www.moniteur.be/index_nl.htm
http://www.senaat.be/
http://www.dekamer.be/
http://justitie.belgium.be/

These are the most important legal documents for the period 2008-2010:

- Draft Act of 29 May 2008 containing various provisions I (Chamber Document 52K1200001, 2nd session of the 52nd parliamentary term 2007-2008).

- Draft Act of 16 October 2008 amending Article 8 of the Act of 11 May 2003 on research on embryos in vitro (Legislative Document no. 4-972/1, session 2008-2009, submitted by Messrs Philippe Mahoux and Philippe Monfils).

- Draft Act of 29 April 2009 to postpone the date of entry into force of the Act of 19 December 2008 on the acquisition and use of human bodily substances for medical use on humans or for scientific research (Legislative Document no. 4-1288/1, session 2008-2009, submitted by Mr Philippe Mahoux c.s.).

- Draft Act of 7 May 2009 amending legislation on stillborn children (Legislative Document no. 4-1318/1, session 2008-2009, submitted by Mrs Sabine de Bethune).

IV.1 Participation in seminars and conferences

IV.1. 1. Annual conference of the European Society of Human Reproduction & Embryology (ESHRE)

ESHRE is the leading European scientific society in the field of human reproduction and embryology (www.eshre.eu) and is the European equivalent of the American Society for Reproductive Medicine - ASRM.

Since the inception of the CFE/FCE's operations, the Scientific Secretary has been a member of ESHRE. The CFE/FCE's members are also ESHRE members. CFE/FCE members who work in this field also take part in the annual conferences. Since 2008 there has always been a CFE/FCE representation at the ESHRE

Annual Meeting:

2008. Barcelona, Spain, B. Jacobs and A. Devos attended.

2009. Amsterdam, the Netherlands. F. Peters attended.

2010. Rome, Italy. B. Jacobs and F. Peters attended.

IV.2. Working group information and consent form for patients

The requests for opinions submitted to the Commission show that drawing up consent forms still poses a number of problems for researchers. A working group was appointed to deal with the issue of the information and consent form in the specific case in which new embryos are used for research. This working group shall determine whether such a form is justified in phased projects and whether a standardized model can be developed to simplify the work of the research teams.

The idea is to continue the initial reflection process. The Commission regularly experiences problems when it comes to harmonizing the required criteria for each research project. In view of the projects' complexity and their execution it is important that the content/wording of information and consent forms be standardized as much as possible.

IV.3. Prospects for 2011 - 2012

The appointment of a level A3 Scientific Secretary would contribute to ensuring continuity in this position at an administrative level. The current situation may give rise to problems stemming from a lack of knowledge of the Commission's procedures, which, in turn, may affect its proper functioning. The position of Deputy Secretary level B will probably be filled again in January 2012.

The Commission wishes to organise a press conference and a workshop in 2011 to contribute to its notoriety.

The Commission also wishes to organise a conference in 2012. Decisions have to be made about the theme, the speakers and the logistical aspects. It is hoped that this will be clarified in early 2012.

The standardization of the information and consent form would also contribute to the Commission's proper functioning and would enable the research teams to save a significant amount of time.

In view of the difficulty related to finding members, the procedure for the Commission's reappointment should be simplified and the tacit renewal of mandates should be possible unless the acting or substitute member asks to be replaced. As a result the Commission's continuity could be guaranteed.

V. Conclusion

The Embryo Commission has continued its work in 2008-2010 as laid down by law. Some activities, such as the planning of a conference, have been postponed because of the unstable situation of the Secretariat in the FPS HFCSE.

The Commission's tasks for 2011 are as follows:

- The Commission needs to continue to carefully map the entire field of medical and scientific research on embryos in vitro in Belgium.

- The Commission must adopt a position on the conditions under which cryo-preserved embryos can be used for research on embryos in vitro. The information included in the consent form according to the Act on Medically Assisted Procreation of 6 July 2007 in many cases will not comply with the conditions imposed according to Article 8 of the Embryo Act of 1 May 2003.

- The Commission wishes to further develop guidelines in working groups, aimed at supporting the Local Ethical Committees, more specifically the « patient information form » and the « patient consent form », as well as practical guidelines relating to research on embryos in vitro, which are aimed at researchers.

This activity report 2008 – 2010 was adopted by the CFE/FCE's plenary (PV 44) on December 19th, 2011.

VI. Appendices

Appendix 1: Attendance at meetings of the Federal Commission for medical and scientific research on embryos in vitro, 2008-2010

		2008								2009								2010			
Leden van de FCE / Membres de la CFE	**Effectif/Effectif - Suppléant/Plaatsvervanger**	14/01/2008	25/02/2008	17/03/2008	7/04/2008	19/05/2008	30/06/2008	15/09/2008	1/12/2008	12/01/2009	2/03/2009	30/03/2009	11/05/2009	22/06/2009	7/09/2009	26/10/2009	30/11/2009	18/01/2010	8/03/2010	10/05/2010	3/06/2010
Jacobs Bénédicte (FR)	Effectif	P	P	P	P	P	P	P	P	P	E	P	P	P	P	P	P	P	E	P	P
Van Steirteghem André (NL)	Effectif	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	E	P
Artsen / Docteurs en médecine																					
Cassiman Jean-Jacques (NL)	Effectif	P	P	E	P	E	P	P	P	P	P	P	P	P	P	E	P	E	P	E	E
Cooreman Gilbert (NL)	Effectif	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
Devreker Fabienne (FR)	Effectif	P	P	P	E	P	P	P	E	P	P	A	P	P	E	P	P	E	P	P	A
Roegiers Luc (FR)	Effectif/Démission	P	A	P	P	P	E	P	P	P	A	E	P	E	E	E	E	E	E	E	A
D'Hooghe Thomas (NL)	Suppléant	P	E	E	E	P	P	E	E	E	A	A	E	E	E	E	E	P	A	P	E
Cosyns Paul (NL)	Suppléant	P	E	P	A	P	E	E	E	A	A	P	E	E	P	E	P	P	P	P	A
Charlier Dominique (FR)	Effectif/Démission	A	A	A	A	A	A	A	A	A	A	E	A	E	E	démission 06/2009					
Perrier d'Hauterive Sophie (FR)	Suppléant/Effectif	aangewezen/nommés 12/2008								E	P	A	E	E	E	P	E	P	E	E	P
in wetenschappen / Docteurs en sciences																					
Pijnenborg Robert (NL)	Effectif/Démission	P	E	P	E	P	E	E	E	E	démission 03/2009										
Van Der Elst Josiane (NL)	Effectif	P	P	E	P	P	P	P	P	P	P	E	E	E	A	E	A	A	A	A	A
Burny Arsène (FR)	Effectif	A	A	A	A	A	A	A	P	E	A	E	E	P	P	P	A	E	E	A	P
Van Cauwenberge Anne (FR)	Effectif	P	E	P	E	P	P	P	P	P	P	E	P	E	P	E	P	P	P	P	E
Hermans Emmanuel (FR)	Suppléant	A	E	P	P	A	E	E	E	A	A	A	E	E	A	E	E	A	A	A	A
Heindrickx Björn (NL)	Suppléant/Effectif	aangewezen/nommés 12/2008								P	P	E	P	P	E	P	P	P	P	P	E
Punjabi Usha Rani (NL)	Suppléant	aangewezen/nommés 12/2008								P	P	P	P	P	P	P	P	P	P	P	P
Jouan Caroline (FR)	Suppléant/Effectif	aangewezen/nommés 12/2008								E	P	P	E	P	A	E	P	P	P	P	E
Juristen / Juristes																					
Van Der Kelen Dirk (NL)	Effectif	P	E	P	P	E	P	P	P	P	P	P	E	P	P	P	P	P	P	P	P
Mewissen Erik (NL)	Suppléant	A	P	A	A	E	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
Gallus Nicole (FR)	Suppléant									P	E	A	P	E	P	E	E	P	E	E	E
e problemen en de sociale wetenschappen / Experts éthique																					
Blancquaert Sofie (NL)	Effectif	E	E	P	E	E	P	E	E	A	E	E	E	E	E	A	E	A	E	E	E
Evers-Kiebooms Gerry (NL)	Suppléant	P	E	E	E	P	P	E	E	P	E	E	E	E	P	E	P	P	E	E	E
Pennings Guido (NL)	Suppléant	P	A	A	P	A	P	E	E	P	A	A	E	E	E	P	P	P	E	E	P
Pinsart Marie-Geneviève (FR)	Effectif	aangewezen/nommés 12/2008								P	P	P	E	E	P	P	E	P	E	P	E
Cailleau Françoise (FR)	Effectif	aangewezen/nommés 12/2008								P	E	P	P	E	P	E	P	P	P	E	E
Ravez Laurent (FR)	Suppléant	aangewezen/nommés 12/2008								P	P	E	E	E	E	P	E	E	P	E	A
Alexandre Henri (FR)	Suppléant	aangewezen/nommés 12/2008								P	P	P	E	P	P	P	P	P	P	E	E

Aanwezig / Présence = P
Verontschuldigd / Excusé = E
Afwezig / Absent = A

Appendix 2. Budget 2008, 2009 and 2010 of the CFE/FCE

Budget 2008 - **Embryocommissie**	**Werkingskosten**
Commission Embryos	**Frais de fonctionnement**

51	7	1	1201

(En milliers d'euros sans décimale – In duizenden euro zonder decimalen)

Aangepast – Adapté 2006	Budget Control 2007
38	39

Niet-gesplitst krediet
Crédit non-dissocié

VOORSTEL PROPOSITION 2008	REALISATIES 2007 REALISATION 2007 CB1/CB3	Raming Estimation 2009	Raming Estimation 2010	Raming Estimation 2011
38	0,1	38	38	38

Verantwoording – Justification

1. Opdrachten/Doelstelling – Missions/Objectif
2. Indicatoren Kostprijs – Indicateurs Prix coûtant
3. Cijfermatige berekening – Calcul chiffré
4. Compensatie - Compensation

(Eéntalig – Unilingue)

BUDGET OWNER
C. DECOSTER

1.Opdrachten/Doelstelling

De wet van 11 mei 2003 betreffende het onderzoek op embryo's in vitro voorziet in de oprichting van een federale commissie voor medisch en wetenschappelijk onderzoek op embryo's in vitro.

3. Ingevolge een beslissing tijdens het conclaaf bij de opmaak van de initiële begroting 2007 werden de werkingsmiddelen van DG1 verminderd met 22.000€. Deze besparing werd aangerekend op drie basisallocaties 1201. Een billijke verdeling van de besparing van 22.000€ over alle basisallocaties 1201 van DG1 brengt het referentiekrediet 2007 voor B.A. 51 71 1201 op **38.000€** binnen de totale enveloppe van 594.000€ voor de basisallocaties 1201 van de OA 51.
De bijdrage van DG1 bij de werking van de Gemeenschappelijke Dienst voor Preventie en Bescherming op het werk (8.000€) werd verdeeld over de basisallocaties 1201. Voor B.A 51 71 1201 werd een bijdrage van 1.000€ verrekend.

- Zitpenningen en reisvergoedingen:	6.000
- Simultaanvertaling:	4.000
- Vergaderkosten:	3.000
- Boeken en tijdschriften:	4.000
- Initiatieven, te ontwikkelen door Commissie:	21.000
Totaal:	**38.000**

Brussel, 17 januari 2008.

De Directeur-generaal,

C. DECOSTER.

E. VERVAET

Budget 2009 - **Embryocommissie**	**Werkingskosten**
Commission Embryos	**Frais de fonctionnement**

51	7	1	1201

(En milliers d'euros sans décimale – In duizenden euro zonder decimalen)

Aangepast – Adapté 2007	Initieel - Initial 2008
39	38

Niet-gesplitst krediet
Crédit non-dissocié

VOORSTEL PROPOSITION 2009	NIEUW INITIATIEF NOUVELLE INITIATIVE	Raming Estimation 2010	Raming Estimation 2011	Raming Estimation 2012
37		37	37	37

Verantwoording – Justification

5. Opdrachten/Doelstelling – Missions/Objectif
6. Indicatoren Kostprijs – Indicateurs Prix coûtant
7. Cijfermatige berekening – Calcul chiffré
8. Compensatie - Compensation

(Eéntalig – Unilingue)

BUDGET OWNER
C. DECOSTER

1.Opdrachten/Doelstelling

De wet van 11 mei 2003 betreffende het onderzoek op embryo's in vitro voorziet in de oprichting van een federale commissie voor medisch en wetenschappelijk onderzoek op embryo's in vitro.

3. - Zitpenningen en reisvergoedingen:	6.000
- aankopen < 5.500€	2.000
- Individuele vorming	1.000
- Vergaderkosten:	3.000
- Boeken en tijdschriften:	4.000
- Symposium:	10.000
- Initiatieven, te ontwikkelen door Commissie:	11.000
Totaal:	**37.000**

4. Compensatie.
Ingevolge een beslissing van het Directiecomité wordt een krediet van 2.000 € overgeheveld naar de horizontale dienst B&Bc die vanaf het begrotingsjaar 2009 de kosten zal dragen voor tolkenprestaties.

Brussel, 19 mei 2008.

De Directeur-generaal,

C. DECOSTER.

E. VERVAET

Budget 2010 - **Embryocommissie**	**Werkingskosten**
Commission Embryos	**Frais de fonctionnement**

51	7	1	1211

(En milliers d'euros sans décimale – In duizenden euro zonder decimalen)

Aangepast – Adapté 2008	Initieel - Initial 2009
39	38

Niet-gesplitst krediet
Crédit non-dissocié

VOORSTEL PROPOSITION 2009	NIEUW INITIATIEF NOUVELLE INITIATIVE	Raming Estimation 2010	Raming Estimation 2011	Raming Estimation 2012
37		37	37	37

Verantwoording – Justification

9. Opdrachten/Doelstelling – Missions/Objectif
10. Indicatoren Kostprijs – Indicateurs Prix coûtant
11. Cijfermatige berekening – Calcul chiffré
12. Compensatie – Compensatio

(Eéntalig – Unilingue)

BUDGET OWNER
C. DECOSTER

1.Opdrachten/Doelstelling

De wet van 11 mei 2003 betreffende het onderzoek op embryo's in vitro voorziet in de oprichting van een federale commissie voor medisch en wetenschappelijk onderzoek op embryo's in vitro.

3. - Zitpenningen en reisvergoedingen:	6
- aankopen < 5.500€	2
- Individuele vorming	1
- Vergaderkosten:	3
- Boeken en tijdschriften:	4
- Symposium:	10
- Initiatieven, te ontwikkelen door Commissie:	11
Totaal:	**37 KEUR**

Brussel, 13 mei 2009.

De Directeur-generaal,

C. DECOSTER.

E. VERVAET

Appendix 3. Overview of the CFE/FCE's opinions for 2008-2010

Opinion	Project name Team Research Centre	Date of reception of the application	Opinion of the local ethical commission	Decision	Date of approval or denial	Term
Adv 012	**1) Human embryonic stem cells as new models for development of new therapies and exploration of mechanisms in monogenic diseases** Prof. Dr. K. Sermon, Prof. Dr. I. Liebaers **UZ Brussel**	19/02/2008		Not in the frame of the Embryo Act		6/12/2008
Adv 013	**(Epi)genetic stability in gametes, preimplantation embryos and human embryonic stem cells with a focus on the behaviour of dynamic mutations causing myotonic dystrophy and fragile X syndrome** Prof. Dr. I. Liebaers, Prof. Dr. K. Sermon **UZ Brussel**	25/02/2008	9/08/2007	Approved	23/05/2008	4 years
Adv 014	**Detection of chromosomal abnormalities in preimplantation embryos by array CGH** Prof. Dr. K. Sermon, Msc Afroditi Mertzanidou, Dr. Claudia Spits, Dr. Catherine Staessen **UZ Brussel**	17/04/2008	2/04/2008	Approved	23/05/2008	4 years
Cons002	**BEST Stem Cells**			Not in the frame of the Embryo Act		
Adv 017	**Optimization of human somatic cell nuclear transfer** Prof. P. De Sutter **UZ Gent**	Negative opinion				
Adv 018	**Optimizing embryo culture and comparison of different sources of embryos for human embryonic stem cell line derivation** Prof. Dr. De Sutter Petra, Dr. Heindryckx Björn, MSc. O'Leary Thomas, Bsc. Lierman Sylvie **UZ Gent**	18/02/2009	16/01/2009	Refused	17/06/2009	
Adv 019	**Study of the PTEN pathway during preimplantation human embryo development (ADV_019)** Pr Y. Englert, Dr. Devreker, Mme. Hoofd **ULB Erasme**	30/04/2009	7/04/2009	Approved	21/08/2009	4 years
Adv 020	**Analysis of calcium pattern in human oocytes and application of various activation stimuli** Prof. De Sutter Petra, Dr. Heindryckx Björn, Prof. Leybaert Luc **UZ Gent**	4/05/2009	31/03/2009	Approved	9/07/2009	4 years
Adv 021	**Chromosomal abnormalities in human preimplantation embryos and embryonic stem cells: causes, mechanisms and consequences for in vitro fertilisation and regenerative medicine** Prof. Dr. Karen Sermon, Dr. Claudia Spits, Msc. Afroditi Mertzanidou **UZ Brussel**	3/06/2009	13/05/2009	Approved	18/12/2009	4 years
Adv 022	**Influence of embryo morphology on stem cell derivation efficiency and molecular characterisation / Identification of intermediary structures between the inner cell mass and stem cell outgrowth** Prof. Dr. De Sutter Petra, Dr. Heindryckx Björn, Msc O'Leary Thomas, BSc Lierman Sylvie **UZ Gent**	17/06/2009	17/06/2009	Approved	2/02/2010	4 years

Cons 003	**Use of vitrification with the aim of improving in vitro fertilization techniques** **ULB Erasme**			Not in the frame of the Embryo Act		
Adv 024	**Optimizing the culture environment during the embryonic development of in vitro matured oocytes from small ovarian follicles** Prof. Dr. De Sutter Petra, M.Sc. Versieren Karen, Dr. Dumortier Frank **UZ Gent**	31/08/2009	16/06/2009	Approved	23/11/2009	4 years
Adv 025	**Totipotency and cell commitment during the human preimplantation development (FWO project)** Prof. I. Liebaers, Van de Velde Hilde, Cauffman Greet, De Paepe Caroline, Verloes An, Petrussa Laetitia **UZ Brussel**	30/10/2009	8/10/2009	Approved	11/05/2010	4 years
Cons 004	**Effect of assisted oocyte activation (AOA) on fertilization in patients with a failed fertilisation after ICSI** Prof. D'Hooghe **UZ Leuven**			Validation of an internal procedure. No request for an opinion.		
Adv 027	**Vitrification of supernumerary embryos and frozen-thawed supernumerary embryos: analysis of the survival** Prof. Dr. De Sutter Petra, M.Sc. Lierman Sylvie **UZ Gent**	2/02/2010	29/12/2009	Approved	11/05/2010	4 years

Appendix 4. Overview of the use of embryos and oocytes for scientific research based on monitoring forms

Advis	**2008**	**2009**	**2010**
Advi011	150 FS in 2 jaar	150 FS in 2 jaar	
Adv 013	x CSE 11 OV 141 E	0 embryo's	
Adv 014	20 CS	6 CS	
Adv 019	*60 S*		
Adv 020		0	250 Cr
Adv 021		0	50 S
Adv 022		*1300 S*	*900 S+ Cr*
Adv 024		*100 Cr*	*100 F*
Adv 025		*200 S + Cr*	*200 S*
Adv 027			120 CS
Adv 028			
TOTAL	**124 OV** **1074 E**	**150 OV** **1921 E**	

Legend: E = embryo, F = fresh, S = supernumerary, C = frozen, Cr = created, OV = ovocyte, I = immature, CSE = embryonic stem cell. The theoretical values, in italic against a grey background.