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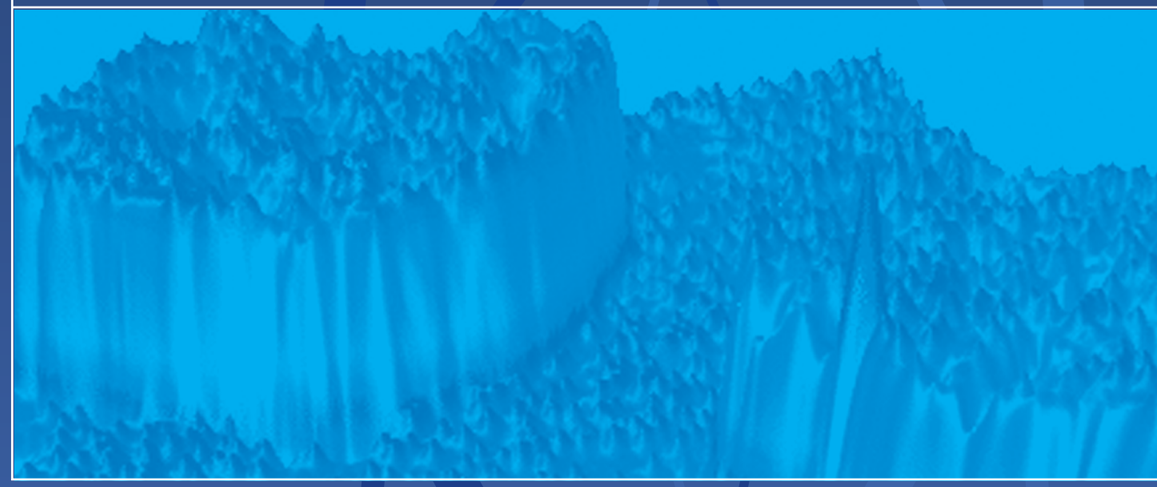
European group
on ethics in sciences
and new technologies
to the european commission

Recommendations on the ethical review of hESC FP7 research projects

OPINION No
22

20 JUNE 2007



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The European Group on Ethics in Science and New Technologies to the European Commission

Recommendations on the ethical review of hESC FP7 research projects

Opinion No 22

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20 June 2007

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Contents

SUMMARY

The European Group on Ethics in Science and New Technologies (EGE) adopted Opinion No 22 on 20 June 2007. The opinion indicates the implementing measures (guidelines) to use during the ethics review of seventh framework programme for research and development (FP7) research projects on human embryonic stem cells (hESCs), as requested by the President of the European Commission, Mr Barroso ([1]), and in line with the adoption of the EU's FP7.

The EGE stressed that, as is the case in the European Union, there are divergent views within the group on the moral legitimacy of research on human embryos and hESCs, ranging from objection to research involving the destruction of human embryos (which makes the full respect of dignity of the human embryo impossible) to a position allowing hESC research under certain conditions or on a broader basis.

The group, however, acknowledged the political decision taken as the starting point for its recommendations, but emphasised that the ethical dilemma regarding the moral status of the human embryo and its use in research still persists both within the EGE members and the EU. Therefore, the group did *not* elaborate ethical arguments on hESC research as such, but worked on recommendations for FP7 ethics review of hESC projects.

The EGE recognised the need for promoting responsible research that is transparent, serves the public interest, respects Member State autonomy, preserves public trust, promotes international cooperation and requires the embedding of ethics within research practice. The group indicated that, in addition to the FP7 ethics rules already adopted in co-decision, among others the following considerations should apply to hESCs funded by the EU:

- FP7 hESC lines have to result from non-implanted IVF embryos;
- if alternatives to hESCs with the same scientific potential as embryo-derived stem cells are found in the future, their use should be maximised;

([1]) Letter sent by European Commission President Barroso to the EGE on 22 November 2006: 'I would like to invite the European Group on Ethics to provide the Commission with an opinion on the implementing measures required during the ethics review of research projects on human embryonic stem cells that will assure that the ethical rules and requirements are fully met.'

- donors' rights (in terms of health, informed consent, data protection and free donation) have to be protected and safeguarded.

The EGE also stressed the following needs:

- to maximise the use of hESCs banked in the European Registry on hESC research;
- to take concrete actions to stimulate public debate on this research sector.

In addition, the EGE expressed the view that the use of human embryos to generate stem cells should be minimised as much as possible in the EU and indicated a number of issues that would deserve interdisciplinary research and further discussion, such as, inter alia, the use of the human body for modern medicine, including commercialisation of products and procedures stemming from the use of human embryonic stem cells; the underlying anthropology of human embryonic stem cell research, especially in the light of hybrids and the chimera research connected to stem cell research; the correlation of human embryonic stem cell research and questions concerning regenerative medicine and health-related justice, including the issue of global justice; the relation between science and humanities and between science and society with respect to the development of new technologies.

The EGE also indicated two topics that the group may address in the future: (1) the patenting of hESC-derived materials, and (2) the tension induced by a policy that encourages both free donation and commercial use of derivates from human substances.

The recommendations were adopted by unanimity and issued to the Commission on 11 July 2007.

RECOMMENDATIONS OF THE EUROPEAN GROUP ON ETHICS IN SCIENCE AND NEW TECHNOLOGIES TO THE EUROPEAN COMMISSION

No 22 **Original in English** **20 JUNE 2007**

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ETHICAL REVIEW OF HESC FP7 PROJECTS

Reference: Request by President Barroso

Rapporteurs: A. Cambon-Thomsen, H. Haker, P. Martinho da Silva

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THE EUROPEAN GROUP ON ETHICS IN SCIENCE AND NEW TECHNOLOGIES (EGE),

I. HAVING REGARD TO

Having regard to the Treaty on European Union as amended by the Treaty of Amsterdam, and in particular Article 6 (formerly Article F) of the common provisions, concerning respect for fundamental rights, Article 152 (formerly Article 129) of the EC Treaty on public health, and in particular paragraph 4(a) referring to substances of human origin, and Articles 163–173 (formerly Articles 130F–130P) on research and technological development;

Having regard to Recommendation (79)5 of the Committee of Ministers of the Council of Europe to Member States concerning international exchange and transportation of human substances, adopted on 14 March 1979 ([2]);

Having regard to the resolutions of the European Parliament namely the resolution on the ethical and legal problems of genetic engineering, and on artificial insemination *in vivo* and *in vitro*, both of 16 March 1989;

([2]) http://www.coe.int/t/e/social_cohesion/health/recommendations/Rec(79)5.pdf

Having regard to Recommendation R(94)1 of the Committee of Ministers of the Council of Europe on human tissue banks adopted on 14 March 1994 ([3]);

Having regard to Directive 95/46/EC ([4]) of the European Parliament and of the Council of the European Union of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data;

Having regard to the Council of Europe Convention on Human Rights and Biomedicine signed on 4 April 1997 in Oviedo ([5]), and the additional protocols to the convention;

Having regards to Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on *in vitro* diagnostic medical devices ([6]);

Having regard to Commission Decision 2002/364/EC ([7]) on common technical specifications for *in vitro* diagnostic medical devices;

Having regard to the Convention on the Grant of European Patents (European Patent Convention) of 5 October 1973 (text as amended by the act revising Article 63 EPC of 17 December 1991 and by decisions of the Administrative Council of the European Patent Organisation of 21 December 1978, 13 December 1994, 20 October 1995, 5 December 1996, 10 December 1998 and 27 October 2005 and comprising the provisionally

([3]) http://www.coe.int/T/E/Social_Cohesion/Health/Recommendations/Rec(1994)01.asp
([4]) OJ L 281, 23.11.1995, pp. 31–50.
([5]) http://conventions.coe.int/treaty/en/treaties/html/164.htm
([6]) OJ L 331, 7.12.1998, pp. 1–37.
([7]) OJ L 131, 16.5.2002, pp. 17–30.

applicable provisions of the act revising the EPC of 29 November 2000) ([8]);

Having regard to Directive 2002/58/EC of the European Parliament and of the Council of 12 July 2002 concerning the processing of personal data and the protection of privacy in the electronic communications sector ([9]);

Having regard to Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use ([10]), as amended in 2003 (Directive 2003/94/EC) ([11]) and 2005 (Directive 2005/28/EC);

Having regard to Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions ([12]);

Having regard to Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data ([13]);

Having regard to the Universal Declaration on the Human Genome and the Rights of Man adopted by Unesco on 11 November 1997 ([14]), the Declaration on Human Genetic Data adopted by Unesco on 16 October

([8]) http://www.european-patent-office.org/legal/epc/e/ma1.html
([9]) OJ L 201, 31.7.2002, pp. 37–47.
([10]) OJ L 121, 1.5.2001, pp. 34–44.
([11]) OJ L 261, 14.10.2003, pp. 22–26.
([12]) OJ L 213, 30.7.1998, pp. 13–21.
([13]) OJ L 281, 23.11.1995, pp. 31–50.
([14]) http://portal.unesco.org/shs/en/ev.php-URL_ID=2228&URL_DO=DO_TOPIC&URL_SECTION=201.html

2003 and the Universal Declaration on Bioethics and Human Rights adopted by Unesco on 19 October 2005;

Having regard to the Convention for the Protection of Individuals with regard to Automatic Processing of Personal Data adopted by the Council of Europe on 1 January 1981 ([15]);

Having regard to the United Nations Declaration on Human Cloning adopted by the UN General Assembly on 8 March 2005;

Having regard to the common position of the Council of Ministers of 23 March 1998 and the second reading of the European Parliament of 17 June 1998 concerning the fifth framework programme;

Having regard to Council Directive 98/44/EC ([16]) of 6 July 1998 on the legal protection of biotechnological inventions, and in particular Article 6 concerning *ordre public* and morality;

Having regard to the decision of the European Parliament and of the Council of 22 December 1998 adopting the fifth framework programme of the European Community for research, technological development and demonstration activities (1998–2002), and in particular Article 7 concerning compliance with fundamental ethical principles;

Having regard to the Council decision of 25 January 1999 concerning the specific programme for research, development and demonstration activities on 'Quality of life and management of living resources', and in particular the ethical requirements in footnote (1) of Annex II;

([15]) http://conventions.coe.int/Treaty/en/Treaties/Html/108.htm
([16]) OJ L 213, 6.7.1998, pp. 13–21.

Having regard to the Charter of Fundamental Rights of the European Union of 28 September 2000, approved by the European Council in Biarritz on 14 October 2000 and proclaimed solemnly in Nice by the European Parliament, the Council and the Commission on 7 December 2000, and in particular Article 1 (human dignity), Article 3 (right to the integrity of the person) and Article 8 (protection of personal data) ([17]);

Having regard to Council Decision 1513/2002/EC ([18]) of 27 June 2002 concerning the sixth framework programme of the European Community for research, technological development and demonstration activities (2002 — 2006), and in particular Article 3;

Having regard to the programme adopted by the Council on 30 September 2002 in implementing the sixth framework programme for research, technological development and demonstration: 'Integrating and strengthening the European research area' (2002–06) (Decision 2002/834/EC) ([19]);

Having regard to the report published by the Commission on 3 April 2003 (SEC(2003) 441) ([20]);

Having regard to the decision of the European Commission on 'Integrating and strengthening the European research area' (2002–06) (Decision 2002/834/EC) ([21]) and the 'procedural modalities for research activities involving banked or isolated human embryonic stem cells in culture to be funded under Council Decision 2002/834/EC' (COM C(2003) 2952);

([17]) OJ C 364, 18.11.2000, pp. 1–22.
([18]) OJ L 138, 21.4.2004, pp. 7–11.
([19]) OJ L 294, 29.10.2002, pp. 1–43.
([20]) http://ec.europa.eu/research/press/2003/pdf/sec2003-441report_en.pdf

Having regard to Decision No 1982/2006/EC of the European Parliament and of the Council of 18 December 2006 concerning the seventh framework programme of the European Community for research, technological development and demonstration activities (2007–13);

Having regard to Regulation (EC) No 1906/2006 ([22]) of the European Parliament and of the Council of 18 December 2006 laying down the rules for the participation of undertakings, research centres and universities in actions under the seventh framework programme and for the dissemination of research results (2007–13);

Having regard to Directive 2001/83/EC ([23]) and Regulation 726/2004/EC ([24]), currently being amended ([25]), on medicinal products for human use: advanced therapy medicinal products;

Having regard to EGE Opinion No 11 'Ethical aspects of human tissue banking' ([26]), published on 21 July 1998;

Having regard to EGE Opinion No 12 'Ethical aspects of research involving the use of human embryo in the context of the fifth framework programme' ([27]), published on 23 November 1998;

Having regard to EGE Opinion No 15 'Ethical aspects of human stem cell research and use' ([28]), published on 14 November 2000;

([22]) OJ L 391, 18.12.2006, pp. 1–18.
([23]) OJ L 311, 28.11.2001, pp. 67–128.
([24]) OJ L 136, 30.4.2004, pp. 1–33.
([25]) http://www.europarl.europa.eu/oeil/FindByProcnum.do?lang=2&procnum=COD/2005/0227
([26]) http://www.ec.europa.eu/european_group_ethics/docs/avis11_en.pdf
([27]) http://www.ec.europa.eu/european_group_ethics/docs/avis12_en.pdf
([28]) http://www.ec.europa.eu/european_group_ethics/docs/avis15_en.pdf

Having regard to EGE Opinion No 16 'Ethical aspects of patenting inventions involving human stem cells' ([29]), published on 14 November 2002;

Having regard the request of November 2006 from the President of the EU Commission to the EGE to issue an opinion on the ethics review of human embryonic stem cell (hESC) projects funded under FP7;

Having heard the rapporteurs A. Cambon-Thomsen, H. Haker, P. Martinho da Silva,

([29]) http://www.ec.europa.eu/european_group_ethics/docs/avis16_en.pdf

II. WHEREAS

II.1. Preamble

It is common knowledge that opinions about the ethical legitimacy of research on human embryos are sharply divided. The controversy is rooted in different ethical, philosophical, and/or religious viewpoints, each of which is acknowledged to be fully legitimate. In this respect, some claim that the divergences are 'intrinsic' and therefore irreconcilable, while others claim that common positions are achievable while respecting the pluralism of European societies, as practical solutions.

The scope of these recommendations, however, is not to address the ethics of human embryonic stem cell research or research on human embryos. These recommendations relate to the political decision reached by the European institutions on the EU's seventh framework research programme and is intended to contribute to the implementation of the mechanism established under the programme for an ethics review of EU-funded research activities involving the use of human embryonic stem cells.

Because of the particular scope of these recommendations, it is important to identify the main requirements regarding the ethics of human embryonic stem cells that have been adopted in co-decision by the European institutions involved: the Council and the European Parliament. In addition, as the current EU framework programme follows on from the previous one, and since both implement the European research area (the policy strategy of the EU in research and development) and are linked to the economic strategy of the EU (the 'Lisbon strategy'), the present document will refer to the previous EU framework programme and its implementation to date by the Commission services.

II.2. The sixth framework programme for research, technological development and demonstration: 'Integrating and strengthening the European research area' (2002–06) (FP6)

On 30 September 2002, the Council adopted the specific programme implementing the sixth framework programme for research, technological development and demonstration: 'Integrating and strengthening the European research area' (2002–06) (Decision 2002/834/EC ([30]) — hereinafter referred to as 'the specific programme').

The specific programme allowed the funding of research activities involving the use of human embryos and human embryonic stem cells except in three areas:

— research activity aiming at human cloning for reproductive purposes (reproductive cloning);

— research activity intended to modify the genetic heritage of human beings which could make such changes heritable (germline gene therapy) ([31]);

— research activities intended to create human embryos solely for the purpose of research or for the purpose of stem cell procurement, including by means of somatic cell nuclear transfer (commonly referred to as therapeutic cloning).

On adopting the programme, however, the Council indicated that 'detailed implementing provisions concerning research activities involving the use of human embryos and human embryonic stem cells shall be established by 31 December 2003'. It asked the Commission to: (1) prepare these provisions; (2) prepare a working paper on the issue; and (3) organise an interinstitutional seminar on bioethics.

([30]) OJ L 294, 29.10.2002, p. 1.
([31]) Research into treatment of cancer of the gonads can be financed.

A moratorium was then implemented by the Commission and no hESC research has since been funded with the exception of proposals for projects that involved the use of already banked or isolated human embryonic stem cells.

The Council asked the Commission to publish a staff report on scientific advances and needs and on the evolution of international and national legislation, regulations and ethical rules regarding research involving the use of human embryonic stem cells. The report was prepared by the Commission, published on 3 April 2003 (SEC(2003) 441 ([32])), and then transmitted to the European Parliament and the Council as a basis for discussion at an interinstitutional seminar on bioethics organised by the Commission ([33]).

On 9 July 2003, the Commission then submitted to the Council a proposal for the modification of the specific programme (COM(2003) 390 ([34])), on which the European Parliament had to express its opinion ([35]). The proposal applied specifically to Community funding of research activities involving the procurement of stem cells from human embryos created as a result of medically assisted *in vitro* fertilisation designed to induce pregnancy and no longer to be used for that purpose (non-implanted human embryos); and it was based on the principles established by the European Group on Ethics, in particular the fundamental ethical principles set out in Opinion No 15 'Ethical aspects of human stem cell research and use' ([36]). This Commission proposal received a favourable opinion from the European Parliament but did not obtain a qualified majority at the Council of 3 December 2003.

([32]) http://europa.eu.int/comm/research/conferences/2003/bioethics/index_en.html

([33]) On 24 April 2003, the interinstitutional seminar on bioethics took place. The seminar addressed issues related to human embryonic stem cell research under the sixth framework programme for research and provided an opportunity for discussion and exchanging of views between experts (scientific, legal, and in ethics) and representatives of the European Parliament, the Council, the Commission, the Member States and the accession and candidate countries.

([34]) Proposal for a Council decision [COM(2003) 390] amending Decision 2002/834/EC on the specific programme for research, technological development and demonstration: 'Integrating and strengthening the European research area' (2002–06).

([35]) http://europa.eu.int/comm/research/conferences/2003/bioethics/index_en.html

([36]) http://europa.eu.int/comm/european_group_ethics/index_en.htm

In parallel, the 'procedural modalities for research activities involving banked or isolated human embryonic stem cells in culture to be funded under Council Decision 2002/834/EC' ([37]) were approved by the Regulatory Committee (comprising representatives of the Member States) on 25 June 2003 and by the Commission on 11 November 2003.

On 31 December 2003, the moratorium ended and the two legal texts on which the Commission based its research implementation were: (1) the specific programme implementing the sixth framework programme for research, technological development and demonstration, 'Integrating and strengthening the European research area' (2002–06) (Decision 2002/834/EC) ([38]); and (2) the 'procedural modalities for research activities involving banked or isolated human embryonic stem cells in culture' (annexed to these recommendations).

II.3. Human embryonic stem cell (hESC) projects financed under FP6

In total, 18 hESC projects were financed under FP6 within the thematic priority 'Life sciences, genomics and biotechnology for health'. These 18 projects accounted for less than 3 % of the total number of projects funded within this thematic priority under FP6. Most FP6 hESC projects also involved research into adult stem cells and/or foetal stem cells (comparative approach), but one of the 18 was entirely dedicated to human embryonic stem cell research (Estools). A detailed list of FP6 projects involving the use of hESCs is annexed to these recommendations.

II.4. The ethics provisions applying to FP6-funded human embryonic stem cell projects

II.4.1. FP6 ethics review

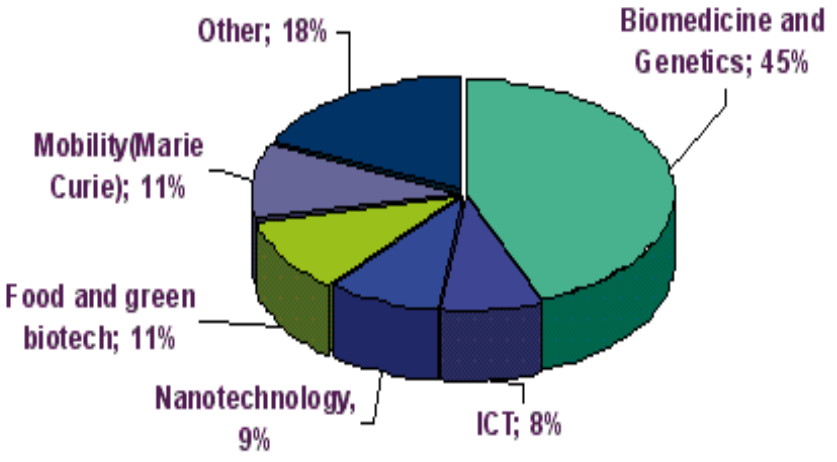
In order to implement Article 6 of the framework programme and Article 15 of the rules for participation, the FP6 evaluation procedure included a check of the ethical issues raised by the proposals. Following the scientific evaluation, an

([37]) C(2003) 2952.
([38]) OJ L 294, 29.10.2002, p. 1.

ethical review of the successful proposals involving sensitive ethical issues was carried out before the final selection by the Commission.

The objective of the ethical review was to make sure that the European Union did not support research contrary to fundamental ethical principles and to examine whether the research complied with the rules relating to ethics set out in the decisions on the sixth framework programme and specific programmes.

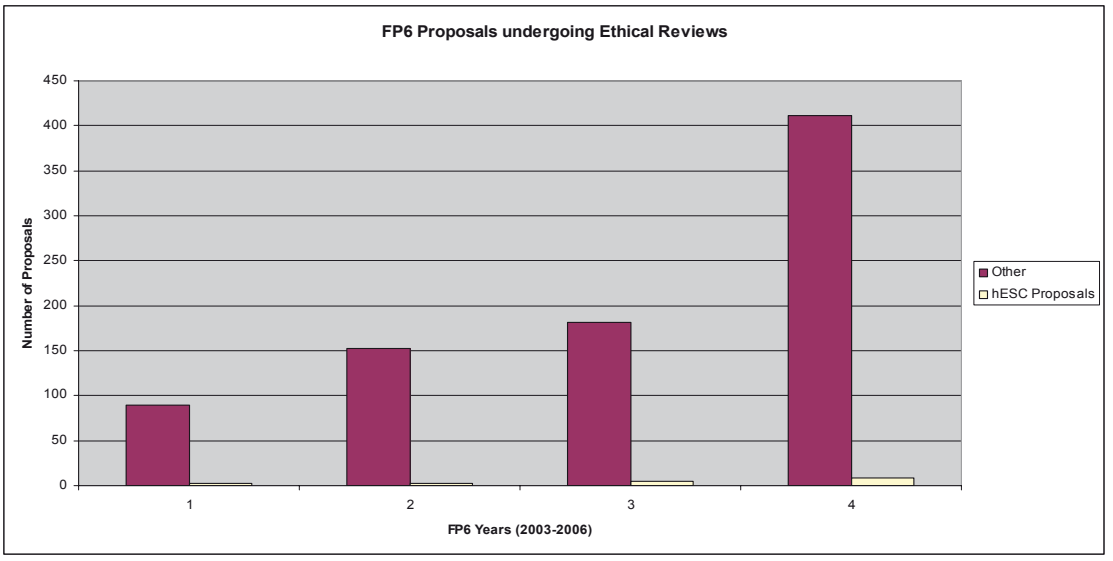
Breakdown of projects subjected to ethical review, by research area



The ethical review was carried out by external experts with the expertise needed for an ethical assessment of the proposals (interdisciplinary approach). The experts were different each time and were selected by the Commission on the basis of expertise, geographical balance and gender balance.

The total number of FP6 proposals that underwent an ethical review was 885 (11 % of FP6 research projects), whereby 18 involved human embryonic stem cell research (around 2 % of the total number of ethically reviewed proposals).

The graph below shows the numbers of FP6 projects subjected to ethical review.



II.4.2. Ethics provisions for FP6 hESC projects

For human embryonic stem cell projects funded under FP6, the following provisions applied.

(a) During the scientific evaluation, independent experts assessed the need to use hESCs to achieve the scientific objectives set forth in the proposal ([39]).

(b) An ethical review was organised by the Commission with independent experts on a case-by-case basis. It was based on the ethical rules embodied in the European Charter of Fundamental Rights and in the different national, EU and international regulations or conventions, also taking into account the opinions of the European Group on Ethics ([40]). In particular, four different criteria were assessed:

- whether the applicants took into account the legislation, regulations, ethical rules and/or codes of conduct in place in the country where the

([39]) The type of stem cells to be used is chosen by the scientists in view of the objectives of the proposal, which should relate to fundamental research questions or medical applications. Then, independent experts evaluate the proposal to assess the appropriateness of the approach chosen by the scientists.

([40]) Council Decision 2002/834/EC, OJ L 294, 29.10.2002; see pp. 7–8 for details.

research using banked or isolated hESCs in culture was to take place, including the procedures for obtaining informed consent ([41]);

- the source of the banked or isolated hESCs in culture;
- the measures taken to protect personal data, including genetic data, and privacy;
- the nature of financial inducements, if any.

(c) A positive opinion from a regulatory committee comprising Member State representatives was required.

(d) Finally, the Commission checked that the participants in research projects had received the approval of the relevant national or local ethics committees prior to the start of research activities.

All these conditions were **cumulative**.

In conclusion, each hESC research proposal supported under FP6 was assessed by at least two independent ethical reviews: one at national level (in the country where the research was to be carried out) ([42]) and one at EU level.

II.5. The seventh framework programme for research, technological development and demonstration (2007–13) (FP7)

As with FP6, ethics and hESCs played a major role in the interinstitutional debate on the seventh framework programme; this was intended to contribute to the

([41]) The EU has never required a uniform regulatory system for all fields of science and technology. The Treaty itself guarantees the autonomy of the Member States. As a consequence, diverse regulatory frameworks coexist (e.g. for research on non-human primates, nuclear research, security and prevention of terrorism, bio-banking, etc.). The principle of subsidiarity is respected in full, assuming respect of fundamental ethical principles.

([42]) If the research raising ethical issues is performed in more than one country (i.e. *n* countries), this implies that more than two ethical reviews will be performed (i.e. in fact *n* + 1 ethical reviews).

implementation of the Lisbon strategy and benefited from a budget of EUR 53 billion for the time frame 2007–13 ([43]).

The Commission proposal for FP7 was adopted on 6 April 2005. As for FP6, the proposal had a specific article (Article 6) stating that 'All the research activities … shall be carried out in compliance with fundamental ethical principles'. The specific programme for FP7 was adopted by the Commission on 21 September 2005. The Commission proposal was then transmitted to the relevant institutions (the European Parliament and the Council) for their approval by co-decision.

The Parliament adopted (first reading) the proposed programme on 15 June 2006 after a preceding vote and a request for amendments by the relevant Parliamentary commission (ITRE) on 30 May 2005. The Commission accepted Parliament's request to have the ethics framework incorporated in the framework programme text, which required a co-decision by the European Parliament and the Council on this issue. This was not the case for FP6, where the ethical framework was included in the specific programme adopted by the Council alone.

After intense discussions, the programme was adopted by the Council on 24 July 2006 (qualified majority). The Council agreement was based on a Commission declaration stating that 'The European Commission will continue with the current practice and will not submit to the Regulatory Committee proposals for projects which include research activities which destroy human embryos, including for the procurement of stem cells. The exclusion of funding of this step of research will not prevent Community funding of subsequent steps involving human embryonic stem cells'.

([43]) A detailed description of the interinstitutional adoption of the programme can be found at http://ec.europa.eu/prelex/detail_dossier_real.cfm?CL=en&DosId=192725

The programme, including the Commission declaration, was then approved at the European Parliament plenary session (second reading) on 30 November 2006 and adopted in co-decision on 18 December 2006.

II.6. Ethics provisions under FP7: hESC research funded by the European Union

The Council agreement made the eligibility of hESC research for EU funding subject to the same specific restrictions and conditions as with FP6.

To ensure an optimal ethics review system, the President of the European Commission asked the EGE on November 2006 to issue an opinion on the ethics review of hESC projects funded under FP7:

I would like to invite the European Group on Ethics to provide the Commission with an opinion on the implementing measures required during the ethics review of research projects on human embryonic stem cells that will assure that the ethical rules and requirements are fully met. Such an opinion would provide guidance (in relation to the values and principles to apply) for the Ethics Review within the frame of the Programme approved by the Council and the European Parliament. It would be important that this opinion is available for use when the first FP7 projects involving human embryonic stem cells are evaluated ([44]).

([44]) Letter by Commission President J. M. Barroso addressed to the EGE on 22 November 2006.

III. BACKGROUND FOR THE ETHICAL REVIEW OF HESC PROJECTS

III.1. Existing ethical guidelines: a brief historical overview

In a fast-developing area such as stem cell research, ethical requirements are assuming increasing importance in project assessment. The process of research approval includes a review of projects by a panel of independent experts (both scientific and ethical).

Up to the present, no clinical research making use of human embryonic stem cells has been carried out. In view of the long-term perspective of FP7, however, all ethical guidelines and regulations must be applied to FP7 projects whenever they involve research on human subjects.

Guidelines and regulations governing the participation of human subjects in biomedical research have been established at international level for many decades. These principles are laid down in internationally recognised research ethics guidelines and other instruments, including (to cite only the most important): the Nuremburg Code of 1947 ([45]), the Declaration of Helsinki of 1964 ([46]) (plus amendments), the Belmont Report of 1979 ([47]), the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine of 1997 (the 'Oviedo Convention') ([48]) and the additional protocols to the convention ([49]), the Unesco Universal Declaration on the Human Genome and Human Rights ([50]) of 1997 and the International Declaration on Human Genetic Data ([51]) of 2003, the Council for International Organisations of Medical Sciences (CIOMS) International Ethical

([45]) http://www.ushmm.org/research/doctors/Nuremberg_Code.htm
([46]) http://www.wma.net/e/ethicsunit/helsinki.htm
([47]) http://ohsr.od.nih.gov/guidelines/belmont.html
([48]) http://conventions.coe.int/treaty/en/treaties/html/164.htm
([49]) http://conventions.coe.int/Treaty/EN/Treaties/Html/168.htm
([50]) http://portal.unesco.org/fr/ev.php-URL_ID=13177&URL_DO=DO_TOPIC&URL_SECTION=201.html
([51]) http://portal.unesco.org/en/ev.php-URL_ID=17720&URL_DO=DO_TOPIC&URL_SECTION=201.html

Guidelines for Biomedical Research Involving Human Subjects of 2002 ([52]), and the Unesco Universal Declaration on Bioethics and Human Rights of 2005 ([53]).

Over the last few years, several international bodies have been established across the world, which give information and guidance in the process of research proposal preparation, application, and definition of standards, both scientific and ethically sound.

As noted before, the volume of documents addressing the ethics of hESCs is vast and diverse. Additional information on relevant initiatives in this area may be found, for example, on the following websites: the BioCentre for Bioethics and Public Policy (CBPP) ([54]), CARE for Europe ([55]), the International Society for Stem Cell Research ([56]), and the Nuffield Council on Bioethics ([57]), along with those of various national institutions ([58])([59]) and international organisations ([60])([61]).

In addition to the abovementioned ethics guidelines produced by relevant international organisations, in 2006 the International Society for Stem Cell Research (ISSCR) published specific guidelines on hESCs (*Guidelines for the conduct of human embryonic stem cell research*).

The guidelines address the procurement, derivation, banking, distribution, and use of cells and tissues taken from pre-implantation stages of human

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([52]) http://www.cioms.ch/

([53]) http://portal.unesco.org/shs/en/ev.php-URL_ID=1883&URL_DO=DO_TOPIC&URL_SECTION=201.html

([54]) http://www.bioethics.ac.uk/

([55]) http://www.careforeurope.org/

([56]) http://www.isscr.org/guidelines/

([57]) http://www.nuffieldbioethics.org/go/ourwork/stemcells/introduction

([58]) http://www.dfg.de/en/news/press_releases/2006/press_release_2006_60.html

([59]) UK HFEA, UK Department of Health, UK Stem Cell Initiative: http://www.hfea.gov.uk/cps/rde/xchg/SID-3F57D79B-370119F4/hfea/hs.xsl/295.html, http://www.dh.gov.uk/PolicyAndGuidance/HealthAndSocialCareTopics/StemCell/fs/en, http://www.advisorybodies.doh.gov.uk/uksci/uksci-reportnov05.pdf

([60]) EMBO: http://www.vr.se/download/18.2aebc6b810f3c933b158000194/EMBO+document+nov+2006.pdf#search='stem+cell'

([61]) European Science Foundation: http://www.esf.org/publication/142/ESPB18.pdf

development; procurements of gametes and somatic tissues for stem cell research; and the use of human stem cell lines ([62]).

III.2. Research using human embryonic stem cells (hESCs)

Human embryonic stem cells are used in a variety of research projects with different scientific goals. Some research protocols focus completely on hESCs, but sometimes they may use human embryonic and adult stem cells for comparative purposes or may use hESCs as a tool to obtain other scientific outcomes (for example, to make *in vitro* tests of a given experimental drug or a new chemical).

The relevance and use of hESCs therefore varies considerably according to the expected scientific outcomes of the research trials. The scientific community is interested in investigating the basic physiology of stem cells, their potential and characteristics. One important aspect of such research is the comparative analysis of hESCs and other types of stem cells, such as umbilical-cord and adult tissue-specific stem cells, in order to address specific questions concerning the suitability of these types of cells. Stem cell research is also done to explore its potential use for regenerative medicine (degenerative diseases such as diabetes and Parkinson's disease) and gene therapy (e.g. for cystic fibrosis and Huntington's disease). At present, there are no indications that clinical trials will be carried out in the near future.

In addition, researchers are exploring the potential use of hESCs in toxicological studies in order to replace animal models with *in vitro* models. Other uses of hESCs, with the exception of the ESTOOL project (see annex to this opinion), are in large multidisciplinary studies, such as those involving genomics and

([62]) http://www.isscr.org/guidelines/ISSCRhESCguidelines2006.pdf

proteomics approaches, which focus on broader contexts with only a subset of experiments specifically dealing with hESCs.

Examples of EU-funded projects that make different uses of hESCs:

(1) EUROSTEMCELL: project aiming to compare adult, foetal, embryonic and tissue-specific stem cells (see http://www.eurostemcell.org/);

(2) BETACELL THERAPY: project aiming to study the generation of insulin-producing pancreatic beta cells for the treatment of diabetes (see http://www.betacelltherapy.org);

(3) CARCINOGENOMICS: project aiming to carry out *in vitro* testing to assess the genotoxic and carcinogenomic properties of chemical compounds (*in silico* models to evaluate the carcinogenic potential of a compound *in vivo*) (see http://www.ecopa.eu/doc/CarcinogenomicsPressRelease-201106.pdf).

III.3. Sources of human embryonic stem cells

The most common source of tissue for human embryonic stem cell isolation is the inner cell mass (ICM) of embryos created using assisted reproduction technologies (ART), but not transferred to the woman's uterus, either because the number of embryos exceeds the number allowed to be transferred under the law (usually two or three) or because of genetic defects detected by pre-implantation genetic diagnostics (PGD) ([63]). In the same way, embryos as a source of stem cells can be created solely for research purposes via *in vitro* fertilisation (IVF), but outside the ART context ([64]).

Another source of human embryonic stem cells, which is allowed in only a few countries ([65]), is their creation by means of somatic nuclear cell transfer (SCNT), where a somatic cell is taken from an adult patient and its nucleus transferred

([63]) This practice is not permitted in all EU Member States.
([64]) This practice is not permitted in most EU Member States. See Table 1, p. 29.
([65]) In the EU, therapeutic cloning is allowed only in the following countries: Belgium, Spain, Sweden and the UK.

into a donated enucleated oocyte. Unlike hESCs derived from a donated IVF embryo, the resulting cell line using SCNT is genetically identical to the donor of the nucleus.

Another possible way of creating stem cells by means of SCNT, but not leading to therapeutic cloning, is to create human/animal hybrids by mixing a human cell with an animal egg in order to obtain 'humanised' stem cells ([66]). There is currently debate on the ethics of human/animal hybrids in several EU and non-EU countries. The EC is at present financing a project on the ethical, legal and social implications of human/animal hybrids ([67]).

III.4. Derivation of new hESC lines

As indicated in Section II.2, the derivation of new totipotent cells or pluripotent stem cell lines from donated pre-implantation human embryos or embryonic cells, or via nuclear reprogramming, is not funded by the EU research programme. The derivation of new hESCs necessarily involves the procurement of biological material from human subjects, which then (when allowed) needs to be approved by institutional oversight bodies with specific responsibility for the protection of human subjects.

III.5. Alternatives to hESC research

As stated in Section II.2, the justification for the use of human embryonic stem cells under FP7 is to be assessed during the scientific evaluation of research proposals. EU projects can be funded only if no suitable alternatives to human embryonic stem cells can be found and the absolute necessity of using hESCs has been scientifically justified and evaluated. With regard to possible

([66]) Recently, British scientists have been seeking HFEA approval to create rabbit–human stem cells by using rabbits' oocytes, in order to overcome the shortage of egg donors in the UK, in a collaboration between King's College in London and Edinburgh University.

([67]) See www.chimbrids.org

alternatives to hESCs, the first factor to consider is the possible use of adult human stem cells.

Adult stem cells are multipotent stem cells, suitable for the treatment of human diseases such as leukaemia, lymphomas and other blood diseases. Such therapies rely on the very well-established practice of transplanting haematopoietic stem cells (blood-forming stem cells) present in bone marrow, placenta or umbilical cord blood cells. Other diseases that may be cured in the near future by using adult stem cells are, for example, diabetes and some forms of cancer (e.g. kidney), for which the clinical potential of adult stem cells looks very promising.

Given the nature of embryonic stem cells and the moral dilemma regarding the destruction of human embryos to obtain embryonic stem cells, research has also been focusing on alternative sources of human embryonic stem cells, an endeavour which received criticisms, both scientific and ethical, as in the case of altered nuclear transfer ([68]), which was developed by scientists as a technological solution to the destruction of human embryos and the related ethical issues ([69])([70]), but implies an epigenetic alteration of the egg to preclude natural embryogenesis.

Nevertheless, some recent promising research into alternatives to hESCs has been carried out, such as for:

- pluripotent stem cells derived from 'arrested' embryos ([71]);

([68]) Melton, D. A., Daley, G. D. and Jennings, C. G. 'Altered nuclear transfer in stem-cell research — A flawed proposal', *The New England Journal of Medicine*, Vol. 351: 2791–2792 (30 December 2004).

([69]) Solter, D. 'Politically correct human embryonic stem cells?', *The New England Journal of Medicine*, Vol. 353: 2321–2323 (1 December 2005).

([70]) Green, R. M. 'Can we develop ethically universal embryonic stem-cell lines?'. *Nature Reviews Genetics* 8: 480–485 (2007).

([71]) Zhang, X. et al. 'Derivation of human embryonic stem cells from developing and arrested embryos', *Stem Cells* 24: 2660–76 (2006).

- pluripotent stem cells via blastomere extraction from developing embryos ([72]);
- pluripotent stem cells via somatic cell dedifferentiation ([73]);
- human materials using cell fusion rather than genetic factors ([74]);
- non-embryonal sources of 'embryonic like', multipotent human stem cells (from human umbilical cord blood ([75]) or from human amniotic fluid ([76])).

III.6. European Registry of existing hESC lines

According to the available data, 81 different hESC lines have at present been established and are used in EU-funded projects. Since there is certain variability from cell line to cell line, the Commission has felt it important to: (1) gather in a centralised manner all information available on each single cell line for comparative purposes; and (2) render such information available at international level.

The European Commission has therefore decided to establish and fund a European Registry for human embryonic stem cell lines ([77]) in order to help researchers to optimise the hESC resources available and avoid duplication of work and/or the creation of new cell lines where possible. This registry is expected to boost the coordination and rationalisation of human embryonic stem cell

([72]) Klimanskya, I. et al. 'Human embryonic stem cell lines derived from single blastomeres', *Nature* 444: 481–485 (2006).

([73]) Takahashi, K. and Yamanaka, S. 'Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors', *Cell* 126: 1–14 (2006).
Wernig, M. et al. '*In vitro* reprogramming of fibroblasts into a pluripotent ES-cell-like state', *Nature*, AOP doi:10.1038/nature05944 (2007).

([74]) Cowan, C. A. et al. 'Nuclear reprogramming of somatic cells after fusion with human embryonic stem cells', *Science*, 309: 1369–1373 (2005).

([75]) Zhao, Y. et al. 'Identification of stem cells from human umbilical cord blood with embryonic and hematopoietic characteristics', *Experimental Cell Research*, 312: 2454–2464 (2006).

([76]) De Coppi, P. et al. 'Isolation of amniotic stem cell lines with potential for therapy', *Nature Biotechnology* 25: 100–106 (2007).

([77]) The project will be funded for three years with grants for a total of EUR 1 million. The registry will be mainly coordinated by two institutions: the Centre of Regenerative Medicine (CRMB) in Barcelona, Spain, and the Berlin-Brandenburg Centre for Regenerative Therapies (BCRT) in Berlin, Germany.

research in Europe. It will provide a platform to maximise reproducibility, comparability and transparency in the field ([78]).

The main objective of this initiative is to provide comprehensive information about all human embryonic stem cell lines available in Europe. The information will be gathered together on a publicly accessible Internet site containing data on the cell lines (e.g. cell characteristics) and their use (e.g. research project outcomes, clinical trials, etc.). The registry will provide information on the sources of the stem cell lines and include comprehensive information on human embryonic stem cell lines obtained from ongoing and future EU-funded projects. The data will be regularly updated and made accessible to the public.

A Steering Committee comprising representatives of the leading European public institutions involved in human embryonic stem cell research has also been established. The committee will be assisted by an Advisory Board, comprising 17 top scientists from Europe and outside Europe in the field of human embryonic stem cell research, and an independent Ethics Advisory Board to ensure compliance with ethical requirements and ethical guidance.

III.7. EU Member States' regulations on hESC research

Among the 27 EU Member States (EU-27), several clusters of countries can be identified according to how they regulate hESC research. However, all countries apply at least some regulations and/or procedural rules to specific projects involving hESCs. Where hESC research is allowed, project proposals have to undergo strict evaluation criteria, both scientific and ethical, decided upon by the competent national bodies ([79]).

([78]) For more information see: www.cmrb.eu; www.cellnet.org; www.ec.europa.eu/research/fp6/index_en.cfm?p=1_stem_projects

([79]) See annex (pp. 52–102) for further details in single Member States.

Permissive position

A few EU Member States have specific legislation for hESC research, covering the procurement of stem cells and their use for research. In Belgium, Spain ([80]), Sweden and the UK, for example, embryo creation is allowed for research purposes.

Permissive position with restrictions

In other EU Member States such as the Czech Republic, Denmark, Greece, France, the Netherlands, Portugal and Finland ([81]), regulations allow the derivation of new hESCs from embryos created as a result of assisted reproduction technology (ART) and *in vitro* fertilisation to induce pregnancy, but only when they can no longer be used for that purpose.

Restrictive position

Germany and Italy have stricter hESC research regulations. Scientists in these countries cannot derive new hES cell lines, but can import them. In Germany, a new discussion has arisen as to whether the 2002 Stem Cell Act regulating the importation of hESC lines should be revised, but no legal proposal has been forthcoming by the date of these recommendations. Italian legislation covers artificial reproduction technology and the production of new hESCs (research involving the destruction of embryos is not allowed). Italy therefore has no legal provision as regards the use of imported hESCs or existing hESCs.

No specific legislation or indirect legislation only

In many Member States, hESC research still has no specific legislation (Bulgaria, Estonia, Ireland, Cyprus, Latvia, Luxembourg and Romania). Ireland, for instance,

([80]) A new law in Spain has just been voted for.
([81]) A new regulation is under way in Portugal.

currently has no specific legislation dealing with embryonic stem cell research and furthermore does not have a legislative basis for the practice of IVF.

Some other EU Member States have no 'specific' regulation on hESC research, but explicitly indicated that they are against it (Lithuania, Malta, Austria, Poland and Slovakia) by voting against hESC research during the Council decision for FP7.

Lastly, in some countries hESC is at present regulated only by indirect legislation for embryo research (Hungary, Slovenia), but without specific reference to hESCs. The table below summarises the current regulatory systems in the EU-27, but specific information on the position of each Member State can be found in the annex to these recommendations (regulatory issues).

Table 1. Regulations in EU Member States regarding hESC research (updated June 2007)

	Allowing procurement of hESCs from supernumerary embryos by law	Specific legislation for embryo research including supernumerary embryos but without specific reference to hESCs	Prohibiting procurement of hESCs from human embryos but allowing importation of hESC lines	No specific regulation on hESC research	Allowing creation of human embryos for procurement of hESCs by law	Countries which signed and ratified the Oviedo Convention of 4.4.1997 (against the creation of human embryos for research purposes)
AT				X ([d])		
BE	X				X	
BG				X		X
CY				X		X
CZ	X					X
DE			X ([a])			
DK	X					X
EE				X		X
EL	X					X
ES	X				X ([c])	X
FI	X					
FR	X					
HU		X				X
IE				X		
IT			X ([b])			
LT				X ([d])		X
LU				X		
LV				X		
MT				X ([d])		
NL	X					
PL				X ([d])		
PT	X					X
RO				X		X
SE	X				X	
SI		X				X
SK				X ([d])		X
UK	X				X	

([a]) Germany has a law and hESC lines have to be derived before 1 January 2002.
([b]) Italy has no law regarding importation.
([c]) Spain allows techniques such as SCNT to obtain hESCs.
([d]) Countries which voted against hESC research during Council decision for FP7.

Country code key:

AT: Austria	DK: Denmark	FR: France	LU: Luxembourg	PT: Portugal
BE: Belgium	EE: Estonia	HU: Hungary	LV: Latvia	SE: Sweden
CY: Cyprus	EL: Greece	IE: Ireland	MT: Malta	SI: Slovenia
CZ: Czech Republic	ES: Spain	IT: Italy	NL: Netherlands	SK: Slovakia
DE: Germany	FI: Finland	LT: Lithuania	PL: Poland	UK: United Kingdom

III.8. Commercialisation and patenting

The directive on the legal protection of biotechnological inventions (98/44/EC) ([82]) regulates patentability of biological material, including hESCs. The debate on patenting hESCs is ongoing at both institutional (European Patent Office, the European Commission ([83])) and academic level. At present, there is no EU consensus on the moral status of the embryo and its products and, reflecting this wide diversity of moral cultures, there are different policies for patenting among national patent offices. The European Group on Ethics (EGE) has evaluated the ethical aspects of patenting inventions involving human stem cells ([84]).

([82]) OJ L 213, 30.7.1998, pp. 13–21.
([83]) See COM(2005) 312
([84]) EGE Opinion No 16, 'Ethical aspects involving the patenting of human stem cells'.

IV. RECOMMENDATIONS

IV.1 Preamble

These recommendations constitute the reply to the request from the President of the European Commission, Mr Barroso ([85]), after the adoption of the EU's seventh framework programme for research and development (FP7), to elaborate an opinion on the implementing measures required during the ethics review of research projects on human embryonic stem cells (hESCs).

As is the case in the European Union, there are divergent views within the European Group on Ethics (EGE) on the moral legitimacy of research on human embryos and hESCs, ranging from objection to research involving the destruction of human embryos (which makes the full respect of dignity of the human embryo impossible), to a position allowing hESC research under certain conditions or on a broader basis.

The group acknowledges the political decision taken as the starting point for its recommendations, but emphasises that the ethical dilemma regarding the moral status of the human embryo and its use in research still persists. The EGE therefore stresses that the ethical differences of opinion concerning hESC research have not been resolved.

However, these recommendations do *not* elaborate ethical arguments on hESC research as such; this is because this was not the task given to the group by the European Commission.

([85]) Letter sent by Commission President Barroso to the EGE on 22 November 2006. 'I would like to invite the European Group on Ethics to provide the Commission with an opinion on the implementing measures required during the ethics review of research projects on human embryonic stem cells that will assure that the ethical rules and requirements are fully met'.

IV.2. Recommendations for the ethical review of research projects involving hESCs

FP7 research projects involving the use of hESCs are subject to stringent rules for selection, are scrutinised at both national and EU level, and undergo both scientific and ethical reviews.

Under FP7, research proposals must include information about ethical aspects of the proposed research, explain in detail the project design, and show that the proposal meets the national legal and ethical requirements of the country where the research is performed.

After successfully passing the scientific evaluation, the selected hESC proposals undergo a specific ethics review organised by the Commission on a case-by-case basis. The objective of the review is to ensure that the European Union does not support research that would not comply with fundamental ethical principles ([86]) and to examine whether the ethics rules set out in FP7 are met.

The ethics review panel is a transnational body composed of experts from different disciplines. The panel produces an ethical review report, which lists the different ethical issues, describes the way these issues were handled by applicants, and gives the recommendations of the panel.

After having successfully passed both the scientific and ethics review, proposals for hESC projects are then handed over to a Regulatory Committee composed of EU Member State representatives, which decides upon the projects on a case-by-case basis.

([86]) Seventh framework programme (Decision No 1982/2006/EC), Article 6(1): 'All the research activities carried out under the Seventh Framework Programme shall be carried out in compliance with fundamental ethical principles.'; Rules for Participation, Article 10: 'A proposal […] which contravenes fundamental ethical principles […] shall not be selected. Such a proposal may be excluded from the evaluation and selection procedures at any time.'

In order to provide guidance to the members of the FP7 hESC ethics review panels who will be asked to review the research projects using hESC lines, and under the specific remit and conditions laid down by the political decision of the European Parliament and of the Council on FP7, and also by the specific request of the President of the European Commission, Mr J. M. Barroso (see above), the EGE elaborated the following guidelines and points to consider when conducting such ethics review of FP7 projects ([87]).

IV.2.1. General criteria

The European Commission has stated that it 'will support actions and initiatives that contribute to coordination and rationalisation of hESC research within a responsible ethical approach' ([88]). In line with this statement, the EGE recognises the need to promote responsible research that is transparent, serves the public interest, respects Member States' autonomy, preserves public trust, promotes international cooperation, and requires the embedding of ethics within research practice ([89]).

Ethically responsible research involving human embryonic stem cells must comply with fundamental ethical principles and human rights in the European Union ([90]), from the procurement of stem cells ([91]) to clinical research based on hESCs.

([87]) According to FP7 rules, evaluators sign a conflict of interest declaration and EC staff verify conflicts with each proposal they evaluate. Evaluation panels of ethics and scientific reviews are anonymous.

([88]) Declaration of the European Commission on 24 July 2006 during the meeting of the Council of Ministers regarding FP7. See OJ L 412, 30.12.2006.

([89]) For example, the Council of Europe Oviedo Convention (Article 2).

([90]) For details, see Section I of this opinion referring to the pertinent documents relevant to the context of medical research.

([91]) FP7 excludes the procurement of hESCs from Community funding (see paragraph II.2). See Decision No 1982/2006/EC of the European Parliament and of the Council of 18 December 2006 concerning the seventh framework programme of the European Community for research, technological development and demonstration activities (2007–13), OJ L 412, 30.12.2006, pp. 1–41.

The fundamental rights include: *protection rights* such as protection of human life, respect of its integrity, protection of health and freedom, *political rights* such as freedom from undue state intervention or participatory rights in political affairs, and *positive rights* such as basic social and economic rights insofar as these contribute to health and a threshold of development, resulting in health-related governance ([92]).

The balancing of these three groups of fundamental rights is by no means easy or pre-determined. Rather, it involves ongoing efforts to ensure their protection, granting and promotion of human dignity and human rights and, more concretely, it involves priority setting with respect to health-related research.

General criteria for research incentives in specific areas incorporate this balancing. They can be summarised as follows:

- **scientific necessity and high-ranking status** of the research ([93]);
- **urgency** ([94]);
- **social desirability**;
- **primacy** of the interest and welfare of the human being over the sole interest of society or science.

Social desirability is open to political and societal discourse on the goals and perspectives of the European Union in the 21st century, in particular the relation between economic growth and social goals, such as the promotion of healthcare standards and their sustainable application at national, international and global level.

([92]) See the United Nations' millennium goals, which the European Union has committed itself to achieving.
([93]) http://ec.europa.eu/research/fp7/index_en.cfm?pg=documents
([94]) http://www.who.int/rpc/en/HealthResearchinPolicyMaking.pdf

As far as hESC research is concerned, there is no consensus on its social acceptability in the European Union, and divergent views coexist. A debate on the best model (e.g. 'minimal consensus' or 'subsidiarity' model) to regulate hESC research at EU level is therefore taking place within and across several EU Member States.

Where morally sensitive means are to be used to achieve well-accepted goals — as in the case of human embryonic stem cells —– where not the *goal* of therapy-oriented research is questioned but the means to accomplish it, the EGE holds that additional criteria apply concerning the **necessity** of the research: (1) **non-availability of validated alternatives**, and (2) the **non-redundancy** of FP7 projects ([95]).

However, all the above criteria, which constitute the key scientific evaluation criteria, need to be assessed from an ethical perspective during the ethics review process. It is clear that the ethics review cannot and should not duplicate the scientific evaluation, which remains the main assessment of the scientific quality of the project proposals. Nevertheless, the two reviews are complementary. As far as FP7 hESC projects are concerned, the Commission should ensure that the scientific evaluation report is available to the ethics review panel and that there is effective communication between the two panels if needed.

To ensure the complementarity of the two reviews, the scientific review report should address at least the points below.

- Applicants must have shown that research with human stem cells derived from alternative sources, such as adult stem cells, amniotic fluid, umbilical cord blood or other relevant ones, cannot achieve the expected goals of the project. This does not apply to research

([95]) However, repetitions are sometimes necessary to provide evidence of success; these are not redundant exercises in the sense used here.

comparing hESCs with human stem cells derived from alternative sources.

- Applicants must have documented the fact that, in accordance with the basic ethical principles of medical research, relevant research on animals and on cell lines of other origin (animal and human) has been adequately carried out before hESC research is performed.

- Applicants must show that their research is aimed at future human health benefit or biomedical knowledge, and cannot be achieved by alternatives. This includes basic research using hESCs, which is allowed in FP7.

- Applicants must have demonstrated that no alternatives can achieve the goals of the project. Although the group is aware of the importance of respecting animal welfare, it is concerned that respect for human dignity may not be maintained when hESCs are used in toxicity testing of industrial or other commercially produced chemicals not related to drugs, such as cosmetics, or for replacement of animal testing. Therefore, particular attention is to be drawn to this issue (see below, paragraph IV.3, point 2).

- Applicants must provide extensive scientific justification when their projects involve toxicity drug testing; this justification should make clear what sort of additional information is expected from the use of hESCs as compared with the established tests.

The scientific panel should ensure that researchers of hESC FP7 projects collaborate nationally and internationally in order to minimise the use of hESCs within FP7-funded projects and to achieve complementary synergy rather than competition.

IV.2.2. Ethical criteria for research projects under FP6

A few conditions have already been laid down under FP6 to ensure that ethical requirements are met, and these can be taken over under FP7.

1. Applicants must explicitly prove that the regulatory criteria are met for the given project and must indicate the relevant national legal and/or regulatory requirements of the country/countries where the research takes place, according to FP7, Article 6(3) ([96]). For further information, see Annex 1.

2. Applicants must provide information that the hESCs used in the given project result from non-implanted IVF embryos (see following paragraph on donors' rights).

3. Applicants must provide information on the protection of personal data and privacy of the donors of embryos for the creation of stem cell lines.

4. Applicants must provide information on the conditions of donation of the embryos (e.g. no financial inducement, number of eggs retrieved, etc.). In order to guarantee the non-commercialisation of the human body and in line with Article 12 of Directive 2004/23/EC, the EGE holds the view that, in order to protect the freedom of donation, human embryo donation should not involve financial inducement, other than the reimbursement of costs incurred.

In addition to these conditions, the EGE recommends that the ethics review panel should ensure that applicants provide information on the points listed below.

([96]) Article 6(3), http://cordis.europa.eu/fp7/ethics-ict_en.html

IV.2.3. Additional criteria for FP7

IV.2.3.1. Use of alternatives to hESCs

Should alternatives to hESCs with the same potential as embryo-derived stem cells be found in the future, the implications of such developments for both scientific and ethical aspects of the hESC-based research projects ought to be taken into account as soon as possible.

IV.2.3.2. Donors' rights

The donation of human embryos for the production of hESCs for research purposes poses a moral dilemma. This arises from the fact that human embryos are not 'neutral objects'. Informed consent should address explicitly this moral dilemma, leaving the decision to the donors.

The protection rights of donors need particular attention, in a very concrete way, meaning that those countries allowing the procurement of hESCs must provide information on the procurement process for the stem cell lines used by the applicant. The information should state that the measures of this process are in accordance with the fundamental ethical principles and human rights in force in the European Union, national legislation applicable at the time of the donation in the country where the donation was carried out and other relevant EU regulations ([97]). Applicants must provide information from the institutes generating the stem cell lines that the following criteria have been met for the procurement of hESCs:

- no pressure has been put on the donors at any stage ([98]);

([97]) See EC/2004/23.

([98]) See ISSCR guidelines (http://www.isscr.org/guidelines/, p. 9, 'Procurement of materials: *For donating embryos or gametes generated in the course of clinical treatment.* Except when specifically authorized by the SCRO (relevant ethics board) process, no reimbursement of direct expenses or financial considerations of any kind may be provided for donating embryos or gametes that have been generated in the course of clinical treatment and are in excess of clinical

- the donor's health has not been put at risk by excessive ovarian stimulation;
- as far as new hESC lines are concerned, informed consent to the donation for research of an embryo, originally planned for reproduction, is given in knowledge of the kind of research intended ([99]), its implications (including commercial) and in respect of the conditions foreseen by law at the time of the donation in the country where the donation was carried out;
- information was given that consent could be withdrawn up to the stage of the creation of stem cells ([100]);
- infertility treatment and research was appropriately separated;
- no financial incentives have been offered to donate embryos for research at any stage, in line with Article 12 of Directive 2004/23/EC ([101]). However, some members of the EGE hold the view that the reduction of IVF costs is acceptable.

If any of these criteria cannot be met because of the former conditions in which cell lines were generated, the applicants must explain why. The ethics review board must then decide how to deal with this matter on a case-by-case basis; for new hESC lines the above criteria are strongly recommended (see following paragraph, IV.2.4).

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need or deemed of insufficient quality for clinical use. Researchers may not request that members of the infertility treatment team generate more embryos or harvest more oocytes than necessary for the optimal chance of reproductive success. People who elect to donate stored materials for research should not be reimbursed for the costs of storage prior to the decision to donate. Reimbursement for direct expenses incurred by donors as a consequence of the consent process may be determined during the SCRO process.)

([99]) ISSCR guidelines, 11.3–11.3a (http://www.isscr.org/guidelines/).

([100]) Informed consent must take into account the fact that the materials will be used in the derivation of cells for research: 'Consent for donation of materials for research should be obtained at the time of proposed transfer of materials to the research team. Only after a rigorous review by a SCRO mechanism or body can permission be granted to use materials for which prior consent exists but for which re-consent is prohibitively difficult.' (ISSCR, http://www.isscr.org/guidelines/).

([101]) Article 12, Directive 2004/23/EC: 'Member States shall endeavour to ensure voluntary and unpaid donations of tissues and cells'.

Researchers must present all the data referred to donors in an anonymous way. The process used to encode the data must be explained and referenced according to relevant provisions ([102])([103]).

IV.2.4. The need for continuous promotion of public governance and science–society dialogue

Apart from consent and respect of donors' rights, hESC research needs appropriate measures to be put in place to promote the public governance and science–society dialogue with regard to its aims, achievements and failures. Adequate means should be established for public access to relevant and comprehensible information on FP7 hESC research to ensure these goals are being continuously fostered and achieved.

As the Council has stated, the Commission is supporting the creation of a European Registry for human embryonic stem cell lines. This registry is intended to allow the *monitoring* of existing hESCs in Europe and to help *maximise their use* by *avoiding unnecessary derivations* of new hESC lines.

In due time, the registry should ask applicants to provide relevant data on hESCs. The registry will store the data according to scientific and ethical standards to be defined by its newly established Scientific and Ethics Advisory Boards.

With regard to the use of the hESC lines banked in the registry, the EGE recommends:

- once the registry is operational, after a necessary transitional period, the use of the hESC lines banked in the registry should be in line with the criteria

([102]) Directive on the protection of personal data (95/46/EC).
([103]) Council of Europe Bioethics Conventions and additional protocols, Council of Europe Convention for the Protection of Individuals with regard to the Automatic Processing of Personal Data (No 108).

indicated in IV.2.3. The Commission should develop and actively maintain the necessary means to ensure this requirement is fulfilled;

- applicants should use hESCs banked in the EU registry. The need to use other hESC lines in FP7 proposals must therefore be justified on both scientific and ethical grounds;
- the registry should prepare and publish (on its website) information on the hESCs banked and on the positive and negative results of the research performed with/on the hESC lines provided to the researchers. At the project's conclusion, in addition to the scientific data, particularly health-related information, the publication of user-friendly information on hESC research, freely accessible to EU citizens, is also highly recommended. The portal should include interactive elements if possible.

Researchers working in the field have a responsibility to inform the public about their work, but also to engage with the social, political and ethical debates. With regard to open questions such as how to balance different rights and how to prioritise conflicting interests, researchers should participate in public discourse and respect the democratic decision-making process with regard to common societal goals. Applicants should therefore commit time, money and activities to advance the dialogue of science and society in the field of human embryonic stem cell research. Applicants for hESC research under FP7 are therefore strongly encouraged to include the science and humanities dialogue, i.e. social, cultural/religious, philosophical and ethical reflection on hESC research, in their projects and to collaborate for this purpose with other disciplines from the humanities.

IV.3. The need for further research and continuous public debate

As the ethical conflicts concerning hESCs have not been resolved either academically or politically, the EGE recommends that, under FP7, funding should

be provided in order to foster further collaborative and multidisciplinary international research on the ethical implications of hESC research and the pertinent surrounding issues, as well as to encourage informed public debate.

The EGE believes the following topics may be of particular immediate interest in such research and discourse:

- the potentially conflicting goals of economic competitiveness and compliance with ethical standards;
- the use of the human body for modern medicine, including commercialisation of products and procedures stemming from the use of human embryonic stem cells;
- the underlying anthropology of human embryonic stem cell research, especially in the light of hybrids and the chimera research connected to stem cell research;
- optimisation of clinical and therapeutic needs of patients suffering from the most common diseases addressed in hESC research on treatment and/or for specific diseases;
- policy regarding numbers and production process of stem cell lines necessary in the case of successful therapies;
- the correlation of human embryonic stem cell research and questions concerning regenerative medicine and health-related justice, including the issue of global justice;
- the relation between science and humanities and between science and society with respect to the development of new technologies;
- the ongoing efforts of scientific alternatives and their anthropological and ethical interpretations.

The EGE also acknowledges that a number of issues will need further clarification, interdisciplinary research, thorough ethical evaluation and, if found necessary in the future, also appropriate legal action. At present, the EGE believes, the following issues require particular attention.

1. The current provisions for patenting hESC-derived materials need to be addressed. Given new developments in research and taking into consideration the ongoing debate on the limits of patenting of biological materials, the EGE would like to deal with this issue at a later point in time ([104]).

2. The tension induced by a policy that encourages both free donation ([105]) and commercial use of derivates from human substances needs to be addressed.

The EGE emphasises its view that the use of human embryos to generate stem cells should be minimised as much as possible. The EGE calls on the European Union to develop appropriate systems to minimise the use of human embryos to cases for which no alternatives exist.

IV.4. Review of recommendations and communication with the Advisory Board of the European Registry on Human Embryonic Stem Cell Research

The EGE would also welcome interaction with the Advisory Board of the European Registry on Human Embryonic Stem Cell Research, in particular with the registry's Ethics Advisory Board, in order to address the ethical concerns regarding the procurement of stem cells and the storing of data in the light of the ongoing progress in this area.

The concrete form and means of this collaboration should be specified and put into place, and should be appropriately supported and funded by the Commission.

([104]) The EGE has issued an opinion on 'Ethical aspects of patenting inventions involving human stem cells' (http://www.ec.europa.eu/european_group_ethics/docs/avis16_en.pdf).

([105]) Article 12, Directive 2004/23/EC: 'The EC encourages Member States to promote the voluntary and unpaid donation of tissue and cells'.

IV. TRANSLATIONS OF THE RECOMMENDATIONS IN FRENCH AND GERMAN ([106])

IV.I. French translation

RECOMMANDATIONS CONCERNANT L'EXAMEN ÉTHIQUE DES PROJETS DE RECHERCHE DU 7E PC DANS LE DOMAINE DES CSEH — Avis n° 22

IV. RECOMMANDATIONS

IV.1. Préambule

Les présentes recommandations constituent la réponse à la demande du président de la Commission européenne, M. Barroso ([107]), après l'adoption du septième programme-cadre de l'Union européenne pour la recherche et le développement (7e PC), de formuler un avis sur les mesures d'exécution requises lors de l'examen éthique des projets de recherche sur les cellules souches embryonnaires humaines (CSEH).

Tout comme au sein de l'Union européenne, il existe des vues divergentes au sein du Groupe européen d'éthique (GEE) quant à la légitimité morale de la recherche sur les embryons humains et les CSEH, qui vont du refus de la recherche comportant la destruction d'embryons humains (rendant impossible le respect total de la dignité de l'embryon humain) à une position permettant la recherche sur les CSEH sous certaines conditions ou sur une base plus générale.

Le groupe prend acte de la décision politique servant de point de départ à ses recommandations, mais souligne que le dilemme éthique subsiste à propos du statut moral de l'embryon humain et de son utilisation dans le cadre de la recherche. Le GEE insiste donc sur le fait que les divergences de vues d'ordre éthique relatives à la recherche sur les CSEH n'ont pas été résolues.

Cependant, ces recommandations ne formulent pas d'arguments éthiques sur la recherche sur les CSEH en tant que telle, car telle n'était pas la mission confiée au Groupe par la Commission européenne.

([106]) Lettre envoyée au GEE le 22 novembre 2006 par M. Barroso, président de la Commission européenne: *«Je souhaiterais inviter le Groupe européen d'éthique à remettre à la Commission un avis sur les mesures d'exécution requises lors de l'examen éthique des projets de recherche sur les cellules souches embryonnaires humaines pour assurer le respect intégral des règles et exigences éthiques».*

([107]) Translations from the English original — only the English text is authentic. Translations in the EU-27 languages are available at: http://ec.europa.eu/european_group_ethics/activities/docs/opinion_22_final_follow_up_en.pdf, or upon request to the EGE Secretariat mailbox (bepa-ethics-group@ec.europa.eu)

IV.2. Recommandations pour l'examen éthique des projets de recherche impliquant des CSEH

Les projets de recherche du 7e PC comportant l'utilisation de CSEH sont soumis à des règles de sélection rigoureuses, sont contrôlés aux niveaux national et communautaire, et font l'objet d'examens scientifiques et éthiques.

Dans le cadre du 7e PC, les propositions de recherche doivent comprendre des informations sur les aspects éthiques de la recherche proposée, expliquer en détail la conception du projet et démontrer que la proposition répond aux exigences juridiques et éthiques du pays dans lequel la recherche est menée.

Après avoir passé avec succès l'étape de l'évaluation scientifique, les propositions CSEH retenues subissent un examen éthique spécifique organisé par la Commission au cas par cas. L'objectif de cet examen est de garantir que l'Union européenne ne soutient pas des recherches qui ne seraient pas conformes aux principes éthiques fondamentaux ([108]) et de contrôler si les règles d'éthique définies dans le 7e PC sont respectées.

Le comité d'examen éthique est un organisme transnational composé d'experts de différentes disciplines. Le comité produit un rapport d'examen éthique, qui énumère les différentes questions éthiques, décrit la manière dont ces questions ont été traitées par les demandeurs et énonce les recommandations du comité.

Après avoir passé avec succès l'examen scientifique et éthique, les propositions de projets CSEH sont ensuite transmises à un comité de réglementation composé de représentants des États membres de l'UE, qui statue sur les projets au cas par cas.

([108]) Septième programme-cadre (décision n° 1982/2006/CE), article 6, paragraphe 1: «Toutes les actions de recherche menées au titre du septième programme-cadre sont réalisées dans le respect des principes éthiques fondamentaux.»; règles de participation, article 10: «une proposition […] allant à l'encontre des principes éthiques fondamentaux […] n'est pas sélectionnée. Une telle proposition peut être exclue à tout moment des procédures d'évaluation et de sélection.»

Afin de fournir des lignes directrices aux membres des comités d'examen éthique du 7e PC en matière de CSEH, qui seront invités à examiner les projets de recherche utilisant des lignées de CSEH, et dans le cadre du mandat et des conditions spécifiques établis par la décision politique du Parlement européen et du Conseil relative au 7e PC, ainsi que par la demande spécifique du président de la Commission européenne, M. J. M. Barroso (voir ci-dessus), le GEE a élaboré les lignes directrices et points suivants à prendre en compte lors de l'examen éthique de projets dans le cadre du 7e PC ([109]).

IV.2.1. Critères généraux

La Commission européenne a déclaré qu'elle «soutiendra les actions et initiatives qui contribuent à coordonner et rationaliser les activités de recherche sur les cellules souches embryonnaires humaines selon une approche déontologique responsable» ([110]). En conformité avec cette déclaration, le GEE reconnaît la nécessité de promouvoir une recherche responsable et transparente, qui sert l'intérêt public, respecte l'autonomie des États membres, préserve la confiance du public, encourage la coopération internationale et exige l'adoption d'une démarche déontologique dans les activités de recherche ([111]).

La recherche sur les cellules souches embryonnaires humaines, menée selon une approche déontologique responsable, doit être conforme aux principes éthiques fondamentaux et aux droits de l'homme dans l'Union européenne ([112]),

([109]) Selon les règles du 7e PC, les évaluateurs signent une déclaration d'absence de conflit d'intérêts, et le personnel de la Commission européenne vérifie les conflits avec chacune des propositions qu'ils évaluent. Les comités d'évaluation des examens éthiques et scientifiques sont anonymes.

([110]) Déclaration de la Commission européenne du 24 juillet 2006, lors de la réunion du Conseil de ministres, à propos du 7e PC. Voir JO L 412 du 30.12.2006, p. 43.

([111]) Par exemple la convention d'Oviedo du Conseil de l'Europe (article 2).

([112]) Pour plus de détails, voir la section I du présent avis relative aux documents pertinents dans le cadre de la recherche médicale.

depuis la fourniture des cellules souches ([113]) jusqu'aux activités de recherche cliniques portant sur les CSEH.

Les droits fondamentaux comprennent: les *droits de protection* tels que la protection de la vie humaine, le respect de son intégrité, la protection de la santé et de la liberté, les *droits politiques* tels que l'absence d'intervention injustifiée de l'État ou les droits participatifs dans le domaine politique, ainsi que les *droits positifs* tels que les droits sociaux et économiques de base dans la mesure où ils contribuent à la santé et à un seuil de développement, avec pour résultat une gouvernance de la santé ([114]).

L'équilibre entre ces trois catégories de droits fondamentaux n'est nullement facile ni prédéterminé, mais implique des efforts continus pour assurer leur protection, la reconnaissance et la promotion de la dignité humaine et des droits de l'homme et, plus concrètement, implique de définir des priorités en matière de recherche médicale.

Les critères généraux des éléments d'incitation de la recherche dans des domaines spécifiques intègrent cet équilibre. Ils peuvent être récapitulés comme suit:

- **la nécessité scientifique et le haut statut** de la recherche ([115]),
- **l'urgence** ([116]) et
- **la désirabilité sociale,**
- **la primauté** de l'intérêt et du bien-être de l'être humain sur l'intérêt exclusif de la société ou de la science.

([113]) Le 7e PC exclut l'approvisionnement en CSEH du financement communautaire (voir paragraphe II.2). Voir décision n° 1982/2006/CE du Parlement européen et du Conseil du 18 décembre 2006 relative au septième programme-cadre de la Communauté européenne pour des actions de recherche, de développement technologique et de démonstration (2007-2013), JO L 412 du 30.12.2006, p. 1-41.

([114]) Cf. les objectifs du millénaire des Nations Unies, que l'Union européenne s'est engagée à réaliser.

([115]) http://ec.europa.eu/research/7PC/index_en.cfm?pg=documents.

([116]) http://www.who.int/rpc/en/HealthResearchinPolicyMaking.pdf.

La désirabilité sociale donne lieu à un discours politique et sociétal sur les objectifs et perspectives de l'Union européenne au XXI^{e} siècle, en particulier sur la relation entre la croissance économique et les objectifs sociaux, tels que la promotion des normes de santé et leur application durable aux niveaux national, international et mondial.

En ce qui concerne la recherche sur les CSEH, il n'y a aucun consensus sur son acceptabilité sociale au sein de l'Union européenne, et des vues divergentes coexistent. Un débat sur le meilleur modèle (par exemple un «consensus minimal» ou la «subsidiarité») pour réglementer la recherche sur les CSEH au niveau de l'UE a donc lieu dans plusieurs États membres de l'UE.

Lorsque des moyens sensibles sur le plan éthique doivent être utilisés pour atteindre des objectifs unanimement acceptés — comme dans le cas des cellules souches embryonnaires humaines —, lorsque la finalité de la recherche thérapeutique n'est pas remise en cause mais les moyens d'y parvenir, le GEE soutient que des critères additionnels s'appliquent en ce qui concerne la ***nécessité*** de la recherche: 1) la ***non-disponibilité d'alternatives validées*** et 2) la ***non-redondance*** des projets du 7^{e} PC ([117]).

Cependant, tous les critères indiqués ci-dessus, qui constituent les principaux critères d'évaluation scientifique, doivent être évalués d'un point de vue éthique au cours du processus d'examen éthique. Il est clair que l'examen éthique ne peut pas et ne doit pas faire double emploi avec l'évaluation scientifique, qui demeure la principale évaluation de la qualité scientifique des propositions de projets. Néanmoins, les deux examens sont complémentaires. En ce qui concerne les projets CSEH du 7^{e} PC, la Commission doit veiller à ce que le

([117]) Des répétitions sont cependant parfois nécessaires pour apporter la preuve de la réussite; il ne s'agit pas d'exercices redondants au sens où on l'entend ici.

rapport d'évaluation scientifique soit à la disposition du comité d'examen éthique et qu'il existe une communication efficace entre les deux comités si nécessaire.

Pour assurer la complémentarité des deux examens, le rapport d'examen scientifique doit porter au moins sur les points suivants:

- les demandeurs doivent avoir démontré que la recherche pratiquée sur des cellules souches humaines dérivées de sources alternatives, telles que des cellules souches adultes, du liquide amniotique, du sang provenant du cordon ombilical ou d'autres sources appropriées, ne permet pas de réaliser les objectifs prévus du projet. Cela ne s'applique pas aux activités de recherche comparant des CSEH à des cellules souches humaines dérivées de sources alternatives;

- les demandeurs doivent avoir documenté le fait que, conformément aux principes éthiques de base de la recherche médicale, des activités de recherche pertinentes sur des animaux et sur des lignées cellulaires d'une autre origine (animale et humaine) ont été menées de façon suffisante avant d'entreprendre des recherches sur les CSEH;

- les demandeurs doivent démontrer que leurs activités de recherche ont pour but des bénéfices futurs en termes de santé humaine ou des connaissances biomédicales, et qu'elles ne peuvent être réalisées par des moyens alternatifs. Cela comprend la recherche fondamentale sur les CSEH, qui est autorisée dans le 7^{e} PC;

- les demandeurs doivent avoir démontré qu'aucune autre solution ne permet de réaliser les objectifs du projet. Bien que le groupe soit conscient de l'importance de respecter le bien-être des animaux, il s'inquiète que le respect de la dignité humaine puisse ne pas être assuré lorsque des CSEH sont utilisées dans le cadre d'essais de

toxicité portant sur des produits chimiques industriels ou du commerce sans rapport avec les médicaments, tels que les cosmétiques, ou en remplacement d'essais sur les animaux. Il convient par conséquent de porter une attention particulière à cette question (voir ci-après le point IV.3.2);

- les demandeurs doivent fournir une justification scientifique complète lorsque leurs projets comportent des essais de toxicité de médicaments; cette justification devra établir clairement le type d'informations additionnelles que l'on peut attendre de l'utilisation de CSEH par rapport aux essais établis.

Le comité scientifique doit veiller à ce que les chercheurs participant à des projets CSEH du 7e PC collaborent sur le plan national et international afin de limiter au minimum l'utilisation de CSEH dans le cadre de projets financés par le 7e PC et pour mettre en place une synergie de complémentarité plutôt qu'une situation de compétition.

IV.2.2. Critères éthiques des projets de recherche dans le cadre du 6e PC

Certaines conditions ont déjà été définies dans le cadre du 6e PC pour assurer le respect des exigences éthiques, et celles-ci peuvent être reprises au titre du 7e PC:

- les demandeurs doivent prouver de façon explicite que le projet en question répond aux critères réglementaires et doivent indiquer les exigences juridiques et/ou réglementaires applicables du/des pays où la recherche a lieu, conformément à l'article 6, paragraphe 3 ([118]), du 7e PC. Pour de plus amples informations, voir l'annexe 1;

([118]) Article 6, paragraphe 3, http://cordis.europa.eu/7PC/ethics-ict_en.html

- les demandeurs doivent indiquer que les CSEH utilisées dans le cadre du projet sont issues d'embryons de FIV non implantés (voir paragraphe suivant sur les droits des donneurs);
- les demandeurs doivent fournir des informations sur la protection des données personnelles et de l'anonymat des donneurs d'embryons pour la production de lignées de cellules souches;
- les demandeurs doivent fournir des informations sur les conditions de don des embryons (par exemple: aucune incitation financière, nombre d'ovules prélevés, etc.). Afin de garantir la non-commercialisation du corps humain et en accord avec l'article 12 de la directive 2004/23/CE, le GEE estime que pour protéger la liberté de don, le don d'embryons humains ne doit pas comporter d'incitation financière autre que le remboursement des frais encourus.

Outre ces conditions, le GEE recommande que le comité d'examen éthique veille à ce que les demandeurs fournissent des informations sur les points énumérés ci-après.

IV.2.3. Critères additionnels pour le 7e PC

IV.2.3.1. Utilisation de solutions alternatives aux CSEH

En cas de découverte future de solutions alternatives aux CSEH présentant le même potentiel que les cellules souches embryonnaires, il conviendra de prendre en compte au plus vite les implications de ces avancées, pour les aspects tant scientifiques qu'éthiques des projets de recherche basés sur les CSEH.

IV.2.3.2. Droits des donneurs

Le don d'embryons humains pour la production de CSEH à des fins de recherche pose un dilemme moral, qui résulte du fait que les embryons humains ne sont pas des «objets neutres». Ce dilemme moral doit faire l'objet d'un consentement éclairé explicite, laissant la décision aux donneurs.

Les droits de protection des donneurs requièrent une attention particulière, sous une forme très concrète, ce qui signifie que les pays autorisant l'approvisionnement en CSEH doivent fournir des informations sur le processus d'obtention des lignées de cellules souches utilisées par le demandeur. Ces informations doivent préciser que les mesures de ce processus sont conformes aux principes éthiques fondamentaux et aux droits de l'homme en vigueur dans l'Union européenne, à la législation nationale applicable au moment du don dans le pays où le don est effectué et aux autres règlements communautaires applicables ([119]). Les demandeurs doivent fournir des informations en provenance des instituts produisant les lignées de cellules souches selon lesquelles les critères énoncés ci-après ont été respectés lors de l'obtention de CSEH:

- aucune pression n'a été exercée à aucun moment sur les donneurs ([120]);

([119]) Voir la directive 2004/23/CE.

([120]) Voir les lignes directrices de l'ISSCR (société internationale de recherche sur les cellules souches) [http://www.isscr.org/guidelines/, p. 9, «Approvisionnement en matériels: *pour les dons d'embryons ou de gamètes produits au cours d'un traitement clinique.* Sauf en cas d'autorisation

- la santé du donneur n'a pas été mise en danger par une stimulation ovarienne excessive;
- pour les nouvelles lignées de CSEH, un consentement éclairé concernant le don pour la recherche d'un embryon initialement destiné à la reproduction est donné en connaissant la nature des recherches prévues ([121]), leurs implications (y compris commerciales) et dans le respect des conditions prévues par la loi au moment du don dans le pays où celui-ci a été effectué;
- le donneur a été informé qu'il pourrait retirer son consentement jusqu'au stade de la création des cellules souches ([122]);
- le traitement de l'infertilité et la recherche sont correctement séparés;
- aucune incitation financière n'a été proposée à aucun moment pour donner des embryons pour la recherche, conformément à l'article 12 de la directive 2004/23/CE ([123]). Cependant, certains membres du GEE estiment acceptable la réduction des coûts de FIV.

Si l'un ou plusieurs de ces critères ne peuvent être respectés en raison des conditions préalables dans lesquelles les lignées cellulaires ont été produites, les demandeurs doivent expliquer pourquoi. Le comité d'examen éthique doit alors statuer au cas par cas sur la manière de traiter cette question; pour les nouvelles

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expresse par le processus du SCRO (comité d'éthique compétent), aucun remboursement de dépenses directes ni rémunération financière d'aucune sorte ne peuvent être accordés pour le don d'embryons ou de gamètes produits au cours d'un traitement clinique et qui excèdent les besoins cliniques ou sont considérés de qualité insuffisante pour un usage clinique. Les chercheurs ne doivent pas demander à ce que les membres de l'équipe de traitement de la stérilité produisent plus d'embryons ou recueillent plus d'ovocytes que nécessaire pour garantir des chances optimales de succès reproductif. Les personnes qui choisissent de faire don de matériels stockés pour la recherche ne doivent pas être remboursées des frais de stockage correspondant à la période précédant la décision du don. Le remboursement des frais directs encourus par des donneurs à la suite du consentement peut être déterminé pendant le processus de surveillance de la recherche sur les cellules souches (SCRO)»].

([121]) Lignes directrices de l'ISSCR, 11.3-11.3.a (http://www.isscr.org/guidelines/).

([122]) Le consentement éclairé doit tenir compte du fait que les matériels seront utilisés afin de produire des cellules pour la recherche: «Le consentement du don de matériels pour la recherche doit être obtenu au moment de la proposition de cession de matériels à l'équipe de recherche. Ce n'est qu'après un examen rigoureux par un mécanisme ou organisme de surveillance de la recherche sur les cellules souches que l'autorisation peut être accordée d'utiliser des matériels pour lesquels il existe un consentement préalable dont le renouvellement s'avère extrêmement difficile» (ISSCR, http://www.isscr.org/guidelines/).

lignées de CSEH, les critères ci-dessus sont vivement recommandés (voir le point IV.2.4).

Les chercheurs doivent présenter de façon anonyme toutes les données faisant référence aux donneurs. Le procédé utilisé pour coder les données doit être expliqué et référencé selon les dispositions applicables ([124]) ([125]).

IV.2.4. Nécessité d'encourager en permanence la gouvernance publique et le dialogue science-société

Indépendamment du consentement et du respect des droits des donneurs, la recherche sur les CSEH nécessite la mise en place de mesures pour favoriser la gouvernance publique et le dialogue science-société en ce qui concerne ses objectifs, réussites et échecs. Des moyens suffisants doivent être établis pour permettre l'accès du public à des informations pertinentes et compréhensibles sur la recherche sur les CSEH dans le cadre du 7e PC, afin de promouvoir et d'atteindre en permanence ces objectifs.

Comme l'a indiqué le Conseil de ministres, la Commission soutient la création d'un registre européen des lignées de cellules souches embryonnaires humaines. Ce registre permettra une *surveillance* des CSEH existant en Europe et favorisera leur utilisation optimale en *évitant d'inutiles dérivations* de nouvelles lignées de CSEH.

Le moment venu, le registre invitera les demandeurs à fournir des données appropriées sur les CSEH. Le registre stockera les données selon des normes scientifiques et éthiques à définir par ses comités consultatifs scientifiques et éthiques récemment formés.

([123]) Article 12 de la directive 2004/23/CE: «Les États membres s'efforcent de garantir les dons volontaires et non rémunérés de tissus et cellules.»

([124]) Directive 95/46/CE du Parlement européen et du Conseil du 24 octobre 1995 relative à la protection des personnes physiques à l'égard du traitement des données à caractère personnel et à la libre circulation de ces données.

([125]) Conventions de bioéthique du Conseil de l'Europe et protocoles additionnels, convention du Conseil de l'Europe pour la protection des personnes à l'égard du traitement automatisé des données à caractère personnel (n° 108).

En ce qui concerne l'utilisation des lignées de CSEH stockées dans le registre, le GEE formule les recommandations suivantes:

- une fois le registre opérationnel, après une période de transition nécessaire, l'utilisation des lignées de CSEH stockées dans le registre devra être conforme aux critères énoncés au point IV.2.3. La Commission devra développer et maintenir activement les moyens nécessaires pour assurer le respect de cette exigence;
- les demandeurs devront utiliser des CSEH stockées dans le registre communautaire. La nécessité d'utiliser d'autres lignées de CSEH dans les propositions du 7e PC devra par conséquent être justifiée sur le plan scientifique et éthique;
- le registre devra préparer et publier (sur son site internet) des informations sur les CSEH stockées en banque et sur les résultats positifs et négatifs des recherches effectuées sur les lignées de CSEH fournies aux chercheurs. En fin de projet, en plus des données scientifiques, en particulier des informations relatives à la santé, il est également fortement recommandé de publier des informations conviviales et librement accessibles aux citoyens de l'UE sur les activités de recherche en matière de CSEH. Le portail devra si possible intégrer des éléments interactifs.

Il incombe aux chercheurs opérant sur le terrain d'informer le public de leurs travaux, mais également de participer aux débats sociaux, politiques et éthiques. Concernant des questions ouvertes telles que «comment trouver l'équilibre entre des droits divergents» et «comment classer des intérêts conflictuels par ordre de priorité», les chercheurs doivent prendre part au débat public et respecter le processus décisionnel démocratique en ce qui concerne les objectifs sociétaux communs. Les demandeurs doivent par conséquent consacrer du temps, de l'argent et des activités pour faire progresser le dialogue de la science et de la société dans le domaine de la recherche sur les cellules souches embryonnaires humaines. Les demandeurs [déposant un dossier] de recherche sur les CSEH

dans le cadre du 7e PC sont donc fortement encouragés à inclure dans leurs projets le *dialogue science et sciences humaines*, c'est-à-dire une réflexion sociale, culturelle/religieuse, philosophique et éthique sur la recherche sur les CSEH, et à collaborer à cet effet avec d'autres disciplines des sciences humaines.

IV.3. Nécessité de recherches complémentaires et d'un débat public permanent

Étant donné que les conflits éthiques concernant les CSEH n'ont pas été résolus au niveau universitaire ou politique, le GEE recommande qu'un financement soit octroyé dans le cadre du 7e PC afin de permettre des recherches internationales complémentaires de nature collaborative et multidisciplinaire sur les implications éthiques de la recherche sur les CSEH et les questions connexes, ainsi que pour encourager un débat public éclairé.

Le GEE estime que les thèmes suivants peuvent présenter un intérêt particulier immédiat dans le cadre de ces recherches et débats:

- les objectifs potentiellement contradictoires de la compétitivité et du respect des normes éthiques;
- l'utilisation du corps humain pour la médecine moderne, y compris la commercialisation de produits et procédures provenant de l'utilisation de cellules souches embryonnaires humaines;
- l'anthropologie sous-jacente de la recherche sur les cellules souches embryonnaires humaines, en particulier à la lumière des hybrides et de la recherche sur les chimères liée à la recherche sur les cellules souches;
- l'optimisation des besoins cliniques et thérapeutiques des patients souffrant des maladies les plus communes visées par la recherche CSEH en matière de traitement et/ou de maladies spécifiques;
- la politique relative au nombre et au processus de production des lignées de cellules souches nécessaires dans le cas de thérapies réussies;

- la corrélation entre la recherche sur les cellules souches embryonnaires humaines et les questions concernant la médecine régénérative, la justice en matière de santé, y compris la question de la justice globale;
- la relation entre la science et les sciences humaines et entre la science et la société en ce qui concerne le développement de nouvelles technologies;
- les efforts continus des solutions alternatives scientifiques et leurs interprétations anthropologiques et éthiques.

Le GEE reconnaît également qu'un certain nombre de questions devront faire l'objet de précisions supplémentaires, d'une recherche interdisciplinaire, d'une évaluation éthique complète et également, si cela s'avère nécessaire dans le futur, d'une action en justice appropriée. Le GEE estime actuellement que les questions suivantes exigent une attention particulière:

- les dispositions courantes de brevetabilité des matériels issus de CSEH doivent être abordées. Étant donné les nouvelles avancées de la recherche et compte tenu du débat en cours sur les limites de brevetabilité des matériels biologiques, le GEE voudrait traiter cette question ultérieurement ([126]);

- la tension induite par une politique qui encourage à la fois le don gratuit ([127]) et l'utilisation commerciale de dérivés de substances humaines doit être abordée.

Le GEE souligne avec insistance le fait que l'utilisation d'embryons humains pour produire des cellules souches doit être limitée au minimum possible. Le GEE invite l'Union européenne à développer des systèmes appropriés pour limiter

([126]) Le GEE a émis un avis sur les aspects éthiques de la brevetabilité des inventions impliquant des cellules souches humaines, http://www.ec.europa.eu/european_group_ethics/docs/avis16_fr.pdf.

([127]) Article 12 de la directive 2004/23/CE: «Les États membres s'efforcent de garantir les dons volontaires et non rémunérés de tissus et cellules.»

l'utilisation d'embryons humains aux cas pour lesquels il n'existe aucune solution de rechange.

IV.4. Examen des recommandations et communication avec le comité consultatif du registre européen des lignées de cellules souches embryonnaires humaines

Le GEE serait également favorable à une interaction avec le comité consultatif du registre européen des lignées de cellules souches embryonnaires humaines, en particulier avec le comité consultatif du registre en matière d'éthique, afin d'aborder les questions éthiques relatives à l'obtention de cellules souches et au stockage des données à la lumière des progrès continus dans ce domaine.

La forme et les moyens concrets de cette collaboration devraient être précisés et mis en place, et devraient être convenablement soutenus et financés par la Commission.

IV.4.1. Nécessité d'une révision

Le GEE propose de réviser les lignes directrices éthiques adoptées à la lumière des avancées scientifiques, juridiques et sociales.

Groupe européen d'éthique des sciences et des nouvelles technologies

Président: Göran Hermerén

Membres:

Emmanuel Agius	Diana Banati	Anne Cambon-Thomsen
Rafael Capurro	Inez de Beaufort	Jozef Glasa
Hille Haker	Julian Kinderlerer	Krzysztof Marczewski
Paula Martinho Da Silva		Linda Nielsen
Pere Puigdomenech-Rosell		Günter Virt

IV.I. GERMAN TRANSLATION[128]

DEUTSCHE ÜBERSETZUNG DER : EMPFEHLUNGEN ZUR ETHISCHEN PRÜFUNG VON FP7-FORSCHUNGSPROJEKTEN MIT HUMANEN EMBRYONALEN STAMMZELLEN - STELLUNGNAHME NR. 22 -

IV. EMPFEHLUNGEN

IV.1 Einleitung

Nach Verabschiedung des Siebten Rahmenprogramms für Forschung und Entwicklung (FP7) forderte der Präsident der Europäischen Kommission, Herr Barroso[129], die Gruppe auf, eine Stellungnahme zu den Durchführungsmaßnahmen auszuarbeiten, die bei der ethischen Prüfung von Forschungsprojekten mit humanen embryonalen Stammzellen (hES-Zellen) erforderlich sind. Die vorliegenden Empfehlungen sind das Ergebnis dieser Arbeit.

Wie in der Europäischen Union generell, so gehen auch innerhalb der EGE die Ansichten über die moralische Legitimität der Forschung an humanen Embryonen und humanen embryonalen Stammzellen auseinander; sie reichen von der Ablehnung der verbrauchenden Embryonenforschung (da diese es unmöglich macht, die Würde des menschlichen Embryos zu wahren) bis zur Position, die Forschung mit hES-Zellen unter bestimmten Bedingungen oder auf breiterer Basis zu erlauben.

Die Gruppe erkennt den politischen Beschluss als Ausgangspunkt dieser Empfehlungen an, betont aber gleichzeitig, dass das ethische Dilemma hinsichtlich des Status des humanen Embryos und seiner Verwendung für Forschungszwecke nach wie vor besteht. Die EGE unterstreicht daher, dass die Meinungsunterschiede in ethischen Fragen im Zusammenhang mit der Forschung an humanen embryonalen Stammzellen nicht ausgeräumt wurden.

In diesen Empfehlungen werden jedoch *keine* ethischen Argumente über die Forschung an humanen embryonalen Stammzellen als solche erarbeitet, da dies nicht dem von der Europäischen Kommission der Gruppe erteilten Auftrag entsprach.

[128] Translations from the English original — only the English text is authentic. Translations in the EU-27 languages are available at: http://ec.europa.eu/european_group_ethics/activities/docs/opinion_22_final_follow_up_en.pdf, or upon request to the EGE Secretariat mailbox (bepa-ethics-group@ec.europa.eu)

[129] Schreiben des Präsidenten der Europäischen Kommission, Herrn Barroso, an die EGE vom 22.11.2006. *„Ich möchte die Europäische Ethikgruppe auffordern, für die Kommission eine Stellungnahme über die Durchführung von Maßnahmen auszuarbeiten, die für die ethische Prüfung von Forschungsprojekten mit humanen embryonalen Stammzellen erforderlich sind, um sicherzustellen, dass die ethischen Regeln und Anforderungen vollständig eingehalten werden."*

IV.2 Empfehlungen zur ethischen Prüfung von Forschungsprojekten mit hES-Zellen

FP7-Forschungsprojekte, in denen hES-Zellen verwendet werden, unterliegen bei der Auswahl strengen Regeln, werden sowohl auf nationaler wie auf EU-Ebene überwacht und durchlaufen sowohl wissenschaftliche als auch ethische Prüfungen.

Forschungsanträge im Rahmen des FP7 müssen Informationen über ethische Aspekte der vorgeschlagenen Arbeit enthalten; die Projektgestaltung ist detailliert zu erläutern und es ist nachzuweisen, dass der Antrag den rechtlichen und ethischen Anforderungen des Landes entspricht, in denen die Forschung durchgeführt wird.

Nachdem die Forschungsvorhaben die wissenschaftliche Prüfung erfolgreich durchlaufen haben, werden die Forschungsprojekte mit hES-Zellen einer speziellen von der Kommission organisierten ethischen Einzelfallprüfung unterzogen. Das Ziel dieser Prüfung ist es sicherzustellen, dass die Europäische Union keine Forschung unterstützt, die mit grundlegenden ethischen Prinzipien unvereinbar ist[130], und es soll überprüft werden, ob die im FP7 festgelegten ethischen Regeln eingehalten werden.

Dem transnational zusammengesetzten Gremium gehören Experten unterschiedlicher Disziplinen an. Es erarbeitet einen Bericht, in dem die verschiedenen ethischen Fragen aufgeführt werden und beschrieben wird, wie die Antragsteller mit ihnen umgehen; außerdem enthält der Bericht die Empfehlungen des Gremiums.

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[130] Siebtes Rahmenprogramm (Beschluss Nr. 1982/2006/EG), Artikel 6 Absatz 1: „Bei allen Forschungsmaßnahmen innerhalb des Siebten Rahmenprogramms werden die ethischen Grundprinzipien beachtet." Regeln für die Beteiligung, Artikel 14 Absatz 2: „Ein Vorschlag, der im Widerspruch zu grundlegenden ethischen Prinzipien steht […], wird nicht ausgewählt. Ein

Vorschläge für hES-Zellforschungen werden, sobald sie die wissenschaftliche und die ethische Prüfung durchlaufen haben, einem Regelungsausschuss vorgelegt, der aus Vertretern der EU-Mitgliedstaaten besteht und auf Einzelfallbasis über die Projekte entscheidet.

Für die Mitglieder der Gremien, die im Rahmen des FP7 die ethische Prüfung von Forschungsprojekten mit hES-Zelllinien vornehmen sollen, hat die EGE entsprechend dem konkreten Mandat und den Bedingungen, die im politischen Beschluss des Europäischen Parlaments und des Rates über das FP7 festgelegt sind, sowie auf die konkrete Aufforderung des Präsidenten der Europäischen Kommission, Herrn J. M. Barroso, hin (siehe oben), für die Durchführung solcher ethischer Prüfungen von FP7-Projekten die folgenden Leitlinien und Kriterien erarbeitet[131].

IV.2.1 Allgemeine Kriterien

Die Europäische Kommission hat erklärt, dass sie „Maßnahmen und Initiativen fördern (wird), die dazu beitragen, dass Forschungsarbeiten mit humanen embryonalen Stammzellen *auf ethisch vertretbare Art und Weise* koordiniert und rationalisiert werden können“[132]. Übereinstimmend mit dieser Erklärung ist auch die EGE der Ansicht, dass nur ethisch vertretbare Forschung gefördert werden kann, die transparent ist, dem öffentlichen Interesse dient, die Autonomie der Mitgliedstaaten respektiert, das Vertrauen der Öffentlichkeit wahrt, die internationale Zusammenarbeit fördert und die ethischen Fragen in der Forschungspraxis verankert[133].

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solcher Vorschlag kann jederzeit von den Bewertungs-, Auswahl- und Gewährungsverfahren ausgeschlossen werden.“

131 Nach den Regeln für die Beteiligung am FP7 unterzeichnen die Bewerter eine Erklärung zum Interessenkonflikt, und die Kommissionsdienststelle überprüft bei jedem Vorschlag, den sie bewertet, ob ein Interessenkonflikt besteht. Die Evaluationsgremien der ethischen und wissenschaftlichen Bewertungen sind anonym.

132 Erklärung der Europäischen Kommission vom 24. Juli 2006 während der Ministerratstagung über das FP7. Siehe ABl. L 412/43 vom 30. Dezember 2006.

133 Siehe beispielsweise das Übereinkommen von Oviedo des Europarats (Artikel 2).

Ethisch vertretbare Forschung mit humanen embryonalen Stammzellen muss von der Beschaffung der Stammzellen[134] bis zu der auf hES-Zellen basierenden klinischen Forschung den grundlegenden ethischen Prinzipien und Menschenrechten der Europäischen Union entsprechen[135].

Zu den Grundrechten gehören: *Schutzrechte,* etwa das Recht auf Leben und auf körperliche Unversehrtheit und der Schutz von Gesundheit und Freiheit, *politische Rechte,* etwa das Recht auf Schutz vor ungerechtfertigtem Eingreifen des Staates oder das Recht auf politische Betätigung, und *positive Rechte,* etwa grundlegende soziale und wirtschaftliche Rechte, soweit sie zur Gesundheit und zum Erreichen einer Entwicklungsschwelle beitragen und die Einführung gesundheitsbezogener Steuerungsmechanismen erfordern.[136]

Der Ausgleich zwischen diesen drei Gruppen von Grundrechten ist keineswegs leicht herzustellen oder gar vorgegeben. Eher ist es so, dass laufend Bemühungen erforderlich sind, um ihren Schutz sicherzustellen und die Menschenwürde und die Menschenrechte zu gewährleisten und zu fördern. Konkret bedeutet dies im Zusammenhang mit gesundheitsrelevanter Forschung auch, Prioritäten zu setzen.

Die allgemeinen Kriterien, nach denen Forschungsförderung betrieben wird, beinhalten eine solche Prioritätensetzung. Diese Kriterien lassen sich folgendermaßen zusammenfassen:

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134 Die Gewinnung humaner embryonaler Stammzellen wird laut FP7 nicht mit Gemeinschaftsmitteln finanziert (siehe Abschnitt II.2). Siehe Beschluss Nr. 1982/2006/EG des Europäischen Parlaments und des Rates vom 18. Dezember 2006 über das Siebte Rahmenprogramm der Europäischen Gemeinschaft für Forschung, technologische Entwicklung und Demonstration (2007 bis 2013), ABl. L 412 vom 30. Dezember 2006, S.1-41.

135 Einzelheiten siehe Abschnitt I dieser Stellungnahme über die relevanten Dokumente im Kontext der medizinischen Forschung.

136 Siehe die Millenniumsziele der Vereinten Nationen, zu deren Realisierung sich die Europäische Union verpflichtet hat.

- ***wissenschaftliche Notwendigkeit und hoher Rang*** der Forschung[137],
- ***Dringlichkeit***[138] und
- ***gesellschaftliche Erwünschtheit,***
- ***Vorrang*** der Interessen und des Wohlbefindens des einzelnen Menschen vor rein gesellschaftlichen oder wissenschaftlichen Interessen.

Die gesellschaftliche Erwünschtheit von Fördermaßnahmen wird im Rahmen des politischen und gesellschaftlichen Diskurses über Ziele und Perspektiven der Europäischen Union im 21. Jahrhundert diskutiert; dabei geht es auch um die Beziehung zwischen Wirtschaftswachstum und sozialen Zielen, etwa der Förderung von Gesundheitsstandards und ihrer nachhaltigen Anwendung auf nationaler, internationaler und globaler Ebene.

Was die hES-Zellforschung betrifft, gibt es in der Europäischen Union keinen Konsens über ihre gesellschaftliche Akzeptabilität, divergente Meinungen stehen nebeneinander. Deshalb werden derzeit in mehreren EU-Mitgliedstaaten und auch über ihre Grenzen hinweg verschiedene Modelle (z. B. das „Minimalkonsens-Modell“ oder das „Subsidiaritäts-Modell“) zur Regulierung der hES-Zellforschung auf EU-Ebene diskutiert.

Wo moralisch sensible Mittel eingesetzt werden, um allgemein akzeptierte Ziele zu erreichen – wie im Falle der humanen embryonalen Stammzellen –, wo also nicht das *Ziel* therapieorientierter Forschung hinterfragt wird, sondern die „Mittel“, mit deren Hilfe es erreicht werden soll, gelten nach Ansicht der EGE zusätzliche Kriterien hinsichtlich der ***Notwendigkeit*** der Forschung: 1) das ***Fehlen validierter Alternativen*** und 2) die ***Nichtredundanz*** von FP7-Projekten[139].

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137 http://ec.europa.eu/research/fp7/index_en.cfm?pg=documents.

138 http://www.who.int/rpc/en/HealthResearchinPolicyMaking.pdf.

139 Wiederholungen sind allerdings zuweilen notwendig, um den Erfolgsnachweis zu erbringen; diese werden nicht im obigen Sinne als redundant angesehen.

Diese zentralen wissenschaftlichen Bewertungskriterien müssen jedoch im Rahmen der ethischen Prüfung aus ethischer Sicht bewertet werden. Selbstverständlich kann und soll die ethische Prüfung nicht eine Wiederholung der wissenschaftlichen Prüfung sein, die nach wie vor für die Beurteilung der wissenschaftlichen Qualität von Projektvorschlägen am wichtigsten ist. Die beiden Prüfungen ergänzen sich vielmehr. Soweit FP7-Projekte mit hES-Zellen betroffen sind, sollte die Kommission sicherstellen, dass der Bericht über die wissenschaftliche Prüfung dem mit der ethischen Prüfung beauftragten Gremium vorliegt und dass die beiden Gremien erforderlichenfalls ungehindert miteinander kommunizieren können.

Um die Komplementarität der beiden Prüfungen zu gewährleisten, sollte aus dem Bericht über die wissenschaftliche Bewertung mindestens Folgendes hervorgehen:

- Die Antragsteller haben deutlich gemacht, dass mit der Forschung an humanen Stammzellen anderer Herkunft, also adulten Stammzellen, Stammzellen aus Fruchtwasser, Nabelschnurblut o. Ä., die angestrebten Ziele des Forschungsvorhabens nicht erreicht werden können. Dies gilt nicht für Forschung zum Vergleich von hES-Zellen mit humanen Stammzellen aus anderen Quellen.

- Die Antragsteller haben die Tatsache dokumentiert, dass in Übereinstimmung mit den grundlegenden ethischen Prinzipien der medizinischen Forschung einschlägige Forschungen an Tieren und an Zelllinien anderer (tierischer und humaner) Herkunft in angemessener Weise durchgeführt wurden, ehe an hES-Zellen geforscht wird.

- Die Antragsteller haben deutlich gemacht, dass sie mit ihrer Forschung künftigen Nutzen für die menschliche Gesundheit oder biomedizinische Erkenntnisse anstreben und dass dies mit alternativen Methoden nicht

erreicht werden kann. Dies gilt auch für die Grundlagenforschung mit hES-Zellen, die im Rahmen des FP7 erlaubt ist.

- Die Antragsteller haben nachgewiesen, dass die Projektziele mit keiner alternativen Methode erreicht werden können. Auch wenn sich die Gruppe der Bedeutung des Tierschutzes bewusst ist, hat sie Bedenken dahingehend, dass die Achtung der Menschenwürde nicht gewährleistet wäre, wenn hES-Zellen in Toxizitätstests für industrielle oder andere kommerziell hergestellte nicht arzneimittelrelevante chemische Produkte wie etwa Kosmetika, oder als Ersatz von Tierversuchen verwendet werden. Dieser Frage ist daher besondere Beachtung zu schenken (siehe Nummer 2 von Absatz IV.3).

- Die Antragsteller haben eine umfassende wissenschaftliche Begründung vorgelegt, wenn in ihrem Projekt Toxizitätstests für Arzneimittel vorgesehen sind; aus dieser Begründung sollte klar hervorgehen, welche Art zusätzlicher Erkenntnisse bei Verwendung von hES-Zellen im Vergleich zu etablierten Tests erwartet wird.

Das mit der wissenschaftlichen Bewertung beauftragte Gremium sollte sicherstellen, dass die Forscher, die an FP7-Projekten mit hES-Zellen arbeiten, national und international kooperieren, um die Verwendung von hES-Zellen im Rahmen FP7-finanzierter Projekte zu minimieren. Bei dieser Forschung geht es mehr darum, Komplementarität und Synergieeffekte anzustreben als Wettbewerb zu fördern.

IV.2.2 Ethische Kriterien für Forschungsprojekte im Rahmen des FP6

Einige wenige Bedingungen wurden bereits im Rahmen des FP6 festgelegt, um sicherzustellen, dass ethischen Anforderungen entsprochen wird, und diese Bedingungen können für das FP7 übernommen werden:

1. Antragsteller müssen ausdrücklich nachweisen, dass bei dem betreffenden Projekt die Regulierungskriterien eingehalten werden, und sie müssen die einschlägigen Rechts- und/oder Verwaltungsvorschriften des Landes/der Länder angeben, in dem/denen die Forschung durchgeführt wird (Artikel 6 Absatz 3 des FP7)[140]. Für weitere Informationen siehe Anhang 1.

2. Antragsteller müssen angeben, dass die im betreffenden Projekt verwendeten hES-Zellen nichtimplantierten IVF-Embryonen entnommen wurden (siehe den nachfolgenden Absatz über die Rechte der Spenderinnen).

3. Antragsteller müssen Angaben über den Schutz der personenbezogenen Daten und der Privatsphäre der Spenderinnen von Embryonen für die Gewinnung von Stammzelllinien machen.

4. Antragsteller müssen Angaben über die Umstände der Embryonenspende machen (z. B. keine finanziellen Anreize, Zahl der gewonnen Eizellen usw.). Um die Nicht-Kommerzialisierbarkeit des menschlichen Körpers und den Schutz der freiwilligen Spende gemäß Artikel 12 der Richtlinie 2004/23/EG zu gewährleisten, sollte nach Auffassung der EGE die Spende menschlicher Embryonen nicht durch finanzielle Anreize gefördert werden und sollten die Spenderinnen nur eine Entschädigung zum Ausgleich der in Verbindung mit der Spende entstandenen Ausgaben erhalten.

Zusätzlich empfiehlt die EGE, das mit der ethischen Prüfung beauftragte Gremium solle sicherstellen, dass die Antragsteller Angaben zu den nachstehend aufgeführten Punkten machen.

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140 Artikel 6 Absatz 3, http://cordis.europa.eu/fp7/ethics-ict_en.html.

IV.2.3 ZUSÄTZLICHE KRITERIEN FÜR DAS FP7

IV.2.3.1 Verwendung von Alternativen zu hES-Zellen

Falls in Zukunft Alternativen zu hES-Zellen gefunden werden, die das gleiche Potenzial aufweisen wie die aus Embryonen gewonnenen Stammzellen, sollten die Folgen dieser Entwicklungen für die wissenschaftlichen und ethischen Aspekte der auf hES-Zellen basierenden Forschungsprojekte so bald wie möglich Berücksichtigung finden.

IV.2.3.2 Rechte der Spendenden

Die Spende von Humanembryonen zur Gewinnung von hES-Zellen für Forschungszwecke wirft ein moralisches Dilemma auf. Dies ergibt sich aus der Tatsache, dass Humanembryonen keine „neutralen Objekte“ sind. Im Rahmen der informierten Einwilligung sollte dieses moralische Dilemma ausdrücklich angesprochen werden und die Entscheidung den Spendenden überlassen bleiben.

Den Schutzrechten der Spendenden muss besondere Aufmerksamkeit gelten, was konkret bedeutet, dass diejenigen Länder, die die Beschaffung von hES-Zellen erlauben, Angaben über das vom Antragsteller angewandte Verfahren zur Beschaffung vorlegen müssen. Die Informationen müssen Aussagen darüber enthalten, dass die entsprechenden Maßnahmen den in der Europäischen Union geltenden grundlegenden ethischen Prinzipien und Menschenrechten, den zum Zeitpunkt der Spende im Land, in dem die Spende erfolgt, geltenden einzelstaatlichen Rechtsvorschriften und anderen einschlägigen EU-Regelungen entsprechen[141]. Die Antragsteller müssen Angaben der Institutionen vorlegen, in denen die Stammzelllinien gewonnen wurden, aus denen hervorgeht, dass bei der Gewinnung der hES-Zellen folgende Kriterien eingehalten wurden:

[141] Siehe Richtlinie 2004/23/EG.

- Die Spendenden wurden in keiner Phase unter Druck gesetzt[142].
- Die Gesundheit der Spenderin wurde nicht durch ovarielle Überstimulation gefährdet.
- Soweit neue hES-Zelllinien betroffen sind, erfolgte die informierte Einwilligung zur Spende eines ursprünglich für die Reproduktion vorgesehenen Embryos zu Forschungszwecken in Kenntnis der Art der geplanten Forschung[143] und ihrer (auch kommerziellen) Implikationen sowie in Übereinstimmung mit den zum Zeitpunkt der Spende in dem Land, in dem die Spende durchgeführt wurde, geltenden Bedingungen.
- Die Spendenden wurden informiert, dass sie bis zur Phase der Gewinnung von Stammzellen ihre Einwilligung zurückziehen können.[144]
- Unfruchtbarkeitsbehandlung und Forschung wurden in angemessener Weise voneinander getrennt.
- Für die Spende von Embryonen zu Forschungszwecken wurden gemäß Artikel 12 der Richtlinie 2004/23/EG in keiner Phase finanzielle Anreize

142 Siehe: die Leitlinien der Internationalen Gesellschaft für Stammzellforschung ISSCR (http://www.isscr.org/guidelines/, S. 9: Gewinnung von ‚Material': Spende von Embryonen und Gameten, die während einer klinischen Behandlung erzeugt wurden. Außer wenn im Rahmen des SCRO-Prozesses (SCRO = zuständiges Ethikgremium) ausdrücklich erlaubt, darf keine Erstattung der direkten Ausgaben und keine finanzielle Vergütung irgendwelcher Art für die Spende von Embryonen oder Gameten gewährt werden, die im Laufe einer klinischen Behandlung erzeugt wurden und die über den klinischen Bedarf hinausgehen oder deren Qualität als für die klinische Verwendung nicht ausreichend angesehen wird. Forscher dürfen nicht verlangen, dass Mitglieder des für die Unfruchtbarkeitsbehandlung zuständigen Teams mehr Embryonen erzeugen oder mehr Oozyten gewinnen, als für eine optimale Chance auf Reproduktionserfolg erforderlich. Personen, die beschließen, ‚gelagertes Material' für Forschungszwecke zu spenden, sollten die Lagerkosten, die vor der Spendenentscheidung entstanden sind, nicht erstattet werden. Die Erstattung direkter Kosten, die den Spendern als Folge des Einwilligungsprozesses entstanden sind, kann im Laufe des SCRO-Prozesses festgelegt werden).

143 Leitlinien der ISSCR, 11.3-11.3a (http://www.isscr.org/guidelines/).

144 Bei der informierten Einwilligung ist die Tatsache zu berücksichtigen, dass das ‚Material' für die Gewinnung von Zellen für Forschungszwecke verwendet wird: „Die Einwilligung zur Spende von ‚Material' für Forschungszwecke sollte zum Zeitpunkt der geplanten Übergabe des Materials an das Forscherteam eingeholt werden. Nur nach einer strengen Prüfung im Rahmen eines SCRO-Mechanismus oder durch ein SCRO-Gremium kann die Verwendung von Material erlaubt werden, für das zwar eine frühere Einwilligung vorliegt, aber die Einholung einer neuen Einwilligung prohibitiv schwierig wäre." (Leitlinien der ISSCR, http://www.isscr.org/guidelines/).

geboten[145]. Allerdings halten einige Mitglieder der EGE eine Reduzierung der IVF-Kosten für akzeptabel.

Kann irgendeines dieser Kriterien wegen früherer Umstände, unter denen Zelllinien gewonnen wurden, nicht erfüllt werden, muss der Antragsteller die Gründe erläutern. Das für die ethische Prüfung zuständige Gremium hat bei jedem Einzelfall zu entscheiden, wie in der Angelegenheit vorzugehen ist. Für neue hES-Zelllinien werden die obigen Kriterien nachdrücklich empfohlen (siehe Absatz IV.2.4).

Forscher müssen alle die Spendenden betreffenden Daten in anonymisierter Form vorlegen. Das Verfahren zur Kodierung der Daten ist zu erläutern und entsprechend den einschlägigen Bestimmungen zu dokumentieren[146,147].

IV.2.4 Die Notwendigkeit, die öffentliche Steuerung und den Dialog zwischen Wissenschaft und Gesellschaft kontinuierlich zu fördern

Abgesehen von der Einwilligung der Spendenden und der Wahrung ihrer Rechte sind geeignete Maßnahmen vorzusehen, um die öffentliche Steuerung und den Dialog zwischen Wissenschaft und Gesellschaft über die Ziele, Errungenschaften und Fehlschläge dieser Forschung zu fördern. Es sollten angemessene Mittel für den Zugriff der Öffentlichkeit auf relevante und verständliche Informationen über die hES-Zellforschung im Rahmen des FP7 bereitgestellt werden, damit diese Ziele kontinuierlich verfolgt und erreicht werden können.
Wie der Ministerrat erklärt hat, unterstützt die Kommission die Einrichtung eines Europäischen Registers für humane embryonale Stammzelllinien. Mit diesem Register soll die *Kontrolle* der vorhandenen hES-Zellen in Europa ermöglicht

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145 Artikel 12 der Richtlinie 2004/23/EG: „Die Mitgliedstaaten streben danach, freiwillige und unentgeltliche Spenden von Geweben und Zellen sicherzustellen."

146 Richtlinie über den Schutz personenbezogener Daten (95/46/EG).

147 Bioethik-Übereinkommen und Zusatzprotokolle des Europarats, Übereinkommen des Europarats zum Schutz des Menschen bei der automatischen Verarbeitung personenbezogener Daten (Nr. 108).

werden, und es soll dazu beitragen, dass *ihre Verwendung* durch *Vermeidung unnötiger Generierung* neuer hES-Zelllinien *maximiert* wird.
In absehbarer Zeit werden die Antragsteller aufgefordert, für das Register einschlägige Daten über hES-Zellen vorzulegen. Sie werden dann entsprechend wissenschaftlichen und ethischen Standards gespeichert, die von den dafür eigens neu eingesetzten Wissenschafts- und Ethikbeiräten festgelegt werden.

Hinsichtlich der Verwendung der im Register eingetragenen hES-Zelllinien empfiehlt die EGE Folgendes:

- Sobald das Register eingerichtet ist, sollte nach der erforderlichen Übergangszeit die Verwendung der eingetragenen hES-Zelllinien den unter IV.2.3 angegebenen Kriterien entsprechen. Die Kommission sollte die Maßnahmen entwickeln und Mittel bereitstellen, die notwendig sind, damit diese Anforderung erfüllt werden kann, und aktiv für ihre Aufrechterhaltung sorgen.
- Die Antragsteller sollten die im EU-Register eingetragenen hES-Zellen verwenden. Wenn andere hES-Zelllinien für FP7-Projekte verwendet werden sollen, muss dies mit wissenschaftlichen und ethischen Gründen begründet werden.
- Auf der Website des Registers sollten Informationen über die eingetragenen hES-Zellen und über die positiven und negativen Ergebnisse der mit/an den zur Verfügung gestellten hES-Zelllinien durchgeführten Forschungen veröffentlicht werden. Nachdrücklich empfohlen wird auch, dass nach Abschluss eines Projekts zusätzlich zu den wissenschaftlichen, insbesondere gesundheitsbezogenen Daten benutzerfreundliche, allen EU-Bürgern frei zugängliche Informationen über die Forschung an hES-Zellen veröffentlicht werden. Das Portal sollte möglichst auch interaktive Elemente umfassen.

Forscher, die in diesem Bereich arbeiten, haben zum einen die Verantwortung, die Öffentlichkeit über ihre Arbeit zu informieren, zum anderen sollen sie sich an den gesellschaftlichen, politischen und ethischen Diskussionen beteiligen. Bei

den offenen Fragen, etwa wie unterschiedliche Rechte gegeneinander abzuwägen sind und wie die Rangfolge widersprüchlicher Interessen festzulegen ist, sollten Forscher am öffentlichen Diskurs teilnehmen und den demokratischen Entscheidungsprozess über gemeinsame gesellschaftliche Ziele respektieren. Die Antragsteller sollten Zeit, Geld und Energie investieren, um den Dialog zwischen Wissenschaft und Gesellschaft im Bereich der Forschung an humanen embryonalen Stammzellen voranzutreiben. Antragsteller, die im Rahmen des FP7 Projekte für Forschungen an hES-Zellen einreichen, werden deshalb mit Nachdruck ermutigt, den *Dialog zwischen Natur- und Geisteswissenschaften*, also die soziale, kulturell/religiöse, philosophische und ethische Reflexion über die Forschung an hES-Zellen, in ihren Projekten zu berücksichtigen und zu diesem Zweck mit geisteswissenschaftlichen Disziplinen zusammenzuarbeiten.

IV.3 Notwendigkeit weiterer Forschung und einer kontinuierlichen öffentlichen Debatte

Da die ethischen Auseinandersetzungen über hES-Zellen weder wissenschaftlich noch politisch gelöst worden sind, empfiehlt die EGE, im Rahmen des FP7 finanzielle Mittel bereitzustellen, um weitere multidisziplinäre, internationale Forschungskooperationen zu den ethischen Implikationen der embryonalen Stammzellforschung zu fördern sowie eine fundierte öffentliche Debatte darüber anzustoßen.

Die EGE betrachtet folgende Themen für diese Forschung und den öffentlichen Diskurs als von besonderem und unmittelbarem Interesse:

- die potentiell konfligierenden Ziele von wirtschaftlicher Wettbewerbsfähigkeit und Vereinbarkeit mit ethischen Standards;
- die Verwendung des menschlichen Körpers für die moderne Medizin einschließlich der Vermarktung von Produkten und Verfahren, die aus der Verwendung humaner embryonaler Stammzelllinien resultieren;

- die Anthropologie, die der Forschung an humanen embryonalen Stammzellen zugrunde liegt, insbesondere unter Berücksichtigung der mit der Stammzellenforschung verbundenen Chimären- und Hybridforschung;
- die Verbesserung der klinischen und therapeutischen Betreuung von Patienten, die unter den am häufigsten auftretenden Krankheiten leiden, mit denen sich die therapeutische und/oder auf bestimmte Krankheiten bezogene hES-Zellforschung befasst, hinsichtlich ihrer Bedürfnisse;
- die langfristige Strategie im Hinblick auf die Anzahl der für erfolgreiche Therapien erforderlichen Stammzelllinien und ihres Gewinnungsprozesses;
- der Zusammenhang zwischen hES-Zellforschung und Fragen der regenerativen Medizin und der gesundheitsbezogenen Gerechtigkeit einschließlich des Aspekts der globalen Gerechtigkeit;
- die Beziehungen zwischen Natur- und Geisteswissenschaften sowie zwischen Wissenschaft und Gesellschaft im Zusammenhang mit der Entwicklung neuer Technologien;
- die laufenden Bemühungen um wissenschaftliche Alternativen zur Forschung an hES-Zellen und deren anthropologische und ethische Interpretation.

Die EGE bekräftigt, dass für zahlreiche Fragen noch weitere Klärung, interdisziplinäre Forschung, gründliche ethische Bewertung und, falls künftig als notwendig erachtet, auch angemessene rechtliche Schritte erforderlich sind. Momentan erfordern nach Ansicht der EGE folgende Fragen besondere Beachtung:

1. Die derzeitigen Bestimmungen für die Patentierung von aus hES-Zellen gewonnenem Material müssen angegangen werden. Angesichts der neuesten Entwicklungen in der Forschung und unter Berücksichtigung der laufenden Debatte über die Grenzen der Patentierung biologischen

Materials möchte sich die EGE mit dieser Frage zu einem späteren Zeitpunkt befassen[148].

2. Die durch eine sowohl die freiwillige Spende[149] als auch die kommerzielle Verwendung von Derivaten humaner Substanzen fördernde Politik verursachte Spannung muss behandelt werden.

Die EGE unterstreicht, dass ihrer Auffassung nach die Verwendung humaner Embryonen zur Erzeugung von Stammzellen so weit wie möglich reduziert werden sollte. Die EGE ruft die Europäische Union auf, geeignete Systeme zu entwickeln, um die Verwendung humaner Embryonen auf Fälle zu reduzieren, in denen es keine Alternative gibt.

IV.4 Prüfung der Empfehlungen und Kommunikation mit dem Beirat des Europäischen Registers für humane embryonale Stammzelllinien

Die EGE würde einen intensiven Austausch mit dem Beirat des Europäischen Registers für humane embryonale Stammzelllinien begrüßen, insbesondere mit dem Ethik-Beirat des Registers. Das Ziel wäre es, die ethischen Bedenken hinsichtlich der Beschaffung von Stammzellen und der Speicherung von Daten im Lichte der laufenden Fortschritte in diesem Bereich gemeinsam behandeln zu können.

Die konkrete Art und Weise dieser Zusammenarbeit sollte spezifiziert und etabliert werden, und sie sollte von der Kommission entsprechend unterstützt und finanziert werden.

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148 Die EGE hat eine Stellungnahme über „Ethische Aspekte der Patentierung von Erfindungen unter Nutzung humaner Stammzellen“ herausgegeben, http://www.ec.europa.eu/european_group_ethics/docs/avis16_en.pdf

149 Artikel 12 der Richtlinie 2004/23/EG: „Die Mitgliedstaaten streben danach, freiwillige und unentgeltliche Spenden von Geweben und Zellen sicherzustellen.“.

IV.4.1 Prüfungsbedarf

Die EGE schlägt vor, die beschlossenen ethischen Leitlinien im Lichte der wissenschaftlichen, rechtlichen und gesellschaftlichen Entwicklungen zu überprüfen.

Die Europäische Gruppe für Ethik in Naturwissenschaften
und neuen Technologien[150]

Der Vorsitzende: Göran Hermerén

Die Mitglieder:

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Hille Haker	Julian Kinderlerer	Krzysztof Marczewski
Paula Martinho Da Silva		Linda Nielsen
Pere Puigdomenech-Rosell		Günter Virt

[150] Translation from the English original — only the English text is authentic — available at: http://ec.europa.eu/european_group_ethics/activities/docs/opinion_22_final_follow_up_en.pdf

ANNEXES

ANNEX I

THE SIXTH FRAMEWORK PROGRAMME

The sixth framework programme covers Community activities in the field of research, technological development and demonstration (RTD) for the period 2002 to 2006

PROCEDURAL MODALITIES FOR RESEARCH ACTIVITIES INVOLVING BANKED OR ISOLATED HUMAN EMBRYONIC STEM CELLS IN CULTURE TO BE FUNDED UNDER COUNCIL DECISION 2002/834/EC

Introduction

Pursuant to the Council decision adopting a specific programme for research, technological development and demonstration, 'Integrating and strengthening the European research area' (2002–06) ([151]), and in particular Article 6(3), the Commission has adopted procedural modalities to clarify the procedure which the Commission will follow when evaluating, selecting and supporting research projects involving the use of banked or isolated human embryonic stem cells in culture.

Procedural modalities for research activities involving banked or isolated human embryonic stem cells in culture to be funded under Council Decision 2002/834/EC ([152])

When evaluating, and selecting proposals involving the use of banked or isolated human embryonic stem cells (hESCs) in culture and negotiating the related contracts, the Commission uses the following procedure:

1. Proposal: Proposers are requested to address, in the application form, the potential ethical aspects of the proposed research in terms of its objectives, methodology and the possible implications of the results. Pursuant to the decision on the work programme in the framework of the specific programme for research, technical development and demonstration on 'Integrating and strengthening the European research area' ([153]) (hereinafter the work programme), they should justify the research design, explain how ethical requirements will be fulfilled and indicate the relevant national legal and/or regulatory requirements of the country(ies) where the research takes place.

([151]) OJ L 294, 29.10.2002, p. 1.
([152]) C(2003) 2952 of 11.11.2003.
([153]) C(2002) 4789 of 9.12.2002.

2. Evaluation: Proposals are evaluated in accordance with the procedure set out in the 'Guidelines on proposal evaluation and selection procedures' established by Decision C(2003) 883 (hereinafter the guidelines) by a panel of independent experts, after those experts have individually examined the projects in the light of each block of evaluation criteria.

The experts also assess whether the use of banked or isolated hESCs in culture is necessary in order to achieve the scientific objectives set forth in the proposal. This point is documented in the consensus report provided for in the guidelines

3. Ethical review: The ethical review is conducted in accordance with the procedure set out in the guidelines and the common evaluation criteria for evaluating proposals set out in Annex B to the work programme.

In the course of that review, the ethical review panel examines whether the proposal complies with the rules relating to ethics set out in Decision No 1513/2002/EC ([154]) and Decision 2002/834/EC.

In addition, that panel assesses:

(a) whether the proposers have taken into account the legislation, regulations, ethical rules and/or codes of conduct in place in the country(ies) where the research using banked or isolated hESC in culture is to take place, including the procedures for obtaining informed consent;

(b) the source of the banked or isolated hESCs in culture;

(c) the measures taken to protect personal data, including genetic data, and privacy;

(d) the nature of financial inducements, if any.

When preparing the ethical review, the Commission may request that the proposers provide additional information on the way the ethical issues raised by the project will be handled.

4. National approvals and opinions of competent ethics committee: The Commission ascertains that the participants have received appropriate approval from the national authority and/or a favourable opinion from the competent ethics committee before the signature of the contract, or before the banked or isolated hESCs in culture are to be used in the project.

5. Negotiation: During the negotiation of the contract, account is taken of the results of the ethical review. The result of the ethical review is reflected in the

([154]) OJ L 231, 29.8.2002, p. 1.

technical annex of the contract. Where the approval of the national authority and/or a favourable opinion from a local ethical committee is/are not obtained before the start of the contract, the contract includes a special clause requiring that the relevant authorisation or opinion be obtained before the start of the corresponding research.

6. Selection: In accordance with Article 6(3) of Decision 2002/834/EC any proposal involving the use of human embryonic stem cells is submitted for an opinion to the Programme Committee established by Article 7(1) of Decision 2002/834/EC.

ANNEX II

Ethical review procedures in FP7

Ethical issues

Describe any ethical issues that may arise in their proposal. In particular, you should explain the benefit and burden of their experiments and the effects it may have on the research subject.

The following special issues should be taken into account.

Informed consent: When describing issues relating to informed consent, it will be necessary to illustrate an appropriate level of ethical sensitivity, and consider issues of insurance, incidental findings and the consequences of leaving the study.

Data protection issues: Avoid the unnecessary collection and use of personal data. Identify the source of the data, describing whether it is collected as part of the research or is previously collected data being used. Consider issues of informed consent for any data being used. Describe how the personal identity of the data is protected.

Use of animals: Where animals are used in research, the application of the 3Rs ('replace, reduce, refine') must be convincingly addressed. Numbers of animals should be specified. Describe what happens to the animals after the research experiments.
Human embryonic stem cells: Research proposals that will involve human embryonic stem cells (hESCs) will have to address all the following specific points:

- the necessity to use hESCs in order to achieve the scientific objectives set forth in the proposal;
- whether the applicants have taken into account the legislation, regulations, ethical rules and/or codes of conduct in place in the country(ies) where the research using hESCs is to take place, including the procedures for obtaining informed consent;
- the source of the hESCs;
- the measures taken to protect personal data, including genetic data, and privacy;
- the nature of financial inducements, if any.

Identify the countries where research will be undertaken and which ethical committees and regulatory organisations will need to be approached during the life of the project.

Include the ethical issues table below. If you indicate YES to any issue, please identify the pages in the proposal where this ethical issue is described. Answering 'YES' to some of these boxes does not automatically lead to an ethical review. It enables the independent experts to decide if an ethical review is required. If you are sure that none of the issues apply to your proposal, simply tick the YES box in the last row.

(No recommended length for section 4 — depends on the number of such issues involved.)

Notes: Only in exceptional cases will additional information be sought for clarification, which means that any ethical review will be performed solely on the basis of the information available in the proposal ([1]). Projects raising specific ethical issues such as research intervention on human beings, research on human embryos and human embryonic stem cells and non-human primates are automatically submitted for ethical review.

To ensure compliance with ethical principles, the Commission services will undertake ethics audit(s) of selected projects at its discretion. A website is being prepared aiming to provide clear, helpful information on ethical issues.

([1]) Such as clinical trials, and research involving invasive techniques on persons (e.g. taking of tissue samples, examinations of the brain).

ETHICAL ISSUES TABLE

	YES	PAGE
Informed consent		
• Does the proposal involve children?		
• Does the proposal involve patients or persons not able to give consent?		
• Does the proposal involve adult healthy volunteers?		
• Does the proposal involve human genetic material?		
• Does the proposal involve human biological samples?		
• Does the proposal involve human data collection?		
Research on human embryos/foetuses		
• Does the proposal involve human embryos?		
• Does the proposal involve human foetal tissue/cells?		
• Does the proposal involve human embryonic stem cells?		
Privacy		
• Does the proposal involve processing of genetic information or personal data (e.g. health, sexual lifestyle, ethnicity, political opinion, religious or philosophical conviction)?		
• Does the proposal involve tracking the location or observation of people?		
Research on animals		
• Does the proposal involve research on animals?		
• Are those animals transgenic small laboratory animals?		
• Are those animals transgenic farm animals?		
• Are those animals cloning farm animals?		
• Are those animals non-human primates?		
Research involving developing countries		
• Use of local resources (genetic, animal, plant, etc.)		
• Benefit to local community (capacity building, i.e. access to healthcare, education, etc.)		
Dual use		
• Research having potential military/terrorist application		
I CONFIRM THAT NONE OF THE ABOVE ISSUES APPLY TO MY PROPOSAL		

ANNEX III

LIST OF PROJECTS SUPPORTED WITHIN THE SIXTH FRAMEWORK PROGRAMME AND WITHIN THE HEALTH DIRECTORATE, INVOLVING HESCS

1. LYMPHANGIOGENOMICS: fundamental research to better understand the lymphatic vasculature with a view to developing therapies to control the growth of lymphatic vessels (e.g. cancer, inflammatory diseases, for tissue ischæmia, lymphœdema)/EUR 9 million, 13 partners, 8 different countries (FI, FR, SE, AT, IT, CH, DE, BE)

2. REPROTECT: model to study reproductive toxicity by a combination of *in vitro* and sensor technologies/EUR 9.1 million, 26 partners, 9 different countries (DE, NL, BE, IT, UK, FR, SE, BG, AT)

3. BETACELL THERAPY: treatment of diabetes: to generate insulin-producing beta cells/EUR 11.8 million, 29 partners, 7 different countries (BE, DK, IL, ES, SE, CH, UK)

4. EUROSTEMCELL: comparison of the properties of adult, foetal and embryonic stem cells for the development of therapies including medicines in different set of diseases/disorders (skin, musculoskeletal, neurodegenerative diseases)/EUR 11.9 million, 14 partners, 7 different countries (UK, SE, FR, IT, DE, CH, DK)

5. HEART REPAIR: underlying principles of cardiac muscle cell formation for stem cell replacement therapies for heart failure and cardiac repair. Comparison of the potential of bone marrow derived stem cells and embryonic stem cells/EUR 11.4 million, 27 partners, 8 different countries (NL, DE, UK, IT, FR, ES, CH, SE)

6. OSTEOCORD: comparison of the properties of embryonic stem cells and umbilical cord blood stem cells in view of new applications and better characterisation of umbilical cord blood stem cells/EUR 2.5 million, 9 partners, 5 different countries (UK, DK, DE, IL, PT)

7. THERCORD: development and preclinical testing of cord blood-derived cell therapy products, where comparative research on the potential of umbilical cord blood stem cells and embryonic stem cell is performed/EUR 1.8 million, 9 partners, 6 different countries (IT, UK, DE, NL, ES, IL)

8. VITROCELLOMICS: on reducing animal experimentation in preclinical predictive drug testing by human hepatic *in vitro* models derived from embryonic stem cells/EUR 2.9 million, 9 partners, 4 different countries (SE, DE, PT, IT)

9. ESTOOLS: better characterisation of 52 different existing human embryonic stem cell lines from all over the world to generate knowledge on the fundamental processes governing stem cell differentiation in view of biomedical discovery. This project will bring a major contribution to the various initiatives launched around the world on the issue of characterisation/EUR 12 million, 20 partners, 10 different countries (UK, CH, IL, FI, DE, IT, ES, CZ, SE, NL)

10. EUROHEAR: fundamental research on the development and function of the inner ear including genetics of hereditary hearing impairments/EUR 12.5 million, 26 partners, 12 different countries (FR, UK, IL, NL, DE, IT, ES, FI, SE, BE, HU, TN)

11. STEMS: preclinical evaluation of stem cell therapy in stroke/ EUR 2.4 million, 9 partners, 5 different countries (FR, SE, DK, DE, CZ)

12. STEMSTROKE: stem cell therapy for stroke. Outcome expected: first clinical protocol for application of stem cell therapy in stroke/EUR 2.5 million, 6 partners, 3 different countries (UK, SE, DE)

13. STEM-HD: using mutant hESC line (with the Huntington genetic defect) to understand Huntington's disease and to perform drug screening/ EUR 2.5 million, 8 partners, 5 different countries (FR, IL, IT, UK, BE)

14. CARCINOGENOMICS: *in vitro* testing to assess genotoxic and carcinogenomic properties of chemical compounds/EUR 10.4 million, 20 partners, 12 different countries (NL, ES, BE, SE, IE, DK, UK, DE, IT, AT, CH, FR)

15. CRYSTAL: cryobanking of stem cells for human therapeutic applications/EUR 2.4 million, 8 partners, 6 different countries (DE, NL, AT, CH, BE, FR)

16. SIROCCO: fundamental research on regulatory RNAs/EUR 11.8 million, 18 partners, 10 different countries (UK, HU, FR, CH, NL, DE, IT, DK, ES, IL)

17. INVITROHEART: *in vitro* testing for cardiotoxicity and drug development/EUR 2.7 million, 9 partners, 4 different countries (SE, DE, DK, BE)

18. NEUROCREEN: screening of neuro-therapeutic molecules/ EUR 2.6 million, 9 partners, 4 different countries (UK, IT, DE, HU)

ANNEX IV

EU MEMBER STATES' REGULATORY FRAMEWORK

FOR HESC RESEARCH

Information provided by EU-27 national ethics councils, updated May 2007

Regulatory frame applying to AUSTRIA

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	The hESC research (Untersuchung/Behandlung rather in the sense of medical examination and treatment) is limited to the field of reproductive medicine. It is therefore covered in the legislation applying to reproductive medicine (Fortplanzungsmedizingesetz §9.(1); http://www.ris.bka.gv.at/bundesrecht/)
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	No
3	**Is hESC research allowed and in what terms and conditions?**
	hESC research in the above mentioned sense is limited to the field of reproductive medicine; other research is not allowed;
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**

5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	No
6	**Is the source of hESC used in research traceable and well documented?**

7	**What are the formal ethical and legal requirements for hESC research approval?**

8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**

9	**Is financial inducement allowed? If so, in what terms?**

10	**Are ad hoc data protection provisions be defined for hESC research?**

11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**

12	**How is patenting of hESC lines regulated?**

Regulatory frame applying to BELGIUM

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	There are several regulations applying on hESC research: 1: Law on organ transplantation 13/06/1986 (applicable on tissues, Published 14/02/1987) 2: Royal Decree on tissue banks of 15/04/1988 (Published 29/04/1988) 3: Embryo Law of 11/05/2003 (Published BS 28/05/2003)
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	Yes: An embryo is a cell or a group of coherent cells that have the capacity to develop into a human being (see Embryo law, Art. 2, cited:) **Loi du 11 mai 2003. Article 2.** Pour l'application de la présente loi, on entend par: 1) «embryon»: la cellule ou l'ensemble organique de cellules susceptibles, en se développant, de donner un être humain
3	**Is hESC research allowed and in what terms and conditions?**
	Yes: At universities or in cooperation with universities, after consent of the local ethical commission and after positive advice (within 2 months) of the Federal Commission for medical and scientific research on embryos *in vitro* **Loi du 11 mai 2003. Article 7, paragraphe 1.** Toute recherche sur des embryons *in vitro* doit être soumise au préalable au comité local d'éthique de l'établissement universitaire concerné et à la Commission fédérale pour la recherche médicale et scientifique sur les embryons in vitro visée à l'article 9. La demande d'avis est introduite conjointement par le chercheur et le chef du laboratoire de procréation médicalement assistée ou de génétique humaine agréé de l'établissement universitaire concerné ou de l'établissement qui a conclu une convention avec un établissement universitaire. La demande d'avis comporte une description détaillée de l'objectif, de la méthodologie et de la durée de la recherche. Elle indique spécialement si la recherche a lieu sur des embryons surnuméraires ou des embryons créés à des fins de recherche. **Paragraphe 2.** L'avis du comité local d'éthique est rendu dans un délai de deux mois suivant la demande d'avis. Si l'avis du comité local d'éthique est négatif, le projet de recherche est abandonné. Le chercheur et le chef de laboratoire portent à la connaissance de la Commission fédérale pour la recherche médicale et scientifique sur les embryons in vitro, visée à l'article 9, leur demande d'avis ainsi que l'avis positif du comité local d'éthique. Si, dans un délai de deux mois après cette transmission, la Commission n'a pas émis d'avis négatif à la majorité de ses membres, le projet de recherche est autorisé et peut être entamé. Toutes les décisions de la Commission fédérale pour la recherche médicale et scientifique sur les embryons in vitro sont motivées.

4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	The Federal Commission for medical and scientific research on embryos *in vitro*
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	Yes, but ONLY if the objective of this research project can't be achieved by using supernumerary embryos and this still under the conditions complying with the embryo law. **Loi du 11 mai 2003. Article 4, paragraphe 1.** La constitution d'embryons in vitro à des fins de recherche est interdite, sauf si l'objectif de la recherche ne peut être atteint par la recherche sur les embryons surnuméraires et pour autant que les conditions de la présente loi soient remplies.
6	**Is the source of hESC used in research traceable and well documented?**
	Actually there is no mandatory traceability. In a short period of time, traceability will be assured by a new law dealing with storage and distribution of cells and tissues
7	**What are the formal ethical and legal requirements for hESC research approval?**
	Cf question 4
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	Yes. Donors give their free and written consent for the use of their gametes for research purposes after being properly informed **Loi du 11 mai 2003. Article 8.** Les personnes concernées donnent leur consentement préalable libre, éclairé et consigné par écrit à l'utilisation des gamètes ou des embryons in vitro à des fins de recherche.
9	**Is financial inducement allowed? If so, in what terms?**
	Yes, for research No, for donation
10	**Are ad hoc data protection provisions be defined for hESC research?**
	Anonymity is guaranteed for the donors of gametes and/or embryos (Medical confidentiality and the law on rights of patients)

11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	The Federal Commission for medical and scientific research on embryos *in vitro* can control the laboratories where research on embryos *in vitro* is ongoing. (Art 10) Every year, the researchers have to procure to the Federal Commission a progress report on their research on embryos (Art 11) **Loi du 11 mai 2003. Article 10, paragraphe 2.** […] Elle peut à tout moment visiter les laboratoires dans lesquels se déroulent les recherches pour lesquelles elle est compétente, afin de faire toutes les constatations utiles à l'exercice de ses missions. **Loi du 11 mai 2003. Article 11.** Chaque chercheur communique à la Commission, au plus tard le 30 avril de chaque année, un rapport décrivant l'état d'avancement de la recherche. Ce rapport mentionne: 1) l'objectif, la méthodologie et la durée de la recherche; 2) les modalités du respect des dispositions de la présente loi; 3) la demande et les avis rendus par le comité local d'éthique et la Commission conformément à l'article 7; 4) l'état d'avancement de la recherche.
12	**How is patenting of hESC lines regulated?**
	In Belgium, patenting of hESC is possible. **Loi du 28 mars 1984** sur les brevets d'invention (*Moniteur belge* du 9.3.1985) modifiée par la loi du 9 mars 1995 (*Moniteur belge* du 7.6.1995), la loi du 28 janvier 1997 (*Moniteur belge* du 4.4.1997), la loi du 26 juin 2000 (*Moniteur belge* du 29.7.2000) et la loi du 12 juin 2001 (*Moniteur belge* du 7.7.2001). Les droits (exploitation exclusive, intervention contre les contrefaçons) d'un titulaire d'un brevet d'invention sont limités dans le temps (maximum 20 ans) et limités au territoire belge. Pour bénéficier des mêmes droits dans d'autres pays, vous devez obtenir ces brevets d'invention dans ces pays aussi, par voie nationale, européenne ou internationale.

Regulatory frame applying to BULGARIA

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	Healthcare Act /Chapter IV, Div. III – 'Artificial Reproduction'/ In force from 01.01.2005 ./ SG N.70/2004., adopt. N.46/2005., N.76/2005., N.85/2005., N.88/ 2005., N.94/2005., N.103/2005., N.18/2006., N.30/2006., N.34/2006., N.59/2006., N.71/2006., N.75/ 2006., N.81/2006., N.95/2006., N.102/ 2006./. Transplantation organ, tissue & cells Act In force from 01.01.2004 ./ SG N.83/2003., adopt..N88/2005.,N.71/2006./.; Ordinance N 37/28.09.2004 for the conditions and order for taking an embryos organs, tissue and somatic, amniotic and placenta cells for transplantation aims. */ SG N.88/8.10.2004г.,adopt. SG N..89/ 12.10. 2004г./* / the object of Ordinance regulation is only the 'embryonic organs, tissue and cells' after abortion — Art.1 and Art.4/ **Remark:** To my opinion, the term 'human embryonic stem sells' have an wide and narrow understanding.. The 'wide' meaning comprises zygotes and life embryo as a source of stem cells. The narrow meaning comprises only life embryo as a source of stem cells. Therefore it will be useful to specify what meaning should be the right contents of the term 'hESC'. Web address: www.bultransplant.bg ; www.mh.government.bg/iat.php;
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	"Embryo' is not defined explicitly. There is a definition of 'embryonic organs, tissue and cells' — Transplantation organ, tissue & cells Act, Additional provisions, &1, point.9.
3	**Is hESC research allowed and in what terms and conditions?**
	No.

4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	see.point.3
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	No.
6	**Is the source of hESC used in research traceable and well documented?**
	See point.5
7	**What are the formal ethical and legal requirements for hESC research approval?**
	Healthcare Act — Art. 134 — 'Gametes and zygotes, which are not used for the purpose of human creation, can be given to the research, academic and medicine entities in the country and outside, for the medicine, scientific and teaching purposes, after written inform consent of the donor, but concerning zygotes – the consent should be taken by the two donors, according to the Ordinance, issued by the Minister of healthcare.
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	See.point.7.
9	**Is financial inducement allowed? If so, in what terms?**
	No
10	**Are ad hoc data protection provisions be defined for hESC research?**
	No
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	N/A
12	**How is patenting of hESC lines regulated?**
	N/A

Regulatory frame applying to CYPRUS

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	There is no specific law for hESC in the Republic of Cyprus. However, the Republic of Cyprus has ratified the 'Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Oviedo Convention' with the Ratification Law N.31(III)/2001. Article 18 of the Convention and the Ratification Law, in relation to the research on embryos *in vitro*, states that: 1. Where the law allows research on embryos *in vitro*, it shall ensure adequate protection of the embryo. 2. The creation of human embryos for research purposes is prohibited.
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	No, it does not provide a definition of 'embryo'.
3	**Is hESC research allowed and in what terms and conditions?**
	There is no law in the Republic of Cyprus allowing research on embryos in-vitro under any circumstances. The hESC research is not allowed in the Republic of Cyprus.
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	The creation of embryos for research purposes is absolutely prohibited in the Republic of Cyprus in accordance with Article 18 (2) of the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, Oviedo Convention'. The Article 18 (2) of the Oviedo Convention states that 'The creation of human embryos for research purposes is prohibited'. The Convention has been ratified by the Law 31 (III)/2001.
6	**Is the source of hESC used in research traceable and well documented?**
	The extraction of embryonic stem cells from embryos in-vitro is prohibited in accordance with Article 18 of the Oviedo Convention and Article 7 of its Ratification Law (No. 31 (III)/2001).
7	**What are the formal ethical and legal requirements for hESC research approval?**
	Having in mind all the above mentioned and in accordance with the information given in paragraphs 3, 5 and 6 above, research on embryonic stem cells is neither legally nor ethically approved by the legislation currently in force, in the Republic of Cyprus.

8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	Not applicable
9	**Is financial inducement allowed? If so, in what terms?**
	Not applicable
10	**Are ad hoc data protection provisions be defined for hESC research?**
	Not applicable
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	Not applicable
12	**How is patenting of hESC lines regulated?**
	Not applicable

Regulatory frame applying to CZECH REPUBLIC

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	Act on Human Embryonic Stem Cell Research (law no. 227/2006 Coll.) passed by the Czech Parliament on 26th of April 2006, in force since June 1 2006. Text available here: http://www.mvcr.cz/sbirka/2006/sb075-06.pdf (also attached)
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	"Human embryo is a totopotent cell or a grouping of cells which are capable develop into human individuum' (law no. 227/2006 Coll., § 2)
3	**Is hESC research allowed and in what terms and conditions?**
	Yes. Conditions: State licensing (given by the Ministry of Education, after approval of the Bioethics Committee of the Research and Development Council of the Czech Government and after positive appraisal of the Research and Development Council) Preconditions: a) Scientific criteria scientifically justifiable – new medical knowledge with applications for humans; scientific necessity (usage of *in vitro* models, animal cells or animals does not provide the necessary knowledge); no alternative research scientific quality of the research team b) Ethical criteria Research project is ethically acceptable (informed consent, donation…)
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	Ministry of Education
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	No. The Czech Republic ratified Oviedo Convention (2001).
6	**Is the source of hESC used in research traceable and well documented?**
	Yes.
7	**What are the formal ethical and legal requirements for hESC research approval?**
	Source of embryos: 'surplus embryos' from IVF (only from licensed IVF centres), no longer than 7 day of development, export of embryos prohibited Informed consent Donation (reimbursement of expenses possible)
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	Yes. Detailed description in § 9 Act no. 227/2006 Coll.

9	**Is financial inducement allowed? If so, in what terms?**
	No. Only reimbursement of real expenses (to the IVF Centre) Reimbursement of real expenses related to the embryo donation (to the donor, payment and other compensation explicitly prohibited)
10	**Are ad hoc data protection provisions be defined for hESC research?**
	Yes. The Act on Personal Data Protection applies.
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	No
12	**How is patenting of hESC lines regulated?**
	No regulation.

Regulatory frame applying to DENMARK

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	Yes www.retsinfo.dk
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	No
3	**Is hESC research allowed and in what terms and conditions?**
	Research is allowed on human fertilized eggs meant for fertilisation of a woman under the conditions mentioned in Lovbekendtgørelse af lov om kunstig befrugtning i forbindelse med lægelig behandling, diagnostic og forskning LBK nr. 923 af 04//09/2006 chapter 7, paragraph 25-27 Kapitel 7 *Forbud mod forskning og forsøg* **§ 25.** Biomedicinske forsøg på befrugtede menneskelige æg samt på kønsceller, der agtes anvendt til befrugtning, må kun foretages i følgende tilfælde: 1) Hvis de har til formål at forbedre in vitro-befrugtning eller lignende teknikker med henblik på at fremkalde en graviditet. 2) Hvis de har til formål at forbedre teknikker til genetisk undersøgelse af et befrugtet æg med henblik på at fastslå, om der foreligger en alvorlig arvelig sygdom eller en væsentlig kromosomabnormitet (præimplantationsdiagnostik). 3) Hvis forsøgene ved anvendelse af befrugtede æg og stamceller herfra har til formål at opnå ny viden, som vil kunne forbedre mulighederne for behandling af sygdomme hos mennesker. *Stk. 2.* Udtagning og befrugtning af æg med henblik på at gennemføre andre forsøg end de i stk. 1 nævnte er ikke tilladt. **§ 26.** Befrugtede æg må kun holdes i live uden for en kvindes livmoder i 14 dage, fra befrugtningen er sket. Den tid, hvori de befrugtede menneskelige æg har været nedfrosset, medregnes ikke. **§ 27.** Befrugtede menneskelige æg, der har været gjort til genstand for biomedicinsk forskning, herunder almindelig kvalitetssikrende forskning ved ægopsætning, må kun opsættes i en kvindes livmoder, hvis det befrugtede æg er genetisk uændret (umodificeret) og den forudgående forskning efter en faglig vurdering i øvrigt ikke må antages at have beskadiget ægget i dets videre udvikling. *Stk. 2.* Forskningsprojekter efter § 25 skal godkendes i det videnskabsetiske komitesystem, der forud for eventuel godkendelse vurderer, om projekterne har det tilladte formål. **§ 28.** Følgende forsøg må ikke foretages: 1) Forsøg, der har til formål at muliggøre fremstilling af arvemæssigt identiske menneskelige individer. 2) Forsøg, der har til formål at muliggøre fremstilling af menneskelige individer ved sammensmeltning af genetisk forskellige fosteranlæg eller dele af fosteranlæg, før

	de sætter sig fast i livmoderen. 3) Forsøg, der har til formål at muliggøre fremstilling af levende menneskelige individer, som er hybrider, med en arvemasse, hvori indgår bestanddele fra andre arter. 4) Forsøg, der har til formål at muliggøre udvikling af et menneskeligt individ i artsfremmed livmoder.
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	The Danish Committees on Biomedical Researchhttp://www.cvk.im.dk/cvk/site.aspx?p=23
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	No
6	**Is the source of hESC used in research traceable and well documented?**
	Yes see provisions of Act on a Biomedical Research Ethics Committee System and the Processing of Biomedical Research Projects http://www.cvk.im.dk/cvk/site.aspx?p=150
7	**What are the formal ethical and legal requirements for hESC research approval?**
	See the Danish act on a Biomedical Research Ethics Committees System and the Processing of Biomedical Research Projects
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?** See the Danish act on a Biomedical Research Ethics Committees System and the Processing of Biomedical Research Projects
9	**Is financial inducement allowed? If so, in what terms?** **No**
10	**Are ad hoc data protection provisions be defined for hESC research?**
	Yes, see the Danish act on a Biomedical Research Ethics Committees System and the Processing of Biomedical Research Projects
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	Yes, see the Danish act on a Biomedical Research Ethics Committees System and the Processing of Biomedical Research Projects
12	**How is patenting of hESC lines regulated?**
	See Danish Law on Patents Paragraph 1A **§ 1 a.** Det menneskelige legeme på alle de forskellige stadier af dets opståen og udvikling og den blotte opdagelse af en del af det, herunder en sekvens eller delsekvens af et gen, kan ikke udgøre patenterbare opfindelser. *Stk. 2.* Uanset stk. 1 kan en del af det menneskelige legeme, der er isoleret herfra eller på anden måde fremstillet ved en teknisk fremgangsmåde, herunder en sekvens

	eller delsekvens af et gen, udgøre en patenterbar opfindelse, selv om en sådan del i sin opbygning er identisk med opbygningen i en naturligt forekommende del. Unofficial translation of the paragraph: “The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including a sequence or partial sequence of a gene, cannot constitute patentable inventions. *Subs. 2.* Notwithstanding subsection 1 hereof, an element isolated from the human body or otherwise produced by means of a technical process, including a sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.’ In the Danish regulations, Article 5, subs. 3 of the EU directive on patenting of human stem cells has been set out in the statutory instrument on patents.

Regulatory frame applying to ESTONIA

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	We have no special regulations of hESC research in Estonia and if needed we take into consideration relevant international documents..
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	–
3	**Is hESC research allowed and in what terms and conditions?**
	The Estonian Council on Bioethics is on the position, that in principle hESC research is acceptable in Estonia.
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	In needed cases the approval will be given by research ethics committees
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	The creation of embryos for research purposes is not allowed by the Estonian law of artificial procreation and embryo protection
6	**Is the source of hESC used in research traceable and well documented?**
	We have no special system for this yet
7	**What are the formal ethical and legal requirements for hESC research approval?**
	They are not fixed yet in Estonia
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	No regulations on it
9	**Is financial inducement allowed? If so, in what terms?**
	It is not regulated
10	**Are ad hoc data protection provisions be defined for hESC research?**
	No
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	No
12	**How is patenting of hESC lines regulated?**
	It is not regulated in Estonia

Regulatory frame applying to FINLAND

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	Medical Research Act, 488/1999. www.finlex.fi Translation: see: http://www.finlex.fi/en/laki/kaannokset/1999/en19990488.pdf
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	Yes. 'embryo' means a living group of cells resulting from fertilisation not implanted in a woman's body
3	**Is hESC research allowed and in what terms and conditions?**
	It is allowed. Embryos shall be used for research only with a written informed consent from the donors of the gametes. Consent can be withdrawn in any time (Act on medical Research, section 12) Only supernumerary embryos shall be used for research. The production of embryos exclusively for the purpose of research is forbidden. (Act on Medical Research, section 13). When hESC lines have been produced, the law does not make any further provisions on the use of these cells. The production of hESC needs the favourable opinion of an ethics committee of a hospital district, and the research on embryos can be done only in the institutions that have got an authorisation from the National Authority of Medicolegal Affairs (TEO) The use of embryos for research is allowed only for 14 days after fertilisation
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	Ethics committees of hospital districts evaluate the research projects, although the research of cell lines is not specifically regulated in the Medical Research Act. The Ministry of Social Affairs and Health has established a working group on Biobanks that is working on the issue of biobanks including ethics evaluation of establishment of biobank and ethics evaluation of the research projects.
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	Medical Research Act states that The production of embryos exclusively for the purpose of research shall be forbidden. However, the Act also determines the embryo as 'the living group of cells resulting from fertilisation'. This can be interpreted so that cells produced by the somatic cell nuclear transfer are not considered as embryos.
6	**Is the source of hESC used in research traceable and well documented?**
	Anonymisation and coding as far as possible should be used in each project
7	**What are the formal ethical and legal requirements for hESC research approval?**
	We have formal ethical and legal requirements for embryo research stated in the Medical Research Act. Further requirements concerning hESC lines have not been established. The working group is working on this issue concerning research on biological sample collections.
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	Ethics committees approve information and consent forms before they can be used in the informed consent procedure
9	**Is financial inducement allowed? If so, in what terms?**

	No; donation must be voluntary. Only compensation of the expenses and harms (healthy donors) is allowed according to Decree 1390/2006. There are not such expenses or harm related to hESC while embryos that could be donated for research are surplus embryos.
10	**Are ad hoc data protection provisions be defined for hESC research?**
	No, regular data protection provisions similar to medical research in general are applied to hESC research.
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	Not necessarily, only when they are published.
12	**How is patenting of hESC lines regulated?**
	We have Act on Patenting (550/1967, amendment 650/2000) that has implemented the EU Directive of biopatenting. It states that (Section 1a and b) human body or its part, whole or partial sequence of a gene or similar finding cannot be patented, but isolated or otherwise produced item, sequence or partial sequence of a single gene form an invention that can be patented, if provisions otherwise are fulfilled, although the structure of this item would be similar to natural item. However, section 1 b states that (3) uses of human embryos for industrial or commercial purposes cannot be patented See translation at: http://www.finlex.fi/en/laki/kaannokset/1967/en19670550.pdf

Regulatory frame applying to FRANCE

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	www.agence-biomedecine.fr http://www.agence-biomedecine.fr/fr/experts/pegh-recherche.aspx Demande d'autorisation de protocoles d'étude et de recherche, d'importation ou de conservation **Le décret n° 2006-121 du 6 février 2006** relatif aux recherches sur l'embryon et les cellules embryonnaires**,** précisant les conditions d'application de la loi du 6 août 2004, prévoit que le directeur général de l'Agence de la biomédecine notifie à l'établissement ou à l'organisme demandeur sa décision d'autorisation ou de refus d'autorisation dans les 4 mois suivant la clôture de la période au cours de laquelle a été déposé le dossier complet. www.legifrance.gouv.fr
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	The embryo in this law is : Obtained during an ART protocol and is no more subject to a parental (pregnancy) project Up to implantation stage
3	**Is hESC research allowed and in what terms and conditions?**
	Subjected to the obtention of a licence for -research project -importation -conservation/storage
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	The agency of biomedicine www.agence-biomedecine.fr
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	No
6	**Is the source of hESC used in research traceable and well documented?**
	It is a condition to fulfil in order to obtain a licence to be able to keep a local registry and tracks of cell culture; The agence de la biomedicine has also to keep a national hESC registry
7	**What are the formal ethical and legal requirements for hESC research approval?**
	The research project should benefit to the progress towards a potential therapeutic use of to progress on human embryo development and medicine. The team involved has to provide proof if feasibility of this research, and to documents the composition of the team, the lab rooms scheme, the traceability of the Es cell lines **See décret n°2006-121 du 6 février 2006**

8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	Yes The law does ask to document the origin of the cell line and to provide the consent form model : both parents should have signed for the use of the embryo for research,
9	**Is financial inducement allowed? If so, in what terms?**
	No The authority in charge of giving licences does not provide funds for research on those topics.
10	**Are ad hoc data protection provisions be defined for hESC research?**
	Yes
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	Yes, they are asked for every licence given, a yearly progress report is asked, and a final report.
12	**How is patenting of hESC lines regulated?**
	Not authorized

Regulatory frame applying to GERMANY

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	1) Act for the Protection of Embryos (Embryo Protection Act), Gesetz zum Schutz von Embryonen (Embryonenschutzgesetz – EschG) *http://bundesrecht.juris.de/eschg/BJNR027460990.html,* 2) Act ensuring protection of embryos in connection with the importation and utilisation of human embryonic stem cells (Stem Cell Act), Gesetz zur Sicherstellung des Embryonenschutzes im Zusammenhang mit Einfuhr und Verwendung menschlicher embryonaler Stammzellen (Stammzellgesetz – StZG) *http://bundesrecht.juris.de/stzg/index.html*
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	For the purpose of the Embryo Protection Act, an embryo means a fertilised human egg capable of developing from the time of fusion of the nuclei, and further each totipotent cell removed from an embryo that is capable of dividing and developing into an individual human being if the necessary conditions prevail. (ESchG §8 (1)). For the Stem Cell Act embryo means any human totipotent cell which has the potential to divide and to develop into a human being if the necessary conditions prevail (StZG §3 (4)).
3	**Is hESC research allowed and in what terms and conditions?**
	According to the Embryo Protection Act the production of hESCs is forbidden. The Stem Cell Act ensures the protection of embryos in connection with the importation and utilisation of human embryonic stem cells. hESC research is only permitted using cell lines created before 1 January 2002 in the country of origin in accordance with relevant national legislation there and kept in culture or subsequently stored using cryopreservation methods. The embryos from which they were derived must have been produced by medically-assisted *in vitro* fertilisation in order to induce pregnancy and definitely no longer used for this purpose and no evidence that this was due to reasons inherent in the embryos themselves. No compensation or other benefit in money's worth may have been granted or promised for the donation of embryos for the purpose of stem cell derivation.
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	The Central Ethics Committee for Stem Cell Research at the Robert Koch Institute (RKI) is in charge of the approval of applications to import hESCs. The RKI is the federal institution responsible for disease control and prevention and the central federal reference institution for applied and response-orientated research as well as for the Public Health Sector.
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	The creation of embryos for research purposes is forbidden in Germany.
6	**Is the source of hESC used in research traceable and well documented?**
	Information on the requested NIH embryonic stem cell lines for the project is registered by the competent agency, the Robert Koch Institute, in a publicly accessible registry on their website

	(*http://www.rki.de/cln_049/nn_207250/DE/Content/Gesund/Stammzellen/Register/reg-20060725-IBMT.html*).
7	**What are the formal ethical and legal requirements for hESC research approval?**
	The hESC research has to serve eminent research aims to generate scientific knowledge in basic research or to increase medical knowledge for the development of diagnostic, preventive or therapeutic methods to be applied to humans and according to the state-of-the-art of science and technology. Firstly the questions to be studied in the research project concerned must been clarified as far as possible through *in vitro* models using animal cells or through animal experiments and secondly the scientific knowledge to be obtained from the research project concerned cannot be expected to be gained by using cells other than embryonic stem cells. Any importation and any utilisation of embryonic stem cells has to be subject to approval by the stem cell ethics committee for stem cell research at the Robert Koch Institute. Applications for approval must be submitted in writing. In the documents accompanying the application, the applicant shall provide the following information in particular: 1. Name and official address of the person responsible for the research project concerned, 2. a description of the research project including scientific reasons showing that the research project meets the requirements described,3. a documentation concerning the embryonic stem cells to be imported or used showing that the requirements have been complied with equivalent evidence. The embryonic stem cells to be imported or used must be identical with those registered in a scientifically recognized, publicly accessible registry maintained by government agencies or agencies authorized by the government.
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	n/a
9	**Is financial inducement allowed? If so, in what terms?**
	For the stem cell lines to be imported no compensation or other benefit in money's worth may have been granted for the donation of embryos for the purpose of stem cell derivation.
10	**Are ad hoc data protection provisions be defined for hESC research?**
	Ad hoc data protection provisions are not mentioned in the Stem Cell Act.
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	An obligation for publication is not mentioned in the Stem Cell Act.
12	**How is patenting of hESC lines regulated?**
	The Biotechnology Patenting Directive (98/44/EC) negotiated by the European Parliament and the European Council on 6 July 1998 provides a uniform procedure for the patenting of biotechnological inventions in all EU Member States. In December 2004 Germany implemented the Biotechnology Patenting Directive and enacted the law 28 February 2005 (Gesetz zur Umsetzung der Richtlinie über den rechtlichen Schutz biotechnologischer Erfindungen (BioPatG), Act Implementing the Directive on the Legal Protection of Biotechnological Inventions in Germany). In December 2006 the German Federal Patent Court partially reversed their 1999 decision on Professor Oliver Brüstle's patent, saying that anything made from human tissue cannot be patented.

Regulatory frame applying to GREECE

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	- Article 1459 c of the Civil Code (Act n. 3089/2002) - Article 11 par. 1 (e) of the Act n. 3305/2005 ("Application of M.A.R.) - - http://www.bioethics.gr/media/pdf/biolaw/human/law_3089_en.pdf?PHPSESSID=c730cd74d93449cca3750bb51c50a228
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	Yes, (article 3 of the Act n. 3305/2005, for the terms 'zygote' and 'fertilized egg' '**Zygote'**: an ovum from its fertilisation until the merger of the two haploid nuclei **"Fertilized egg'**: an ovum after the penetration or initiation of sperm
3	**Is hESC research allowed and in what terms and conditions?**
	Yes. Under certain conditions: - Only on surplus embryos (up to the 14th day after fertilisation) - Prior written informed consent of the donors - Prior approval of the protocol (from the National Authority on M.A.R.) - Prior research on laboratory animals (if possible) - The research team should possess the necessary equipment and know-how - It is not allowed to implant the embryos that have been used
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	The National Authority on Medically Assisted Reproduction (an independent regulatory agent, nominated by the Parliament)
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	No
6	**Is the source of hESC used in research traceable and well documented?**
	Yes

7	**What are the formal ethical and legal requirements for hESC research approval?**
	See above (3)
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	See above (3)
9	**Is financial inducement allowed? If so, in what terms?**
	No (only compensation for justifiable expenses, medical services or undue damages is allowed)
10	**Are ad hoc data protection provisions be defined for hESC research?**
	No. The law on sensitive data protection (Act n. 2472/1997) is applicable, binding the research team. The Data Protection Authority is responsible for relevant controls.
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	No
12	**How is patenting of hESC lines regulated?**
	By the presidential decree n. 321/2001 (on the Directive 98/44/EC)

Regulatory frame applying to HUNGARY

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	The human embryonic stem cells research and use is regulated by law and five decrees. The 1997. CLIV. law about the health regulated the general conditions of the use and research of the human embryonic stem cells (180- 182 paragraphs.(The 2006 CXV. law about the health reform. The 21/1998. (VI.3.) MH decree contains the minimum conditions of the use of human embryonic stem cells (15/B attachment). The 22/1998. (VI.3.) MH decree contains the detailed regulation of the transplantation of different organs and tissues. The 31/1998. (VI.24.) MH decree regulated the ethical approval system of biomedical research. The 22/2002. (V.9.) MH decree regulated the ethical approval system of biomedical research. The 1/2007. (I.24.) MH decree regulated the ethical approval system of biomedical research.
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	embryo is defined as every living human embryo following the completion of fertilisation until 12th week of pregnancy. The foetus is the human being developing within the uterus after the 12th week of pregnancy.
3	**Is hESC research allowed and in what terms and conditions?**
	Research on embryos can be carried out on the basis of an authorisation of the Hungarian Reproduction Commission. Embryos can only be used for research purposes and experiments can only be made on embryos for the research purposes that the Health Care Act fixes with regard to medical research.
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	Hungarian Reproduction Commission
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	Embryos cannot be created for research purposes, only embryos created in medically assisted human procreation procedures (MAP) can be used for research and experiments, either on the basis of the decision of those entitled to decide, or in case of damage of the embryo. If an embryo was donated for a MAP procedure, but not used within 10 years following the donation, the embryo can be used for research purposes.
6	**Is the source of hESC used in research traceable and well documented?**
	The source of the hESC is traceable and well documented in every cases.
7	**What are the formal ethical and legal requirements for hESC research approval?**
	The formal ethical and legal requirements for hESC research approval are regulated in the 1/2007. (I.24.) MH decree. The decree accepted the EC recommendations.
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**

	There is no embryo donation for research.
9	**Is financial inducement allowed? If so, in what terms?**
	Financial inducement is not allowed.
10	**Are ad hoc data protection provisions be defined for hESC research?**
	Data protection is according to EU regulations.
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?** It is not.
12	**How is patenting of hESC lines regulated?**
	Patenting of hESC lines is not regulated.

Regulatory frame applying to IRELAND

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	Ireland currently has no specific legislation dealing with embryonic stem cell research and furthermore does not have a legislative basis for the practice of IVF and therefore has no legislation pertaining to use of embryos (supernumerary or otherwise) for research. The Medical Council's Guide to Ethical Conduct and Behaviour 6th edition 2004 states that in relation to IVF 'that any fertilised ovum must be used for normal implantation and must not be deliberately destroyed". They also state 'the creation of new life forms for experimental purposes or the deliberate and intentional destruction of in-vitro human life already formed is professional misconduct". It should be noted that the Medical Council only regulate physicians and therefore scientists are not bound by the guide, e.g. it would appear that there is currently no legal impediment on importation or use of embryonic stem cells lines by scientists. Following a referendum some years ago, The Irish Constitution was amended and Article 40.3.3 of the Constitution acknowledges the right to life of the unborn. However, no legislation followed this amendment e.g. to articulate what is defined as 'unborn', would this include supernumerary embryos in storage etc. This Constitutional Amendment has been interpreted by some to mean that embryonic stem cell research would be prohibited by our constitution. A recent high court judgment (Nov 2006) found that three frozen embryos resulting from IVF are not 'unborn" as defined under the Constitution. This judgment has been appealed to the Supreme Court.
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	N/A
3	**Is hESC research allowed and in what terms and conditions?**
	There is no legislation prohibiting ESC research in Ireland. It would appear from the Recent High Court Judgement that ESC research is also not prohibited under the Irish Constitution. Further clarification will be forthcoming following a decision from the Supreme Court
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	Situation has not arisen to legal uncertainty in this area but it would come under research ethics committee review.
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	No legislation/Regulation in this area.
6	**Is the source of hESC used in research traceable and well documented?**
	N/A
7	**What are the formal ethical and legal requirements for hESC research approval?**
	N/A

8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	N/A
9	**Is financial inducement allowed? If so, in what terms?**
	N/A
10	**Are ad hoc data protection provisions be defined for hESC research?**
	N/A
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	N/A
12	**How is patenting of hESC lines regulated?**
	N/A

Regulatory frame applying to ITALY

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	Italian discipline applying to human embryonic stem cells research consists in Law 19 February 2004, n. 40 (Law 40/2004), on medically assisted reproduction ("Norme in materia di procreazione medicalmente assistita'), published in Gazzetta Ufficiale n. 45, February 24, 2004.
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	The law does not provide a definition of 'embryo'. However, it aims to protect the rights of all the subjects involved in the medical assisted reproduction, included the conceived subject (see Art. 1, No 1, which specifies the scopes of the law).
3	**Is hESC research allowed and in what terms and conditions?**
	Art. 13, n. 1, of Law 40/2004 that has regards to the experimentation on human embryos ("Sperimentazione sugli embroni umani') expressly prohibits any experimentation on human embryos.
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	See answer No 3.
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	Art. 13, n. 3 *a)*, of Law 40/2004 expressly prohibits the creation of human embryos for research purposes or for experimentation.
6	**Is the source of hESC used in research traceable and well documented?**
	See answers No 3 and 5.
7	**What are the formal ethical and legal requirements for hESC research approval?**
	See answers No 3 and 5.
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	The donation of embryos for research is not allowed by Italian law.
9	**Is financial inducement allowed? If so, in what terms?**
	See answer No 8.
10	**Are ad hoc data protection provisions be defined for hESC research?**
	See answers No 3 and 5.

11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	See answers No 3 and 5.
12	**How is patenting of hESC lines regulated?**
	See answers No 3, 5, 8.

Regulatory frame applying to LATVIA

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	It is not regulated by legislation in Latvia
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	No
3	**Is hESC research allowed and in what terms and conditions?**
	It is not prohibited by legislation
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	Central Medical Ethics Committee
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	It is prohibited by Latvian Reproductive Medicine Act; "The creation of human embryos for research purposes is prohibited. The human biological material or embryo shall not, as such, give rise to financial gain. '
6	**Is the source of hESC used in research traceable and well documented?**
	We have no experience
7	**What are the formal ethical and legal requirements for hESC research approval?**
	It is not regulated by legislation
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	It is not regulated by legislation
9	**Is financial inducement allowed? If so, in what terms?**
	It is not regulated by legislation
10	**Are ad hoc data protection provisions be defined for hESC research?**
	It is regulated for any research **Law on Data Protection** Personal data processing is permitted only if not prescribed otherwise by law, and at least one of the following conditions exist: 1) the data subject has given his or her consent;

	2) the personal data processing results from contractual obligations of the data subject; 3) the data processing is necessary to a system controller for the performance of his or her lawful obligations; 4) the data processing is necessary to protect vitally important interests of the data subject, including life and health; 5) the data processing is necessary in order to ensure that the public interest is complied with, or to fulfil functions of public authority for whose performance the personal data have been transferred to a system controller or transmitted to a third person; and 6) the data processing is necessary in order to, complying with the fundamental human rights and freedoms of the data subject, exercise lawful interests of the system controller or of such third person as the personal data have been disclosed to. The processing of sensitive personal data is prohibited, except in cases where: 1) the data subject has given his or her written consent for the processing of his or her sensitive personal data; 2) special processing of personal data, without requesting the consent of the data subject, is provided for by regulatory enactments which regulate
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?** **Yes, but it is not regulated by legislation.**
12	**How is patenting of hESC lines regulated?**
	It is not regulated

Regulatory frame applying to LITHUANIA

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	As for today (16 March, 2007) embryonic stem cell research has not been specifically addressed in the law. However, Lithuanian Law on Ethics of Biomedical Research allows only observational studies on human embryo, all other research activities on human embryo are prohibited (Article 3, Paragraph 2; http://www3.lrs.lt/pls/inter2/dokpaieska.showdoc_l?p_id=148740)
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	As for today (16 March, 2007) the regulation does not provide a definition of embryo
3	**Is hESC research allowed and in what terms and conditions?**
	hESC would not be allowed in the country because Lithuanian Law on Ethics of Biomedical Research allows only observational studies on human embryo, all other research activities on human embryo are prohibited.
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	NA
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	The creation of human embryos is prohibited by the law (Law on Ethics of Biomedical Research, Article 3, Paragraph 2)
6	**Is the source of hESC used in research traceable and well documented?**
	NA
7	**What are the formal ethical and legal requirements for hESC research approval?**
	NA
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	NA
9	**Is financial inducement allowed? If so, in what terms?**
	NA
10	**Are ad hoc data protection provisions be defined for hESC research?**
	NA
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	NA
12	**How is patenting of hESC lines regulated?**
	NA

Regulatory frame applying to GRAND-DUCHÉ DE LUXEMBOURG

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	There is, at present, no legal or regulatory framework for human embryonic stem cells research in Luxembourg. However, a new law is under preparation: Projet de loi 5528/00 portant approbation: — de la convention pour la protection des droits de l'homme et de la dignité de l'être humain à l'égard des applications de la biologie et de la médecine: convention sur les droits de l'homme et la biomédecine, ouverte à la signature, à Oviedo, le 4 avril 1997; — du protocole additionnel à la convention pour la protection des droits de l'homme et de la dignité de l'être humain à l'égard des applications de la biologie et de la médecine, portant interdiction du clonage d'êtres humains, ouvert à la signature, à Paris, le 12 janvier 1998; — du protocole additionnel à la convention sur les droits de l'homme et la biomédecine relatif à la transplantation d'organes et de tissus d'origine humaine, ouvert à la signature, à Strasbourg, le 24janvier 2002; — du protocole additionnel à la convention sur les droits de l'homme et la biomédecine, relatif à la recherche biomédicale, ouvert à la signature, à Strasbourg, le 25 janvier 2005, et modifiant la loi du 25 novembre 1982 réglant le prélèvement de substances d'origine humaine.
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	No definition of 'embryo' is provided in the draft law.
3	**Is hESC research allowed and in what terms and conditions?**
	No human embryonic stem cells research is being done in Luxembourg at this time.
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	n/a
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	n/a The draft law mentioned above doesn't allow research on human embryos *in vitro* (article 6).
6	**Is the source of hESC used in research traceable and well documented?**
	n/a
7	**What are the formal ethical and legal requirements for hESC research approval?**
	n/a
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	n/a

9	**Is financial inducement allowed? If so, in what terms?**
	n/a
10	**Are ad hoc data protection provisions be defined for hESC research?**
	n/a
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	n/a
12	**How is patenting of hESC lines regulated?**
	n/a However, 'the use of human embryos for industrial and commercial purposes is not patentable.' («les utilisations d'embryons humains à des fins industrielles ou commerciales ne sont pas brevetables»), article 5, loi du 7 avril 2006 modifiant la loi modifiée du 20 juillet 1992 portant modification du régime des brevets d'invention.

Regulatory frame applying to MALTA

Currently there is no Embryonic Stem Cell or other embryonic regulation at all in Malta.

Regulatory frame applying to NETHERLANDS

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	The Dutch 'Act containing rules relating to the use of human gametes and embryos' (Embryos Act) came into force on September 1th 2002. A translation can be found at: http://www.minvws.nl/en/folders/ibe/2002/introduction-embryo-act.asp
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	Embryos Act, Section 1: In this Act the following words shall have the following meanings: (….) c. embryo: a cell or a complex of cells with the capacity to develop into a human being; (…) This definition is criticised as being too narrow (excluding non-viable embryos). Cf: -Health Council of the Netherlands: Embryonic stem cells without moral pain? (2005). Translated report: http://www.gr.nl/pdf.php?ID=1270&p=1 -Report of the recent evaluation of the Embryos Act (2006). Translated summary: http://www.zonmw.nl/fileadmin/cm/vraagsturing/documenten/Evaluatie_regelgeving/embryos_act_en_sum.pdf
3	**Is hESC research allowed and in what terms and conditions?**
	hESC research is allowed. There are no special conditions for hESC research using existing stem cell lines. hESC involving the use of human embryos is subjected to the general conditions for research using human embryos set in the Embryos Act (including the moratorium regarding the creation of embryos for other purposes than pregnancy; cf sub question 5).
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	Only hESC research involving the use of human embryos requires special approval. The Central Committee on Research Involving Human Subjects and Embryo Research (CCMO) is in charge of this. Website: www.ccmo.nl The head of the bureau of the national review committee (CCMO) is dr. Marcel Kenter; e-mail ccmo@ccmo.nl Tel +31 70 3406700.

5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	The Embryos Act prohibits the creation of embryos for purposes other than reproduction (section 24a). This also applies to 'therapeutic cloning' using human stem cells. However, the Act also contains the provision that this ban shall lapse on a date to be determined within five years after the coming into force of the Act (i.e. before September 2007), thus effectively turning the ban into a moratorium (section 33 sub 2). The Act already contains provisions for the handling of embryos created for purposes other than reproduction which would come into force after the lifting of the ban (sections 9 and 11). Section 11 limits the types of research for which embryos may then be created to 1) research which is reasonably likely to lead to new insights in the fields of infertility, 2) artificial reproduction techniques, 3) hereditary or congenital diseases or 4) transplant medicine. This complex construction was chosen in order to allow for making a reservation to Article 18 of the European Convention on Human Rights and Biomedicine (forbidding the creation of embryos for research purposes) when ratifying that Convention (as the Netherlands intends to do). The report of the recent evaluation of the Embryos Act (2006) has called for a swift end to the present moratorium on creating embryos for other purposes than pregnancy. Translated summary of report: http://www.zonmw.nl/fileadmin/cm/vraagsturing/documenten/Evaluatie_regelgeving/embryos_act_en_sum.pdf However, the new government coalition formed early 2007 (Labour & two Christian Democrat parties) has announced its intention to maintain the current ban (possibly in the form of extending the moratorium for some further years). No formal decision about this has as yet been taken.
6	**Is the source of hESC used in research traceable and well documented?**
	No special regulations
7	**What are the formal ethical and legal requirements for hESC research approval?**
	Cf questions 4 and 8
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	Yes. As specified in section 8.2 of the Embryos Act, embryos may be made available only by means of a written donation and without consideration, and only after the persons concerned (which may also include a gamete donor), have been informed by the person storing the embryos regarding the nature and the purpose thereof. Where a difference of opinion arises between the parties concerned, the embryos shall not be made available. Any of the persons concerned may revoke his/her decision at any time before the embryos have been used, without giving reasons. In the report of the recent evaluation of the Embryos Act (2006), it is pointed out that the Act does not provide sufficient guidance as to the required specificity of the information to be given about the nature of the research. Cf summary of report: http://www.zonmw.nl/fileadmin/cm/vraagsturing/documenten/Evaluatie_regelgeving/embryos_act_en_sum.pdf

9	**Is financial inducement allowed? If so, in what terms?**
	No, cf question 8: embryos may only be donated 'without consideration'. The same holds for the donation of gametes. In practice, a remuneration of expenses is accepted. The report of the recent evaluation of the Embryos Act (2006) contains the recommendation to further debate the desirability/acceptability of a larger recompensation for women donating oocytes for research. Cf summary of report: http://www.zonmw.nl/fileadmin/cm/vraagsturing/documenten/Evaluatie_regelgeving/embryos_act_en_sum.pdf
10	**Are ad hoc data protection provisions be defined for hESC research?**
	No special regulations
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	No special regulations
12	**How is patenting of hESC lines regulated?**
	No special regulations

Regulatory frame applying to POLAND

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	In Poland there is no research on embryonic stem cells. Polish legal rules do not include distinct regulations for human embryonic stem cells research. There is also no legal definition for embryo stage of life. The fundamental legal act in Poland is **the Constitution of the Republic of Poland** (http://www.sejm.gov.pl/prawo/konst/angielski/kon1.htm), which was passed by the National Assembly on April 2nd, 1997. In accordance with Art.38 of this Law the Republic of Poland shall ensure the legal protection of the life of every human being Regulations referring to legal protection and conduct rules in the pre-birth stage of human life are included in **the Act of January 7th, 1993 on Family Planning, Protection of Human Foetus and Admissible Conditions for an Abortion**. In accordance with Art.1 of this Law, the right to life is protected, including also the prenatal stage, in the scope stipulated by the Law. The Law also includes regulations concerning the conceived child that is from the moment of conception through the embryo and foetal stages until birth. According to Art.157a of **the Criminal Code** any person except for child's mother who commits any infringement to a conceived child, will be punished. The rule does not include a physician who undertakes medical action necessary to exclude danger-threatening mother's or child's health or life. What's more, under **the Act of December 5th, 1996 on Medical Profession's**, human embryos (conceived children) may not be used for therapeutic research (Art. 26 paragraph 1). Not directly refers to this matter the **ruling of the Constitutional Court of the Republic of Poland from the 28th May 1997**, which says: 'A democratic state governed by the rule of law holds man and his most precious weal as a supreme value. By this weal, we understand life which in a democratic state governed by the rule of law must enjoy constitutional protection in each stage of its development'.
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	As mentioned above, there is no legal definition for embryo stage of life.
3	**Is hESC research allowed and in what terms and conditions?**
	In Poland, human embryo research is prohibited.
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	NA
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	Is not allowed.
6	**Is the source of hESC used in research traceable and well documented?**
	NA
7	**What are the formal ethical and legal requirements for hESC research approval?**
	NA

8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	NA
9	**Is financial inducement allowed? If so, in what terms?**
	NA
10	**Are ad hoc data protection provisions be defined for hESC research?**
	NA
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
12	**How is patenting of hESC lines regulated?**
	NA

Regulatory frame applying to PORTUGAL

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	In Portugal, **Law n. 32/2006, of the 26th of July**, concerning Medically Assisted Reproduction, addresses hESC research. The text is available on http://www.dre.pt/pdfgratisa5/2006/07/14300.pdf (Portuguese version only)
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	The Portuguese regulation doesn't provide a definition of 'embryo'.
3	**Is hESC research allowed and in what terms and conditions?**
	The article n. 9 of the law forbids the deliberate production of human embryos specifically for research purposes. However, scientific hESC research can be allowed provided it is reasonable to expect that the investigation project will benefit mankind. Research must aim: Prevention, diagnosis or therapy on embryos; Perfection of Medically Assisted Reproduction techniques; Creation of stem cell banks for transplantation programs or other therapeutic purposes.
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	The law n. º 36/2006 created the National Council for Medically Assisted Reproduction, in charge of the approval of the investigation projects for hESC research.
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	As mentioned above, the deliberate production of human embryos specifically for research purposes is forbidden. According to Arts. 9, 24 and 25, IVF techniques must ensure only the necessary number of embryos for the success of the IVF process. Only embryos whit particularly severe genetic anomalies with no conditions to be preserved or implanted, embryos not derived by fertilisation of a human oocyte by human sperm, or those created to enhance the success rate of IVF who became supernumerary and no longer a part of a parental project, can be used for research purposes.
6	**Is the source of hESC used in research traceable and well documented?**
	According to Art. 16, personal genetic and health data regarding medically assisted reproduction techniques is regulated by **Law n.º 12/2005, of the 26th of January**, concerning genetic and health personal information. The text is available on http://www.dre.pt/pdfgratisa5/2005/01/018A00.pdf (Portuguese version only) Further regulation on data documentation, storage and access is being prepared.

7	**What are the formal ethical and legal requirements for hESC research approval?**
	The regulation of the conditions under which the investigation projects will be evaluated is being prepared. However, in Art. 9º the actual law still requires that scientific hESC research is made for prevention, diagnosis or therapy on embryos, for the perfection of Medically Assisted Reproduction techniques or for the creation of stem cell banks for transplantation programs or other therapeutic purposes. Additionally, research can be allowed provided it is reasonable to expect that the investigation project will benefit mankind.
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	According to the present law, the use of supernumerary embryos or of embryos with particularly severe genetic anomalies entails previous informed consent from donors. This consent must also be express, free and conscientious. It is expected that the regulation to further to the law establishes further requirements for consent.
9	**Is financial inducement allowed? If so, in what terms?**
	Art. 18 states that the purchase or sell of embryos or any other biological material obtained from the use of Medically Assisted Reproduction techniques is forbidden.
10	**Are ad hoc data protection provisions be defined for hESC research?**
	This regulation is being prepared.
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	At this time, there is no knowledge of research involving human embryos being made in Portugal. The regulatory framework under which the investigation projects will be made is being prepared.
12	**How is patenting of hESC lines regulated?**
	By the **Decree-Law n.º 36/2003, of the 5th of March**, Portugal transposed the Directive 98/44/CE of the European Parliament and the Council of the 6th of July, regarding the legal protection of biotechnological inventions. Art. 53º of this decree-law states that the use of human embryos for industrial or commercial purposes, as well as the human body, in his various stages of development or by the mere discovery of one of his elements, aren't patentable. The text is available on http://www.dre.pt/pdfgratisa5/2003/03/054A00.pdf (Portuguese version only)

Regulatory frame applying to ROMANIA

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	In Romania there is no specific regulation applying to hESC. In the field of research on hESC the following general regulation could be applied: 1. Law 206/2004 regarding good conduct in scientific research, technological development and innovation, www.cdep.ro 2. Law 17/2001 regarding the ratification of Oviedo Convention, www.cdep.ro 3. Law 95/2006 regarding the reform in health care system, www.cdep.ro 4. The Code of Deontology for Physicians of the Romanian College of Physicians, www.cmr.ro
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	No Romanian law provides a definition of ‘embryo’.
3	**Is hESC research allowed and in what terms and conditions?**
	There is no specific legal provision to forbid hESC research.
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	Ethics commissions organized according to law 206/2004 (art.12) must supervise the research projects in order to respect the protection of human being, including the protection of human embryos
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	No
6	**Is the source of hESC used in research traceable and well documented?**
	No
7	**What are the formal ethical and legal requirements for hESC research approval?**
	There are not specific formal ethical and legal requirements for hESC research approval
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	In such situations the general legislation mentioned in point 1 could be applied.
9	**Is financial inducement allowed? If so, in what terms?**
	The financial inducement is not allowed according to law 95/2006, title VI- organ and tissue donation must be purely altruistic

10	**Are ad hoc data protection provisions be defined for hESC research?**
	There are not specific provisions for ad hoc data protection in hESC research. There are general laws regarding personal data protection: 1. Law 667/2001, www.cdep.ro 2. Law 676/2001, www.cdep.ro
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	I do not have such information
12	**How is patenting of hESC lines regulated?**
	I do not have certain information regarding this issue. I do not think that in Romania there are specific provisions regarding this issue

Regulatory frame applying to: SLOVAK REPUBLIC

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	No specific regulations exist at present. There is an extensive governmental regulation in preparation, however, to deal with the 'donation, procurement, testing and distribution of organs, tissues and cells, and processing, conservation and storage of tissues and cells' (transposition of the requirements of the Dir. 2006/17/EC, ev. Dir. 2004/23/EC). It could tackle on some closely related issues, but probably not specifically on hESCs.
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	N.A. (non-applicable)
3	**Is hESC research allowed and in what terms and conditions?**
	hESC research is not specifically prohibited by a law, however, according to the position the Slovak Republic (SR) has taken so far on the issue, it probably would not be allowed to take place in the country (as destroying of a human embryo is necessary to obtain the hESCs lines for research). The 'non-therapeutic' research on human embryo and fetus, as well as human cloning are prohibited both by the SR's health law (law No. 576/2004 Coll. as later amended) and by SR's Penal Code (law No. 300/2005 Coll.) – making both a criminal offence.
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	N.A. (non-applicable)
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	NO, it is prohibited as a criminal act (see 3, above).
6	**Is the source of hESC used in research traceable and well documented?**
	N.A. (non-applicable)
7	**What are the formal ethical and legal requirements for hESC research approval?**
	N.A. (non-applicable)
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	N.A. (non-applicable)
9	**Is financial inducement allowed? If so, in what terms?**
	N.A. (non-applicable)
10	**Are ad hoc data protection provisions be defined for hESC research?**
	N.A. (non-applicable)
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	N.A. (non-applicable)
12	**How is patenting of hESC lines regulated?**
	N.A. (non-applicable)

Regulatory frame applying to SLOVENIA

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	Explicit legal regulation on hESC does not exist. However, the Law on treatment of infertility and biomedically assisted fertilisation (Zakon o zdravljenju neplodnosti in postopkih oploditve z biomedicinsko pomocjo, /ZZNPOB/ 3307, Uradni list Republike Slovenije 70/2000, 8. 8. 2000, UL ONLINE) contains provisions that apply to research on embryos from IVF procedures and may apply to procurement of hESC. Web address (Ministry of Health): http://www.mz.gov.si
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	Article 4: The embryo is created by fertilisation of the ovum. For the purposes of this Law, the early embryo is a zygote or an embryo that has developed outside the uterus for less than 14 days or until the appearance of the primitive streak.
3	**Is hESC research allowed and in what terms and conditions?**
	As said above, research on hESC is not specifically regulated. Slovenia is party to the Oviedo Convention and the protocol on prohibition of human cloning. Its Law on treatment of infertility and biomedically assisted fertilisation forbids the creation of human embryos for research, the production of cloned embryos and the use of *in vitro* fertilisation for any purpose other that birth of a child. Also prohibited is the use of parts of embryo for any purpose other than is explicitly allowed by law. However, the law allows research on surplus embryos from *in vitro* fertilisation procedures (and thus also procurement of hESC), if several conditions are fulfilled: *Article 38 (unofficial translation)* Scientific research on the gametes and early embryos (= *in vitro* embryos) is allowed exclusively for the purposes of (promoting knowledge on) protection and improvement of human health. It may be carried out on early embryos only if it cannot be done on animal embryos or otherwise with comparable efficiency. Early embryos may only be used for research after a written informed consent has been obtained for their parents who had undergone medically assisted reproduction. The research must be authorised by the National Commission for Assisted Reproduction and must be approved and supervised by the National Medical Ethics Committee (NMEC). Permission may be granted for embryos that, according to medical knowledge, are not suitable to be transferred into woman's body or for storage, or would have to be left to perish according to the Article 35 of the Law (end of the maximum storage period). In research on embryos, current medical knowledge, experience, established practices and principles of general medical ethics must be taken into account.

4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	The National Medical Ethics Committee, after authorisation has been obtained from the National Commission for Assisted Reproduction.
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	No.
6	**Is the source of hESC used in research traceable and well documented?**
	Traceability and full documentation of biological materials of human origin is legally required.
7	**What are the formal ethical and legal requirements for hESC research approval?**
	Full compliance with the law (see answer to Q 3).
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	The regulatory framework (the Law on treatment of infertility and biomedically assisted fertilisation does not provide for any specific rules, except that written informed consent must be obtained from both partners.
9	**Is financial inducement allowed? If so, in what terms?**
	All financial inducement is strictly forbidden.
10	**Are ad hoc data protection provisions be defined for hESC research?**
	This Q is slightly difficult to understand (syntactic error?). Until now, the National Medical Ethics Committee has received only one application for approval of a study on hESC derived from embryos and has approved harvesting hESC from nonviable embryos from *in vitro* fertilisation procedures. The usual rules of confidentiality and data protection apply.
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	Yes. This is among the requirements of the NMEC.
12	**How is patenting of hESC lines regulated?**
	Specific regulation does not exist.

Regulatory frame applying to SPAIN

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	Law 14/2006 about Human Assisted Reproduction Techniques (HARTAct): http://www.boe.es/boe/dias/2006/05/27/pdfs/A19947-19956.pdf http://www.boe.es/g/es/bases_datos/doc.php?coleccion=iberlex&id=2006/09292&txtlen=1000 Act of 2007, on Biomedical Research (BMRAct) (It has not been published in the State Official Journal) Other regulations: Research with spare frozen embryos after assisted reproduction techniques: http://www.isciii.es/htdocs/terapia/legislacion/Terapia_RD_2132_2004.pdf Organization of the National Bank of Stem Cell Lines: http://www.boe.es/boe/dias/2006/02/18/pdfs/A06637-06641.pdf
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	Yes, it does. In the Spanish legislation there are two definitions, on the human pre-embryo and on the human embryo: a) Pre-embryo: the *in vitro* embryo as constituted by a group of cells derived of the continuous division of the fertilised oocyte until 14 days later (art. 1.2 of HARTAct and art. 3, s, BMRAct) b) Embryo: A step of embryonic development, which includes the time in what the fertilised oocyte is located in the uterus of a woman until the time of the beginning of the step of the formation of organs, it is to say, 56 days after fertilisation occurs, regardless the time during such development could be stopped (art. 3, l, BMRAct).
3	**Is hESC research allowed and in what terms and conditions?**
	Yes, this type of research is allowed but only under case by case scrutiny. The research project has to fulfil, by the research group, the ethical guarantees requested. A) From surplus pre-embryos HARTAct): Article 15. Using pre-embryos for research purposes. a) Informed consent of the couple or of the single woman. *b)* The pre-embryo shall not be developed *in vitro* more than 14 days, regardless the time it could be cryo-preserved *c)* Research shall be performed in authorised centres *d)* Research will be done on the basis of a research project authorised by the competent authority, previous the perceptive and favourable Commission (see down). B) From cloned pre-embryos (BMRAct): Article 34 Guarantees and requisites for research 1. Research or experimentation with surplus oocytes and pre-embryos from the application of assisted

	reproduction techniques, or from their biological structures, with the aim to obtain, develop and use embryonic stem cell lines or with other purposes not associated with the development and application of assisted reproduction techniques, shall be undertaken in accordance with the conditions established in Law 14/2006, of 26 May, and comply with the following requisites: a) That the research abides by the applicable ethical principles and legal regulations, especially in that provided in this Law and its development of rules and guidelines in law, and that it follows the principles of relevance, feasibility and suitability, specifically of the main researcher, of the research team and of the facilities of the centre that shall undertake the research. b) That it is based on a research project authorised by the relevant State or autonomous authorities, after a favourable report by the Commission for establishing guarantees in the donation and use of human cells and tissues, in the event that the project deals with matters provided in article 35. 2. The authorisation of the research projects shall be conditioned on the project including at least the following elements: a) The authorisation by the management of the centre that shall undertake the research, as well as the favourable report of the corresponding Research Ethics Committee. b) The notification of the common relations and interests, of any nature or the absence of such, between the team and the centre that have undertaken each of the processes of assisted reproduction that have generated pre-embryos or have intervened in the obtaining of oocytes. c) The written commitment to supply to the corresponding public authority the data that will permit to identify and know the storage of the cell lines that could be obtained as a consequence of the development of the research. d) The commitment of the free conveyance of line cells that could be obtained in the development of the research, for its use by other researchers. e) When using oocytes or pre-embryos, the indication and justification of its size, origin and the document of the informed consent signed by the donors or progenitors respectively.
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	A) For researches related with the application and implementation of human assisted reproductive techniques: the National Commission on Assisted Human Reproduction (art. 15.1, d, HARTAct) 'Comision de Garantías para la Donación y Utilización de Células y Tejidos Humanos' B) For researches related with the gain, implementation and use of hESC lines: the Commission for Establishing Guarantees in the donation and use of human cells and tissues (art. 35 BMRAct) In both cases the previous review by a local Research Ethics Committee is also needed.
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	The new law explicitly prohibits the creation of pre-embryos and embryos for the exclusive use of research, although it permits the use of any other technique, including nuclear transfer, aimed to obtaining human embryonic stem cells for research or therapy (BMRAct): Article 33 Obtaining of embryonic cells 1. The creation of human pre-embryos and embryos solely for experimentation purposes shall be prohibited. 2. The use of any technique for obtaining human stem cells for therapeutic or research purposes shall be permitted, when it doesn't entail the creation of a pre-embryo or embryo solely for this purpose, in the terms provided in this Law, including the activation of oocytes through nuclear transfer. A perceptive and favourable previous opinion by the Commission for Establishing

	Guarantees in the donation and use of human cells and tissues is needed, as well as the authorisation of the Autonomous Community Authority.
6	**Is the source of hESC used in research traceable and well documented?**
	Yes, it is (art. 8 BMRAct).
7	**What are the formal ethical and legal requirements for hESC research approval?**
	1-Informed consents from the parents of all embryos used; 2-approval by the ethical committee of the institution or the autonomous community and 3-approval by the ad hoc 'Comision de Garantías para la Donación y Utilización de Células y Tejidos Humanos' (See on this previous answer to question Nr 4).
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	Yes. If embryos are going to be used for a research project, parents must sign an informed consent specific for that project. The informed consent form includes the name of the research project, a short summary of the main research objectives, the name of the IP and a disclosure of any financial interest (Art. 15.1, a of HARTAct).
9	**Is financial inducement allowed? If so, in what terms?**
	No, it is not. (See art. 7 BMRAct and art. 15.1, a of HARTAct).
10	**Are ad hoc data protection provisions be defined for hESC research?**
	Yes, they are. (arts. 5 and 53 of BMRAct): Article 5 Protection of personal data and Confidentiality (general provisions on the use of human biological material). Article 53 Genetic analysis on pre-embryos, embryos and foetuses. The results of genetic analysis on per-embryonic, embryonic and foetal material shall be submitted to the principles of data protection and confidentiality established in this Act.
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	Yes, they are, although it is not required to be provided in form of publications.
12	**How is patenting of hESC lines regulated?**
	In the same conditions as it is at the Directive 98/44/EC, on the legal protection of biological inventions. See the Act 11/1986 of 26 March, on Patent, as modified by Act 10/2002 of 29 April, transposing that Directive.
	Information provided by Prof. C.M. Romeo-Casabona (Universidad de Deusto, Bilbao) and Dr. Javier Arias (Institut de salud Carlos III, Madrid)

Regulatory frame applying to SWEDEN

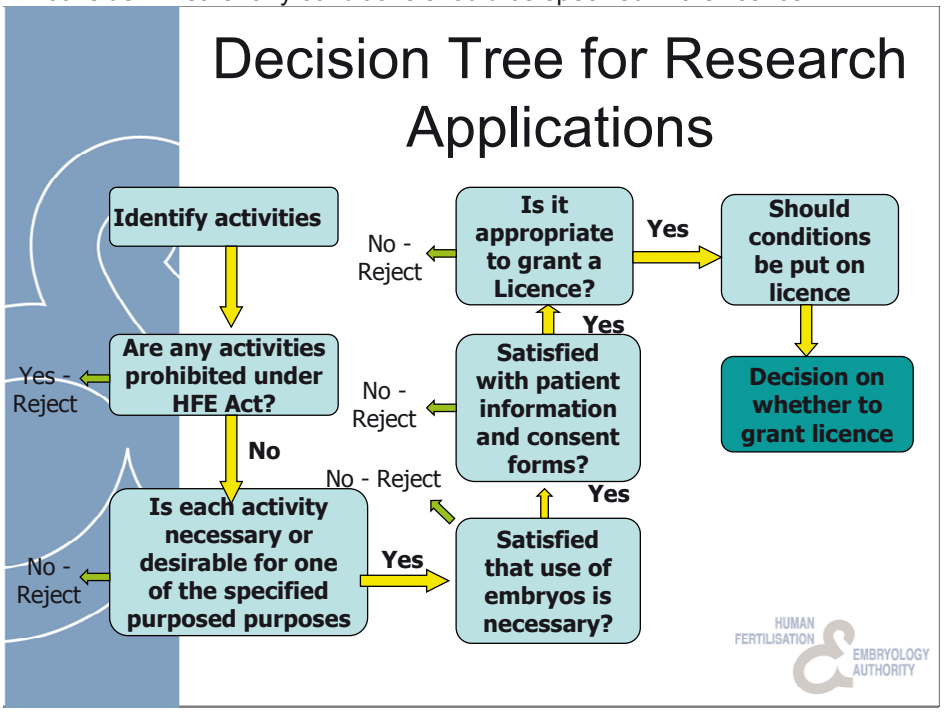
Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	The Act (2006:351) on genetic integrity etc.. The Biobanks in Medical Care Act (2002:297) The Act (2003:460) on ethics review of research on humans http://www.epn.se/eng/start/index.aspx The Transplantation Act (1995:831) Guidelines issued by the Swedish Research Council
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	The word used in Sweden is ‘fertilised egg’. There is a 14 day limit for its use.
3	**Is hESC research allowed and under what terms and conditions?**
	Yes. Approval by regional research ethics authority. Consent from both donors.
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	see above
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes under what conditions?**
	same as 3
6	**Is the source of hESC used in research traceable and well documented?**
	Yes
7	**What are the formal ethical and legal requirements for hESC research approval?**
	same as 3
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	Consent should be informed. Procedures are reviewed by the Regional Research Ethics Authority.
9	**Is financial inducement allowed? If so, on what terms?**
	No. Normally, only reimbursement of costs allowed
10	**Are ad hoc data protection provisions defined for hESC research?**
	The Patient Records Act and the Personal Data Act apply
11	**Are data deriving from hESC projects necessarily (?) provided, whether positive or negative (in form of publications)?**
	No different from other research
12	**How is patenting of hESC lines regulated?**
	Indirectly in the Transplantation Act

Regulatory frame applying to UNITED KINGDOM

Please the information here provided should concern current regulatory requirements and not other reference documents having not a legal personality.

1	**Please list existing regulation applying to human embryonic stem cells (hESC) research (web address where to get the texts would be welcomed).**
	The use of embryos to derive hES cell lines is regulated by the Human Fertilisation and Embryology Authority (HFEA) in the UK (www.hfea.gov.uk). The UK Stem Cell Bank Steering Committee also issues guidelines on the use of hES cell lines in the UK (www.ukstemcellbank.org.uk)
2	**Does the regulation provide a definition of 'embryo', if so which one?**
	The Human Fertilisation and Embryology Act (HF&E Act) 1990 provides that 'an embryo means a live human embryo where fertilisation is complete, and references to an embryo include an egg in the process of fertilisation, and, for this purpose, fertilisation is not complete until the appearance of a two cell zygote'.
3	**Is hESC research allowed and in what terms and conditions?**
	The HFEA regulates the use of embryos to derive hES cell lines. The use of hES cell lines in research is permitted in the UK but is not within the remit of the HFEA.
4	**If yes, which body is in charge of the approval of hESC research (ethics review)?**
	The HFEA regulates the use of embryos to derive hES cell lines.
5	**Is the creation of embryos for research purposes, or stem cells procurement, allowed in your country, if yes at what conditions?**
	Yes the creation of embryos for use in research, including the derivation of hES cell lines, is permitted in the UK. An explanation of how the HFEA licences research projects can be found on our website at www.hfea.gov.uk.
6	**Is the source of hESC used in research traceable and well documented?**
	Yes
7	**What are the formal ethical and legal requirements for hESC research approval?**
	The use of embryos to derive hES cell lines requires a licence from the HFEA. ***The HFEA has set up a dedicated Research Licence Committee. Under section 9(5) of the 1990 Act, a Licence Committee is required to include at least 1 member who is not authorised to carry on or participate in any activity under the authority of a licence and would not be so authorised if outstanding applications were granted. In addition to this requirement, and in accordance with the recommendations of the Better Regulation Task Force, the Research Licence Committee has a lay chair and a lay majority.*** In considering whether to grant or renew a licence, the Committee will have access to the following documentation: • Application form signed by the Person Responsible and the Nominal Licensee • *Curricula vitae* of the principal personnel involved in the research • Approval of a properly constituted local research Ethics Committee, • Report of the inspection of the research centre • Comments from 2 peer reviewers • The centre's licensing history

	• Copies of relevant publications • Patient Information and Consent Forms Before considering whether it is appropriate to grant or renew a licence the Research Licence Committee has to be satisfied that activities proposed in the licence application are necessary or desirable for one or more of the purposes set out in Schedule 2 to the HF&E Act 1990 (as amended by the Research Purposes Regulations 2001). In addition, the Research Licence Committee has to be satisfied that any proposed use of embryos is necessary for the purposes of the research. In addition the Research Licence Committee has to be satisfied that the character, qualifications and experience of the Person Responsible are such as are required to supervise the activities that s/he will discharge their duties under section 17 of the HF&E Act 1990 and that the premises where the research is to be carried out are suitable for the activities. To aid the Licence Committee in its consideration of research applications a decision making tool (the Decision Tree) which was formulated on the basis of legal advice and includes the statutory criteria that the Committee is required to consider. If the Licence Committee decides to grant or renew a licence, the Licence Committee will consider whether any conditions should be specified in the licence. 
8	**Does the relevant regulatory frame foresee informed consent procedures from individuals involved in embryo donation for research, if so could you please describe them?**
	The HFEA, as part of the licensing procedure, see and must approve the patient information and consent forms used in obtaining consent from patient donating gametes and/or embryos in licensed research projects. These documents must also be approved by a local research ethics committee. Furthermore, all research centres are inspected, by the HFEA, annually and as part of this process, the HFEA examines the process used by the centre in obtaining the

	consent of patients whose gametes and/or embryos are used in licensed research.
9	**Is financial inducement allowed? If so, in what terms?**
	Women will not be paid for donating their eggs. Researchers will have to follow the same system as donation for treatment. Non patient donors can only claim back the expenses that they have actually incurred i.e. in money or money's worth, a donor may be given reasonable, demonstrable expenses which she has incurred, within the UK, in connection with the donation. Donors may be compensated for loss of earnings (but not for other costs or inconveniences) up to a daily maximum of £55.19 but with an overall limit of £250 (or the equivalent in local currency) for each cycle of egg donation. Patient participating in egg sharing schemes will be permitted to receive treatment services in exchange for sharing a proportion of the eggs collected.
10	**Are ad hoc data protection provisions be defined for hESC research?**
	This is not within the remit of the HFEA
11	**Are data deriving from hESC projects necessarily provided, whether positive or negative (in form of publications)?**
	This is not within the remit of the HFEA
12	**How is patenting of hESC lines regulated?**
	This is not within the remit of the HFEA

When clinical experiments are carried out, the Ethics Review Board must broaden its review to cover research ethics questions and consider patients' protective rights as laid down in the general medical ethics principles and guidelines. It may be necessary at that point to review these guidelines, as they are based upon the current status quo in human embryonic stem cell research.

APPENDIX:

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