



European Group on Ethics in
Science and New Technologies
(EGE)



Bureau of European Policy Advisers
(BEPA)

Gene, cell Therapy, stem cells regulatory issues

**The view I express are my own and do not necessarily
reflect those of the European Commission**

**Maurizio SALVI
BEPA
European Commission**



Regulation on advanced therapy medicinal products

- These three kinds of **advanced therapies** (**gene therapy, somatic cell therapy, and tissue engineering**) are expected to have a major impact on public health. Moreover, they constitute a coherent ensemble insofar as they share several key scientific, regulatory and economic features:
 - – They are based on **complex, highly innovative manufacturing processes**. The specificity of the product precisely lies *in* the process.
 - – **Traceability from the donor to the patient, long-term patient follow-up and a thorough post-authorisation risk management strategy** are crucial aspects to be addressed when evaluating advanced therapies.
 - – Advanced therapy products are subject to **rapid and often radical innovation**



Regulation on advanced therapy medicinal products

- The Parliament adopted, on **25 April 2007**, the amended report by a MEP on the Commission proposal (November 2005) for a regulation on advanced therapies. The MEPs rejected all ethical amendments proposed to the report.
- An informal triologue between the Commission, the Parliament and the Council (**early 2007**) aimed for adoption of the dossier in the first reading in the Parliament. The inclusion of ethical amendments into the compromise proposal was raised and additional time then needed.
- Due to controversy on inclusion of ethical amendments to the report, the EP's ENVI committee rejected the committee's first draft report in **September 2006**. A new report was adopted on **30 January 2007**.
- **Directive EC/2004/23 on the safety and quality aspects of dealing with human tissues and cells** came into force in **April 2004**. Its provisions needed to be transposed by the member states by April 2006..
- **31 May 2007**, agreement was reached by European Health Ministers on a **Regulation on advanced therapy medicinal products (ATMPs)**, including tissue engineering.
- On **30 October 2007**, the Council has formally adopted the Regulation on advanced therapy medicinal products.



Regulation on advanced therapy medicinal products

Legal basis and procedure

- The proposal is based on **Article 95** of the EC Treaty. Article 95, which prescribes the codecision procedure described in Article 251, is the legal basis for achieving the aims set out in **Article 14 of the Treaty, which includes the free movement of goods** (Article 14(2)), in this case advanced therapy medicinal products for human use.

The overall aim of the new Regulation is:

- - **to improve patients' access to ATMPs;**
- - **to provide legal certainty** in order to foster development in the European biosciences industries;
- - **to harmonise market access** in the European Union by establishing a comprehensive regulatory framework for ATMPs.



Regulation on advanced therapy medicinal products

- The Regulation provides for a **centralised authorisation procedure for marketing** of these innovative products.
- the European Medicines Agency (EMA) will act a specific role for scientific advices.
- The Regulation recognises that there is **no consensus among Member States** upon which harmonised decisions could be taken on the use or prohibition of **ATMPs containing certain types of cells** (such as embryonic stem cells) so this would remain a national responsibility.



What is required?





Regulation on advanced therapy medicinal products

- **evaluation and authorisation**: marketing authorisation procedure, post-authorisation vigilance, traceability, etc. Such Regulation builds on already-existing legislation, in particular:
 - – **Directive 2004/23/EC**, which lays down quality and safety standards in respect of human tissues and cells. It is important to bear in mind that these standards would apply to the donation, procurement and testing of human tissues and cells contained in advanced therapy products;
 - – **Regulation (EC) No 726/2004**, which establishes the so-called ‘centralised procedure’ and the role/structure of the **European Medicines Agency (EMA)**;
 - – **Directive 2001/83/EC** on medicinal products;
 - – **Council Directive 93/42/EEC** concerning medical devices and Council Directive 90/385/EEC on active implantable medical devices..



Regulation on advanced therapy medicinal products

- **Technical requirements.** It is well acknowledged that advanced therapy products are neither medical devices nor conventional medicines: therefore, the technical requirements necessary to demonstrate their **quality, safety and efficacy** (e.g. the type of pre-clinical and clinical data required) will be highly specific, and should depend on the level of risks associated with these products.
- a centralised authorisation procedure, involving a single scientific evaluation of the quality, safety and efficacy of the product, which is carried out to the highest possible standard by **EMA**



Regulation on advanced therapy medicinal products

Donation.

- Conformity with **2004/23** (anonymity of both donor and recipient, altruism of the donor and solidarity between donor and recipient should be respected. As a matter of principle, human cells or tissues contained in advanced therapy medicinal products should be procured from voluntary and unpaid donation.)



Regulation on advanced therapy medicinal products

- **Traciability:** A system allowing complete traceability of the patient as well as of the product and its starting materials is essential to monitor the safety of advanced therapy medicinal products. The establishment and maintenance of that system should be done in such a way as to ensure coherence and compatibility with **traceability requirements laid down in Directive 2004/23/EC in respect of human tissues and cells, and in Directive 2002/98/EC** of the European Parliament and of the Council of 27 January 2003 setting **standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components**.



Regulation on advanced therapy medicinal products

- **Data Protection.** 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 the free movement of such data
- **Clinical trials:** Conformity with EC 2001/20 (informed consent, ethics review)



Regulation on advanced therapy medicinal products

Labelling:

- The requirements in **Directive 2001/83/EC** as regards the summary of product characteristics, **labelling and the package leaflet** should be adapted to the technical specificities of advanced therapy medicinal products by laying down specific rules on those products



Regulation on advanced therapy medicinal products

Guidelines:

Detailed guidelines. As for gene and somatic cell therapy products, it is proposed to establish detailed technical guidance for tissue engineered products through guidelines (EC or EMEA).



Regulation on advanced therapy medicinal products

hESC:

FP7 agreement

- No consensus in the EU
- EGE Opinion on ethics review of hESC FP7 projects
- EGE Opinions on Stem Cells and Patenting of Stem Cells



hESC legislation

BE, SE,
UK, Israel

FI, DK, FR, LV,
EE, SI, EL, ES,
HU, NL, CZ,
PTCH ↓

IT^s ↓

DE ↓

AT, PL, LU
LT, SK, MT
CY IE, LU

European Picture

*Broader
research
on hESC*

*No research
on hESC*

↑
USA non-federal
funds, Australia
China, India
Singapore, South Korea

↑
Brazil
Canada
Japan, Taiwan

↑
USA federal funds

§ law prohibiting procurement
but no law on existing hESC



hESC EU policy

- EU has **no legal competency** to regulate in this sector of ethics
- The **Commission has the responsibility to implement** the EU research programs even where some areas of research raise important ethical issues.
- **Respect of national rules** is a fundamental principle ⇒ no research forbidden in a Member State supported by EU funds there



Specific Procedural Modalities for research involving hESC

■ Scientific Evaluation:

Independent experts assess the necessity of using hESC for achieving the objectives set forth in the proposal.

All proposals for funding involving the use of hESC and/or foetal issues will be automatically submitted to an ethical review panel.



Procedural Modalities for hESC

Once the scientific evaluators confirm the necessity of using hESC in the research proposal, the ethical review panel assesses:

- That the proposal does not include research activities which destroys embryos including for the procurement of stem cells;
- Whether the consortium has taken into account the legislation, regulations, ethical rules and/or codes of conduct in place in the country(ies) where the research using hESC is to take place, including the procedures for obtaining informed consent*
- The source of the hESC;
- The measures taken to protect personal data, including genetic data, and privacy;
- The nature of financial inducements, if any

* Cf. Directive 2004/23/EC



Procedural Modalities for hESC

- In addition, when research proposals involve the use of hESC, the following procedures are required:
 - A **positive opinion from a Regulatory Committee** constituted by Member States' representatives is required .
 - Participants in research projects must seek the **approval of the relevant national or local ethics committees** prior to the start of the research activities (**General Clause in the contract!**)



**the European
Group on Ethics of
Science and new
Technologies
(EGE)**



The EGE





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EGE



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- In order to equip itself with expertise on bioethics, in 1991 the Commission set up the **European Group on Ethics in Science and New Technologies (EGE)**, an independent group, with the mandate to advise the Commission on ethical questions related to sciences and new technologies.
- Following President Barroso's requests, in 2006-2008 the EGE has issued Opinions on
 - (1) **ethics and nanomedicine,**
 - (2) ***ethics review of FP7 human embryonic stem cells projects,***
 - (3) ***ethical aspects of animal cloning for food supply***
 - (4) ***ethical aspects of modern developments in agriculture technologies.***



FP7 ethics and hESC; EGE Position

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.



EGE: FP7 ethics and hESC

Principles advocated by the EGE:

the principle of respect for human dignity

the principle of individual autonomy (entailing the informed consent, and respect for privacy and confidentiality of personal data)

the principle of justice and of beneficence (namely with regard to the improvement and protection of health and quality of life of present and future patients)

the principle of freedom of research (which is to be weighed up against other fundamental principles)

the principle of proportionality (including the reflection on research methods necessary to the aims pursued and the factuality that no alternative methods that would be more acceptable are available).



EGE Position: FP7 ethics and hESC;

The Group indicated that, **additionally** to the FP7 ethics rules already adopted in co-decision, the following considerations have to apply to hESC funded by the EU:

FP7 hESC lines have to result from non-implanted IVF embryos.

there is a need of maximising the use of alternatives to hESCs with the same potential as embryo-derived stem cells

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

The EGE also stressed the need of maximising the use of hESC banked in the European Registry on hESC Research, and stressed the need of taking concrete actions for public debate on this research sector.



And now?





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NO



Yes





Ethics in the EC

Issues that deserve specific efforts:

- how to deal with diversity on ethics and hESC?
- Implementing measures by EMEA?
- Clarification of informed consent procedures
- Free donation of biological material
- international debate (EMEA-FDA)?

•DISPUTATUR INTER SAPIENTES!!!



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(BEPA)

Contact:

Maurizio SALVI, PhD

Bureau of European Policy Advisers, (BEPA)

Head of the EGE Secretariat

Chair EC Inter-service Platform on Ethics and EU Policies

European Commission, Rue de la Loi 200, BERL 8/146

B-1049 Brussels, Belgium

e-mail: maurizio.salvi@ec.europa.eu

Information available:

EGE homepage: http://europa.eu.int/comm/european_group_ethics/index_en.htm

BEPA homepage: http://ec.europa.eu/dgs/policy_advisers/index_en.htm