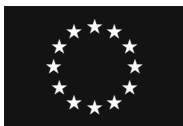


EUROPEAN PARLIAMENT

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2009

Committee on Legal Affairs

PROVISIONAL
2005/0227(COD)

19.6.2006

DRAFT OPINION

of the Committee on Legal Affairs

for the Committee on the Environment, Public Health and Food Safety

on the proposal for a regulation of the European Parliament and of the Council
on advanced therapy medicinal products and amending Directive 2001/83/EC
and Regulation (EC) No 726/2004
(COM(2005)0567 – C6-0401/2005 – 2005/0227(COD))

Draftswoman: (*) Hiltrud Breyer(*) Enhanced cooperation between
committees – Rule 47 of the Rules of
Procedure

PA_Legam

SHORT JUSTIFICATION

The Commission's proposal seeks to regulate placing on the European market of products based on gene therapy, cell therapy and tissue engineering. These products are of growing importance for modern medicine and can potentially help a lot of patients, but some serious health risks might occur in case of improper regulation. Especially in the area of tissue engineering no harmonised European approach exists.

In general, the Commission's proposal is welcome by all stakeholders but the public debate and discussion in Parliament committees has shown that there are some points that urgently need clarification to make the proposal legally consistent, to exclude controversial interpretations, to make the proposal coherent with the current legislation and to safeguard Parliament's rights. This is why your draftsman proposes a number of amendments.

1. The rights of the Parliament in the comitology procedure.

The Commission's proposal foresees to delegate almost all important questions to the comitology procedure. In such a highly political issue it is important to safeguard Parliament's rights. The Parliament should have the right to examine and to block such decisions. It is unacceptable that Art. 8 of this proposal refers to the comitology procedure although the Commission has not even submitted to the Parliament a draft of adequate technical requirements. The European institutions are getting close to a new agreement on the comitology procedure which is a step forward in balancing their powers. In the meantime, a proposed amendment introduces a procedure strengthening Parliament's role.

2. Legal safety on the issue of subsidiarity.

There is broad agreement that the European Union should not harmonise the legislation on the use of human embryos and human embryonic stem cells. The Commission proposes to safeguard the legislative right of the Member States in Article 28(2). However, this provision is not adequate and may be challenged in the Court of Justice, as it causes serious problems with regard to the legal basis of the proposal. It can not be excluded that the proposed Regulation constitutes a complete harmonisation. Therefore, the proposed Art. 28(2) would be an alien substance and breach of Community law would not be excluded.

The draftsman therefore supports the approach to exclude certain delicate areas such as embryonic stem cells from the scope of the Regulation in Article 1. It would make clear that there will be no harmonization in these delicate areas. In addition, the wording of Art. 28(2) of the proposal should be changed to underline that Member States, acting on the basis of Art. 30 TEC can further ban or limit the use, the sale, the placing on the market of human and animal cells as well as the use of medicinal products which contain, consist or are derived from such cells.

3. To make the proposal coherent with the current EU legislation, some technologies that are banned in other European legislation should also not get authorisation under the current Commission's proposal.

Regardless of the competence of the Member States there should not be any compromises regarding human rights and constitutional law, even if progress in some areas is rapid. The

principle of the non-commercialization of the human body has to be respected. The integrity of the person is protected under the Oviedo Convention and the Charter of Fundamental Rights. The production of human-animal hybrids or chimeras constitutes a breach of the principle of the integrity of the person and of the principle of inviolability of human dignity. Interventions in the human germ line are explicitly named in the Oviedo Convention as endangering human dignity. Products which intervene in the human germ line are excluded from clinical trials in Directive 2001/20/EC and are non patentable according to Directive 98/44/EC as are also human-animal hybrids being against ordre public.

4. To insure the voluntary and unpaid donation of human tissues and cells the Directive 2004/23/EC must be amended.

Straight in connection with advanced therapies which are subject to rapid development and for products of which the human tissue and cells are increasingly needed, the principle of the non-commercialization of the human body requires Member States to ensure the voluntary and unpaid donation and procurement of human cells and tissues. Therefore the Directive 2004/23/EC must be amended for the purposes of the suggested Regulation.

AMENDMENTS

The Committee on Legal Affairs calls on the Committee on the Environment, Public Health and Food Safety, as the committee responsible, to incorporate the following amendments in its report:

Text proposed by the Commission	Amendments by Parliament
Amendment 1 TITLE	
Proposal for a Regulation of the European Parliament and of the Council on advanced therapy medicinal products and amending Directive 2001/83/EC <i>and</i> Regulation (EC) No 726/2004	Proposal for a Regulation of the European Parliament and of the Council on advanced therapy medicinal products and amending Directive 2001/83/EC, Regulation (EC) No 726/2004 <i>and Directive 2004/23/EC</i>
<i>Justification</i>	
<i>The title of the proposal need to be changed, as Directive 2004/23/EC is also amended (see amendment 20).</i>	
Amendment 2 RECITAL 6	
(6) The regulation of advanced therapy medicinal products at Community level should not interfere with decisions made by	(6) <i>Legislation in force in Member States concerning the use of certain types of cells, such as embryonic stem cells, varies</i>

Member States on whether to allow the use of any specific type of human cells, such as embryonic stem cells, or animal cells. It should also not affect the application of national legislation prohibiting or restricting the sale, supply or use of medicinal products containing, consisting of or derived from these cells.

considerably. The regulation of advanced therapy medicinal products at Community level should not interfere with decisions made by Member States on whether to allow the use of any specific type cells. It should also not affect the application of national legislation prohibiting or restricting the sale, supply or use of medicinal products containing, consisting of or derived from these cells. ***Moreover, it is impossible to assess when, if ever, research on these cells will reach the stage at which commercial products made from these cells could be placed on the market. In order to respect the basic principles and the proper functioning of the internal market and to ensure legal certainty, this Regulation should apply only to products made of cells, for which marketing is feasible in the near future and which do not raise major ethical controversies.***

Justification

The legal base of this regulation (Article 95 TEC) is a single market harmonisation measure. It is not designed to cover situations in which significant national legislative differences are intended to remain (c.f. ECJ Case C-376/98). It is therefore necessary to exclude from the scope of this regulation products using materials which are ethically controversial and for which differing Member States legislative provisions are intended to remain. In any case, products using these materials are unlikely to be ready to be placed on the market in the foreseeable future.

Amendment 3 RECITAL 7 A (new)

(7a) This Regulation fully respects the prohibition on making the human body and its parts as such a source of financial gain, as set out as an inalienable minimum safeguard in the Charter of Fundamental Rights of the European Union and further underlined by the European Parliament in its resolution of 10 March 2005 on the trade in human egg cells¹. To that end, it is necessary to ensure that the donation of tissues and cells is voluntary and unpaid and that their procurement is carried out

on a non-profit basis. Voluntary and unpaid tissue and cell donations also contribute to high safety standards for tissues and cells and therefore to the protection of human health.

¹ *OJ C 320 E, 15.12.2005, p. 251.*

Justification

Rapid developments in biotechnology and biomedicine must not be allowed to compromise the protection of fundamental rights. These rights of which one of the most important one is the right to the integrity of the person are laid down in the Oviedo Convention as well as in the Charter of Fundamental Rights. These standards should be met especially for tissue- and cell-based advanced therapy medicinal products as highly innovative new products. In this context, voluntary and unpaid donation as well as procurement on a non-profit basis are the key principles that should be imperatively respected in the Community.

Amendment 4

RECITAL 7 B (new)

(7b) Directive 2001/20/EC¹ prohibits gene therapy trials that result in modifications to a subject's germ line genetic identity. Directive 98/44/EC² provides that processes for modifying the human germ line genetic identity are to be regarded as unpatentable. To ensure legal consistency, this Regulation should prohibit any authorisation of products that modify the germ line genetic identity of human beings.

¹ *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 (OJ L 121, 1.5.2001, p. 34).*

² *Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions (OJ L 213, 30.7.1998, p. 13).*

Justification

As Articles 1 and 13 of the Oviedo Convention make it clear, human dignity is compromised when the inheritance of genetic identity is altered. Products which are neither properly

subject to clinical trials under Directive 2001/20/EC nor legally patentable under Directive 98/44/EC should not be eligible for authorisation under this regulation.

Amendment 5
RECITAL 7 C (new)

(7c) This Regulation should prohibit any authorisation of products derived from human-animal hybrids or chimeras or containing tissues or cells originating or derived therefrom. This provision should not exclude the transplantation of somatic animal cells or tissues to the human body for therapeutic purposes, in so far as it does not interfere with the germ line.

Justification

The physical and mental integrity of the person and human dignity must be respected, as underlined in Articles 1 and 3 of the Charter of fundamental rights of the European Union. The creation of human-animal hybrids or chimeras is a threat to the right to integrity of a person and a violation of human dignity. Therefore, no authorisation for products containing or originating from human-animal hybrids or chimeras should be granted under this Regulation. However, the Xenotransplantation for therapeutic purposes should not be excluded, as far as it does not interfere with the germ line.

Amendment 6
RECITAL 14

(14) As a matter of principle, human cells or tissues contained in advanced therapy medicinal products should be procured from voluntary and unpaid donation. Voluntary and unpaid tissue and cell donations are a factor which may contribute to high safety standards for tissues and cells and therefore to the protection of human health. ***deleted***

Justification

This recital shall be deleted as a consequence to the introduction of a new recital 7(a) and new Articles 3(a) and 28(a).

Amendment 7

RECITAL 28

(28) Directive 2001/83/EC **and** Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing European Medicines Agency should therefore be amended accordingly,

(28) Directive 2001/83/EC, Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing European Medicines Agency **and Directive 2004/23/EC** should therefore be amended accordingly,

Justification

This is a consequential amendment to the introduction of Article 28(a) (new) modifying Directive 2004/23/EC on tissues and cells.

Amendment 8 ARTICLE 1 A (new)

Article 1 a

Exclusions

This Regulation shall not apply to any advanced therapy medicinal products that contain or are derived from:

(a) human embryonic and foetal cells, primordial germ cells and cells derived from those cells,

(b) cells derived from human parthenogenesis or material derived from cloned human embryos, human embryos produced by somatic cell nuclear transfer and somatic stem cells reprogrammed through fusion with embryonic stem cells,

(c) embryonic stem cells obtained through nuclear transfer of a human somatic cells nucleus in an enucleated oocyte from an animal, or

(d) non-human cells (isolated cells, tissues and organs), so long as there remain problems over the identification of endogen retroviruses in the external cells

and in the recipients, the possible creation of new viruses, possible immune reactions, the possible development of cancer or the lengthy isolation of human recipients which is necessary for security reasons and which has serious consequences for their personal freedom.

Justification

The legal base of this regulation (Article 95 TEC) is a single market harmonisation measure. It is not designed to cover situations in which significant national legislative differences are intended to remain (c.f. ECJ Case C-376/98). It is therefore necessary to exclude from the scope of this regulation products using materials which are ethically controversial and for which differing Member States legislative provisions are intended to remain. In any case, products using these materials are unlikely to be ready to be placed on the market in the foreseeable future.

Amendment 9

ARTICLE 2, PARAGRAPH 1, POINT (D A)(new)

(da) chimera means:

- an embryo into which a cell of any non-human life form has been introduced; or***
- an embryo that consists of cells of more than one embryo, foetus or human being;***

Justification

This definition is introduced for the purpose of Article 3(c) of the present Regulation. Source: Canadian assisted human reproduction act 2004.

Amendment 10

ARTICLE 2, PARAGRAPH 1, POINT (D B) (new)

(db) hybrid means:

- a human ovum that has been fertilised by a sperm of a non-human life form;***
- an ovum of a non-human life form that has been fertilised by a human sperm;***
- a human ovum into which the nucleus of a cell of a non-human life form has been introduced;***
- an ovum of a non-human life form into which the nucleus of a human cell has***

*been introduced; or
- a human ovum or an ovum of a non-human life form that otherwise contains haploid sets of chromosomes from both a human being and a non-human life form.*

Justification

This definition is introduced for the purpose of Article 3(c) of the present Regulation. Source: Canadian assisted human reproduction act 2004.

Amendment 11
ARTICLE 3

Where an advanced therapy medicinal product contains human cells or tissues, the donation, procurement and testing of those cells or tissues shall be made in accordance with the provisions laid down in Directive 2004/23/EC.

Where an advanced therapy medicinal product contains human cells or tissues, the donation, procurement and testing of those cells or tissues shall be made in accordance with the provisions laid down in Directive 2004/23/EC. ***The Committee for Medicinal Products for Human Use of the European Medicines Agency, hereinafter “the Agency”, shall verify the assurances (or the documentation) of the holder of the marketing authorisation with regard to the voluntary and unpaid donation of tissues and cells as laid down in Directive 2004/23/EC.***

Amendment 12
ARTICLE 3 A (new)

Article 3a

Prohibition of commercialisation of the human body

Where an advanced therapy medicinal product contains human tissues or cells, every stage of the authorisation procedure shall be carried out in accordance with the principle of non-commercialisation of the human body or its parts as such. To that end, and for the purposes of this Regulation, Member States shall ensure

that:
- the donation of human cells and tissues is voluntary and unpaid and is made of the donor's free will without payment except compensation; and
- the procurement of tissues and cells is carried out on a non-profit basis.

Justification

Rapid developments in biotechnology and biomedicine must not undermine the protection of fundamental rights. These rights, of which one of the most important ones is the right to the integrity of the person, are laid down in the Oviedo Convention as well as in the Charter of Fundamental Rights. These standards can only be upheld by careful observation at every stage of the authorisation process. Therefore EMEA should be subject to this specific obligation and Member States should ensure voluntary and unpaid donation and guarantee the procurement of tissues or cells on a non-profit basis.

Amendment 13
ARTICLE 3 B (new)

Article 3b

Prohibition of products modifying the human germ line

No authorisation shall be granted for products which modify the germ line genetic identity of human beings.

Justification

As Articles 1 and 13 of the Oviedo Convention make it clear, human dignity is compromised when the inheritance of genetic identity is altered. Products which are neither properly subject to clinical trials under Directive 2001/20/EC nor legally patentable under Directive 98/44/EC should not be eligible for authorisation under this Regulation.

Amendment 14
ARTICLE 3 C (new)

Article 3c

Prohibition of products derived from human-animal hybrids or chimeras

No authorisation shall be granted for products derived from human-animal hybrids or chimeras or containing tissues

or cells originating or derived therefrom. This provision shall not preclude the transplantation of somatic animal cells or tissues to the human body for therapeutic purposes, in so far as it does not interfere with the germ line.

Justification

The physical and mental integrity of the person and human dignity must be respected, as underlined by the Charter of fundamental rights of the EU. The creation of human-animal hybrids or chimeras is a breach of the right to integrity of a person and a violation of human dignity. In addition, the Directive 98/44/EC on the legal protection of biotechnological inventions stresses that the production of chimeras from germ cells is excluded from patentability. Therefore, no authorisation under this regulation should be granted to products containing or derived from such tissues and cells.

Amendment 15
ARTICLE 24

The Commission shall, in accordance with procedure referred to in Article 26(2), amend Annexes **I** to IV in order to adapt them to scientific and technical evolution.

The Commission shall, in accordance with procedure referred to in Article 26(2), amend Annexes **II** to IV in order to adapt them to scientific and technical evolution.

Justification

Annex I contains a fundamental and substantial definition. We therefore consider that it should not be subject to any changes through comitology. Should any changes be necessary due to scientific progress, they should be adopted in codecision, fully involving the European Parliament.

Amendment 16
ARTICLE 25

Reporting

Within 5 years of entry into force of this Regulation, the Commission shall publish a general report on its application, which shall include comprehensive information on the different types of advanced therapy medicinal products authorised pursuant to this Regulation.

Report and review

Within 5 years of entry into force of this Regulation, the Commission shall publish a general report on its application, which shall include comprehensive information on the different types of advanced therapy medicinal products authorised pursuant to this Regulation.

In that report, the Commission shall also assess the impact of technical progress on the application of this Regulation and, if

necessary, submit a legislative proposal for a review of its scope to include novel therapies which are neither gene therapy, nor cell therapy nor tissue engineering.

Justification

Scientific advances may make additional novel therapies possible which are neither gene therapy, nor cell therapy nor tissue engineering. It would be in the interest of patients for these to be included at some future date in order to allow European authorisation of the resulting products.

Amendment 17
ARTICLE 25 A (new)

Article 25a

The Commission shall by no later than the end of 2007 submit a legislative proposal in order to ensure that products used for cosmetic purposes which contain human or animal cells or tissues are also covered by adequate Community legislation.

Justification

Until now products used for cosmetic purposes containing human or animal cells or tissues, although already being placed on the market, are not regulated under Community law. This regulation gap needs to be closed.

Amendment 18
ARTICLE 26, PARAGRAPH 2, SUBPARAGRAPH 1

2. Where reference is made to this paragraph, Articles 5 and 7 of Decision 1999/468/EC shall apply, having regard to the provisions of Article 8 thereof.

2. Where reference is made to this paragraph, ***and without prejudice to Article 26a***, Articles 5 and 7 of Decision 1999/468/EC shall apply, having regard to the provisions of Article 8 thereof.

Justification

This is a consequential amendment to the introduction of the new Article 26(a) below.

Amendment 19
ARTICLE 26 A (new)

Article 26a

For the purposes of this Regulation, the following procedure shall apply:

1. The Commission shall without delay submit the draft implementing measures to the European Parliament.

2. The European Parliament, acting by a majority of its component members, may oppose the adoption of the draft by the Commission on the grounds that the draft exceeds the implementing powers provided for in this Regulation or is incompatible with the aim or the content of this Regulation or does not respect the principles of subsidiarity or proportionality.

3. If within three months of the date of their submission the European Parliament opposes the draft measures, the latter shall not be adopted by the Commission. In that event, the Commission may submit an amended draft of the measures or present a new legislative proposal.

4. If the European Parliament has not opposed the draft measures within the above-mentioned period, they shall be adopted by the Commission.

Justification

There is a lack of transparency and democratic control in the Commission's decisions on delegated legislation. The Parliament should have the right to examine and to block such decisions. It is unacceptable that Article 8 of this regulation refers to the comitology procedure although the Commission has not even submitted a draft to the Parliament. European institutions are getting close to make a new agreement on the comitology procedure which is a step forward in balancing their powers. In the meantime, we introduce the above mentioned procedure strengthening the Parliament's role.

Amendment 20

ARTICLE 28, PARAGRAPH 2

“5. This Directive and all Regulations referred to therein shall not affect the application of national legislation prohibiting or restricting the use of any specific type of human or animal cells, or the sale, supply or use of medicinal products containing, consisting of or derived from

“5. This Directive and all Regulations referred to therein shall not affect the application of national legislation prohibiting or restricting the use of any specific type of human or animal cells, or the sale, supply or use of medicinal products containing, consisting of or derived from

these cells. ***The Member States shall communicate the national legislation concerned to the Commission.***"

these cells, ***by virtue of the Article 30 of the Treaty establishing the European Community.***"

Justification

As this regulation is a partially harmonizing measure, it should be made clear that Member States has the right to refer to the Article 30 of the TEC when it comes to the access of certain medicinal products to their market. With regard to the Article 95, paragraph 4 of the TEC, the obligation to communicate the national legislation concerned to the Commission is only appropriate if the community measure is a fully harmonizing one.

Amendment 21
ARTICLE 28 A (new)
Article 2, paragraph 1 (Directive 2004/23/EC)

Article 28a

Amendment to Directive 2004/23/EC

In Article 2(1) of Directive 2004/23/EC, the second subparagraph shall be replaced by the following:

"Where such manufactured products are covered by other Community legislation, this Directive shall apply only to donation, procurement and testing. However, the donation, procurement and testing provisions of this Directive shall be without prejudice to more specific provisions contained in other Community legislation."

Justification

According to the existing legislation, the donation, procurement and testing of human tissues and cells should comply with high standards of quality and safety in order to ensure a high level of health protection in the Community. Moreover, it also has to be ensured that the human body or its parts as such are not commercialised. Therefore, for the purposes of this Regulation, Member States shall have an imperative obligation to ensure voluntary and unpaid donation and to guarantee that the procurement of tissues or cells is carried out on a non-profit basis.

Amendment 22
ANNEX II, POINT 2.2.

2.2. qualitative and quantitative composition
in terms of the active substances and other

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in terms of the active substances and other

constituents of the product, knowledge of which is essential for proper use, administration or implantation of the product. Where the product contains cells or tissues, a detailed description of these cells or tissues and of their specific origin shall be provided.

constituents of the product, knowledge of which is essential for proper use, administration or implantation of the product. Where the product contains cells or tissues, a detailed description of these cells or tissues and of their specific origin, **including the species of animal in cases of non-human origin**, shall be provided.

Justification

This amendment aims at ensuring that potential recipients having various cultural considerations are duly informed before taking their decision.

Amendment 23
ANNEX III, POINT (B)

(b) A description of the active substance(s) expressed qualitatively and quantitatively, including, where the product contains cells or tissues, the statement “This product contains cells of human/animal [as appropriate] origin” together with a short description of these cells or tissues and of their specific origin;

(b) A description of the active substance(s) expressed qualitatively and quantitatively, including, where the product contains cells or tissues, the statement “This product contains cells of human/animal [as appropriate] origin” together with a short description of these cells or tissues and of their specific origin, **including the species of animal in cases of non-human origin**;

Justification

This amendment aims at ensuring that potential recipients having various cultural considerations are duly informed before taking their decision.

Amendment 24
ANNEX IV, POINT (A), POINT (III)

(iii) where the product contains cells or tissues, a description of those cells or tissues and of their specific origin;

(iii) where the product contains cells or tissues, a description of those cells or tissues and of their specific origin, **including the species of animal in cases of non-human origin**;

Justification

This amendment aims at ensuring that potential recipients having various cultural considerations are duly informed before taking their decision.