

# EUROPEAN PARLIAMENT

2004



2009

Committee on the Environment, Public Health and Food Safety

22.6.2006

PE 374.483v01-00

## AMENDMENTS 48-120

### Draft report

(PE 371.745v02-00)

Miroslav Mikolášik

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

Proposal for a regulation (COM(2005)0567 – C6-0401/2005 – 2005/0227(COD) - amending act)

Text proposed by the Commission

Amendments by Parliament

Amendment by John Bowis

### Amendment 48 RECITAL 2

(2) Insofar as these advanced therapy products are presented as having properties for treating or preventing diseases in human beings, or that they may be used in or administered to human beings with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, they are biological medicinal products within the meaning of Article 1(2) and Annex I to Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use. Thus, the essential aim of any rules governing their production,

(2) Insofar as these advanced therapy products are presented as having properties for treating or preventing diseases in human beings, or that they may be used in or administered to human beings with a view to restoring, correcting or modifying physiological functions by exerting *principally* a pharmacological, immunological or metabolic action, they are biological medicinal products within the meaning of Article 1(2) and Annex I to Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use. Thus, the essential aim of any rules

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distribution and use must be to safeguard public health.

governing their production, distribution and use must be to safeguard public health.

Or. en

*Justification*

*The Medical Devices Directives (MDD) provide a regulatory framework which is readily adapted to the control of devices containing or made of tissue engineered products. If a tissue engineered product falls within the definition of “medical device” in Article 1 of the MDD (and therefore does not have a mode of action which is primarily pharmacological, immunological or metabolic), it should be regulated under the MDD although additional specific requirements may be necessary.*

Amendment by Urszula Krupa

Amendment 49  
RECITAL 2

Insofar as these advanced therapy products are presented as having properties for treating or preventing diseases in human beings, or that they may be used in or administered to human beings with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, they are biological medicinal products within the meaning of Article 1(2) and Annex I to Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use. Thus, the essential aim of any rules governing their production, distribution and use must be to safeguard public health.

Insofar as these advanced therapy products are presented as having properties for treating or preventing diseases in human beings, or that they may be used in or administered to human beings with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, they are biological medicinal products within the meaning of Article 1(2) and Annex I to Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use. Thus, the essential aim of any rules governing their production, distribution and use must be to safeguard public health **and individual well-being.**

Or. pl

*Justification*

*Public health protection is a general idea. In connection with treatment methods that are so innovative and of such importance to health, account should be taken of individual well-being.*

Amendment by Frédérique Ries

Amendment 50  
RECITAL 3 A (new)

***(3a) For reasons of efficacy, the directives on which this proposal for a regulation is based, and notably Directive 2004/27/EC on medicinal products for human use<sup>1</sup>, Directives 2004/23/EC<sup>2</sup> and 2006/17/EC<sup>3</sup> on human tissues and cells and Commission Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use<sup>4</sup>, should be transposed within the deadlines, or at the earliest opportunity, by all Member States;***

<sup>1</sup> Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on a Community code relating to medicinal products for human use (OJ L 136, 30.4.2004, p. 34).

<sup>2</sup> Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells (OJ L 102, 7.4.2004, p. 48).

<sup>3</sup> Commission Directive 2006/17/EC of 8 February 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells (OJ L 38, 9.2.2006, p. 40).

<sup>4</sup> OJ L 91, 9.4.2005 p. 13.

Or. fr

Amendment by Urszula Krupa

Amendment 51  
RECITAL 4

(4) Because of the novelty, complexity and technical specificity of advanced therapy medicinal products, specially tailored and harmonised rules are needed to ensure the free movement of those products within the Community, and the effective operation of the internal market in the biotechnology sector.

(4) Because of the novelty, complexity and technical specificity of advanced therapy medicinal products, specially tailored and harmonised rules are needed to ensure the free movement **and control** of those products within the Community, and the effective operation of the internal market in the biotechnology sector.

Or. pl

*Justification*

*To prevent improper use - particularly in ethical terms -being made of advanced therapies.*

Amendment by Frédérique Ries

Amendment 52  
RECITAL 6

(6) 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 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.

(6) 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 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. ***It should also fully respect the freedom of therapeutic research and in particular Community financing of research on the use of adult and embryonic stem cells, in line with the position adopted by the European Parliament on 15 June 2006 on the Seventh framework programme of the European Community for research, technological development and demonstration activities (2007 to 2013)***<sup>1</sup>.

<sup>1</sup> *Texts adopted of that date, P6\_TA-PROV(2006)0265.*

Or. fr

### *Justification*

*This amendment aims to support the hundreds of thousands of Europeans fighting any one of the 6 000 rare diseases currently on record and the hope they place in different forms of medical research and their future therapeutic applications.*

Amendment by Miroslav Mikolášik

Amendment 53  
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, set out as an inalienable minimum protection 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 cells<sup>1</sup>. To achieve this objective 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.***

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<sup>1</sup> OJ C 320 E, 15.12.2005, p. 251.

Or. en

### *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 all around the Community.*

Amendment by Cristina Gutiérrez-Cortines

Amendment 54  
RECITAL 7 A (new)

***(7a) These provisions should not affect 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.***

Or. en

*Justification*

*This regulation should not introduce concepts that can affect national regulations allowing already existing techniques*

Amendment by Cristina Gutiérrez-Cortines

Amendment 55  
RECITAL 10

(10) The Committee for Advanced Therapies should gather the best available Community expertise on advanced therapy medicinal products. The composition of the Committee for Advanced Therapies should ensure appropriate coverage of the scientific areas relevant to advanced therapies, including gene therapy, cell therapy, tissue-engineering, medical devices, pharmacovigilance and ethics. Patient associations and ***surgeons*** with scientific experience of advanced therapy medicinal products should also be represented.

(10) The Committee for Advanced Therapies should gather the best available Community expertise on advanced therapy medicinal products. The composition of the Committee for Advanced Therapies should ensure appropriate coverage of the scientific areas relevant to advanced therapies, including gene therapy, cell therapy, tissue-engineering, medical devices, pharmacovigilance and ethics. Patient associations and ***physicians*** with scientific experience of advanced therapy medicinal products should also be represented.

Or. en

*Justification*

*For the sake of being more precise it is necessary to apply the technical term.*

Amendment by Dagmar Roth-Behrendt

Amendment 56  
RECITAL 10

(10) The Committee for Advanced Therapies should gather the best available Community expertise on advanced therapy medicinal products. The composition of the Committee for Advanced Therapies should ensure appropriate coverage of the scientific areas relevant to advanced therapies, including gene therapy, cell therapy, tissue-engineering, medical devices, pharmacovigilance and ethics. Patient associations and *surgeons* with scientific experience of advanced therapy medicinal products should also be represented.

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Or. en

*Justification*

*This amendment brings the proposal in line with existing legislation.*

Amendment by Urszula Krupa

Amendment 57  
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.

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

Or. pl

*Justification*

*The principle of voluntary tissue and cell donation must ensure the safety of both recipients and donors.*

Amendment by Urszula Krupa

Amendment 58  
RECITAL 15

(15) Clinical trials on advanced therapy medicinal products should be conducted in accordance with the overarching principles and the ethical requirements laid down in 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. However, tailored rules should be laid down, adapting Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products, in order to fully take into account the specific technical characteristics of advanced therapy medicinal products.

(15) Clinical trials on advanced therapy medicinal products should be conducted in accordance with the overarching principles and the ethical requirements laid down in 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. However, tailored rules should be laid down, adapting Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products, in order to fully take into account the specific technical characteristics **and ethical significance** of advanced therapy medicinal products.

Or. pl

*Justification*

*Given the specific nature of advanced therapies, emphasis should be placed on the significance of bioethical principles.*

Amendment by Dagmar Roth-Behrendt

Amendment 59  
RECITAL 15

(15) Clinical trials on advanced therapy medicinal products should be conducted in accordance with the overarching principles and the ethical requirements laid down in Directive 2001/20/EC of the European

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Or. en

#### *Justification*

*This amendment shall ensure that clinical trials are conducted in the safest possible manner.*

Amendment by Dagmar Roth-Behrendt

#### Amendment 60 RECITAL 18

(18) Specific rules should be laid down, adapting the requirements in Directive 2001/83/EC as regards the summary of product characteristics, labelling and package leaflet to the technical specificities of advanced therapy medicinal products.

(18) ***Patients have the right to know the nature of the origin of any tissues and cells used in the preparation of advanced therapy medicinal products.*** Specific rules should be laid down, adapting the requirements in Directive 2001/83/EC as regards the summary of product characteristics, labelling and package leaflet to the technical specificities of advanced therapy medicinal products.

*Justification*

*This amendment makes a necessary clarification with regard to the rapporteur's amendment 13. Patients have of course the right to be informed about the entire composition of an advanced therapy medicinal product but that cannot include e.g. any confidential information on the identity of individual donors.*

Amendment by Anne Ferreira

Amendment 61

RECITAL 19

(19) Long-term patient follow-up and pharmacovigilance are crucial aspects of advanced therapy medicinal products.  
***Where justified on public health grounds, the holder*** of the marketing authorisation should therefore be ***required*** to put in place a suitable risk management system to address those aspects.

(19) Long-term patient follow-up and pharmacovigilance are crucial aspects of advanced therapy medicinal products.  
***(deletion) The granting*** of the marketing authorisation should therefore be ***conditional on the holder of that authorisation putting*** in place a suitable risk management system to address those aspects.

*Justification*

*See amendment to Article 17(5).*

Amendment by John Bowis

Amendment 62

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

***Tissue engineered products containing or made exclusively of human or animal tissues and/or cells, which do not act principally by pharmacological, immunological or metabolic action, are excluded from this definition.***

*Justification*

*The Medical Devices Directives (MDD) provide a regulatory framework which is readily adapted to the control of devices containing or made of tissue engineered products. If a tissue engineered product falls within the definition of “medical device” in Article 1 of the MDD (and therefore does not have a mode of action which is primarily pharmacological, immunological or metabolic), it should be regulated under the MDD although additional specific requirements may be necessary.*

Amendment by Dagmar Roth-Behrendt

Amendment 63

ARTICLE 2, PARAGRAPH 1, POINT (D), INDENT 2

- *its* cellular or tissue part ***must be liable to act upon the human body with action that cannot be considered as ancillary to that of the devices referred to.***

- ***it contains a*** cellular or tissue part.

Or. en

*Justification*

*In order to enhance legal certainty and the safety of advanced medicinal products, a combined product should fall under this regulation if it contains parts of cells or tissues.*

Amendment by Cristina Gutiérrez-Cortines

Amendment 64

ARTICLE 2, PARAGRAPH 1, POINT (D), INDENT 2

- its cellular or tissue part must be liable to act upon the human body with ***action*** that cannot be considered ***as ancillary to that*** of the devices referred to.

- its cellular or tissue part must be liable to act upon the human body ***with a function*** that cannot be considered ***the prime function, above that*** of the devices referred to.

Or. es

*Justification*

*If the incorporated part is an instrument, it must be considered as part of the whole and not on its own.*

Amendment by Miroslav Mikolášik

Amendment 65  
ARTICLE 3 A (new)

**Article 3 a**

***Ban of products modifying the human  
germ line***

***No authorisation shall be granted to  
products modifying the germ line genetic  
identity of human beings, except for those  
intended to treat cancers of the gonads.***

Or. en

*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. Nevertheless, products for the treatment of cancer of the gonads should be permitted to have European marketing authorisation.*

Amendment by Anne Ferreira

Amendment 66  
ARTICLE 4, PARAGRAPH 3 A (new)

***3a. Concerning the provisions referred to  
in paragraphs 2 and 3 of this article, each  
proposal by the Commission, including any  
amendments, shall be referred to the  
Committee for Advanced Therapies for its  
opinion. Each opinion shall be made public  
at the earliest opportunity.***

Or. fr

*Justification*

*The need to adapt the texts to scientific developments, without their systematic passage before Parliament, must not lead to the interests of the patient being overlooked. Amendment of the rules governing clinical trials and the manufacture of advanced therapy medicinal products, as laid down in this proposal for a regulation, can only be envisaged if there is utmost transparency. The regulation should therefore set out very clearly that the Commission must justify any adaptations and the decision-making process, and that the Committee on*

*Advanced Therapies should systematically be involved.*

Amendment by Anne Ferreira

Amendment 67

ARTICLE 5

Detailed guidelines in line with the principles of good manufacturing practice and specific to advanced therapy medicinal products shall be published ***by the Commission***.

Detailed guidelines in line with the principles of good manufacturing practice and specific to advanced therapy medicinal products shall be published ***on the Agency's website at the earliest opportunity***.

Or. fr

*Justification*

*It seems essential for the guidelines to be made public and disseminated via the Agency's website.*

Amendment by Anne Ferreira

Amendment 68

ARTICLE 8, PARAGRAPH 1 A (new)

***Each amendment proposed by the Commission shall be referred to the Committee for Advanced Therapies for its opinion. Each opinion shall be made public at the earliest opportunity.***

Or. fr

*Justification*

*The need to adapt the texts to scientific and technical developments, without their systematic passage before Parliament, must not lead to the interests of the patient being overlooked. Amendment of the rules governing clinical trials and the manufacture of tissue engineering products, as laid down in this proposal for a regulation, can only be envisaged if there is utmost transparency. The regulation should therefore set out very clearly that the Commission must justify any adaptations and the decision-making process, and that the Committee for Advanced Therapies should systematically be involved.*

Amendment by Dagmar Roth-Behrendt

Amendment 69

ARTICLE 9, PARAGRAPH 2 A (new)

***2a. The rapporteur or co-rapporteur shall be entitled to question the applicant directly. The applicant may also offer to be questioned. The rapporteur or co-rapporteur shall inform the Committees involved in writing without delay of the details of contacts with the applicant.***

Or. en

*Justification*

*The amendment aims at enhancing a more transparent procedure.*

Amendment by Anne Ferreira

Amendment 70

ARTICLE 9, PARAGRAPH 2 A (new)

***2a. The Committee for Advanced Therapies shall adopt its draft opinion for the Committee on Medicinal Products for Human Use by a majority of its members. The draft opinion shall set out any divergent opinions and the grounds for these. The reasoned opinion shall be made public at the earliest opportunity.***

Or. fr

*Justification*

*The Committee for Advanced Therapies has a major role to play. It seems essential for its decision-making processes to be laid down and for all its decisions to be made public and disseminated.*

Amendment by John Bowis

Amendment 71

ARTICLE 10, PARAGRAPH 1

1. Where a combined advanced therapy medicinal product is concerned, ***the whole product, including any medical device or any active implantable medical device incorporated in the medicinal product, shall be evaluated by the Agency.***

1. Where a combined advanced therapy medicinal product is concerned, ***the Agency shall evaluate the quality and safety of the advanced therapy medicinal element of the product together with the compatibility of that element with the device element of the product. The Agency shall also seek an opinion on the device element of the product from the notified body appointed by the manufacturer of the device. The notified body shall provide its opinion on the conformity of the medical device with the relevant essential requirements referred to in Annex I of Directive 93/42/EEC or Directive 90/385/EEC as applicable. The Agency shall take account of the results of that assessment in its evaluation of the advanced therapy medicinal product concerned.***

Or. en

#### *Justification*

*The EMEA should evaluate the efficacy of the medicinal element of an advanced therapy product, whilst a Notified Body (under the Medical Devices Directives) should examine the device element of the product. A clearer definition of the responsibilities of the EMEA and Notified Bodies should avoid duplication and reduce unnecessary delays.*

Amendment by Peter Liese

Amendment 72

ARTICLE 10, PARAGRAPH 1

1. Where a combined advanced therapy medicinal product is concerned, ***the whole product, including any medical device or any active implantable medical device incorporated in the medicinal product, shall be evaluated by the Agency.***

1. Where a combined advanced therapy medicinal product is concerned, ***the Agency shall evaluate the quality and safety of the advanced therapy medicinal element of the product together with the compatibility of that element with the device element of the product. The Agency shall also seek an opinion on the device element of the product from the notified body appointed by the manufacturer of the device. The notified body shall provide its opinion on the conformity of the medical device with the relevant essential requirements referred***

***to in Annex I of Directive 93/42/EC or Directive 90/385 EC as applicable. The Agency shall take account of the results of that assessment in its evaluation of the advanced therapy medicinal product concerned.***

Or. en

*Justification*

*The specific knowledge of the Agency of medicinal products and of the Notified Bodies of medical devices shall be appropriately exploited, while avoiding redundancies and / or overlaps. A clear definition of roles and duties will also reduce unnecessary delays.*

Amendment by Frédérique Ries

Amendment 73

ARTICLE 10, PARAGRAPH 2, SUBPARAGRAPH 1 A (new)

***Where the medical device or active implantable medical device which is not intended exclusively for use in the given combination and is reusable, has never been assessed by a notified body, the application for a marketing authorisation shall include an assessment by a notified body identified in conjunction with the applicant.***

Or. en

*Justification*

*This is a compromise between the initial text of the Commission and the amendment 28 tabled by the rapporteur in order to ensure a flexible and efficient evaluation procedure of the medicinal product concerned.*

Amendment by Peter Liese

Amendment 74

ARTICLE 14, PARAGRAPH 2

***2. The package leaflet shall reflect the results of consultations with target patient groups to ensure that it is legible, clear and***

***2. Where products are exclusively applied to patients by medical practitioners, the summary of product characteristics***

*easy to use.*

***pursuant to Article 11 of Directive 2001/83/EC can be used as the package leaflet.***

Or. en

*Justification*

*Since the predominant majority of Advanced Therapy Medicinal Products will not come into the hands of patients but will be applied by medical practitioners directly, information about the therapy, especially in cases of autologous products, must be given to patients even before the starting material is removed. Therefore the possibility should be introduced to use the summary of product characteristics as package leaflet. Because the package will not come into the hand of patients the necessity for consultations with target patient groups could be deleted.*

Amendment by Dagmar Roth-Behrendt

Amendment 75

ARTICLE 14, PARAGRAPH 2 A (new)

***2a. The package leaflet and the product characteristics can be combined if the advanced therapy medicinal product is only applied directly and exclusively by the medical practitioner to the patient.***

Or. en

*Justification*

*Advanced therapy products will often only be applied by medical professionals directly to the patient and, therefore, make a package leaflet obsolete as information is required by the medical practitioner before the application. Consequently, a combination of package leaflet and summary of product characteristics is adequate in those cases and would reduce administrative burden.*

Amendment by Dagmar Roth-Behrendt

Amendment 76

ARTICLE 15, PARAGRAPH 1

1. In addition to the requirements for pharmacovigilance laid down in Articles 21 to 29 of Regulation (EC) No 726/2004, the applicant shall detail, in the marketing

1. In addition to the requirements for pharmacovigilance laid down in Articles 21 to 29 of Regulation (EC) No 726/2004, the applicant shall detail, in the marketing

authorisation application, the measures envisaged to ensure the follow-up of efficacy of advanced therapy medicinal products.

authorisation application, the measures envisaged to ensure the follow-up of efficacy **and adverse reactions** of advanced therapy medicinal products.

Or. en

*Justification*

*This amendment would ensure a better coherence with existing pharmaceutical legislation and a high standard of pharmacovigilance.*

Amendment by Anne Ferreira

Amendment 77

ARTICLE 15, PARAGRAPH 2

**2. Where there is particular cause for concern, the Commission may, on the advice of the Agency, require as part of the marketing authorisation that a risk management system designed to identify, prevent or minimise risks related to advanced therapy medicinal products, including an evaluation of the effectiveness of that system, be set up, or that specific post-marketing studies be carried out by the holder of the marketing authorisation and submitted for review to the Agency.**

**2. The granting of marketing authorisation shall be conditional on the company putting in place a risk management system. The authority may also, if necessary, require the authorisation holder to conduct specific studies after the placing on the market of the medicinal product concerned. The risk management system shall comprise a series of pharmacovigilance activities and measures designed to identify, prevent or minimise risks related to advanced therapy medicinal products, including an evaluation of the effectiveness of that system. The Agency may be asked for an opinion, pursuant to the provisions of Article 57(1) of Regulation (EC) No 726/2004.**

Or. fr

*Justification*

*Despite the inherent nature of advanced therapy medicinal products, Article 15 introduces hardly any new measures over and above those already applicable to medicinal products for adult use. The competent authority can call for specific studies or a 'system of risk management' after marketing authorisation has been granted, but only, as stated in the original paragraph 2 of this article 'where there is particular cause for concern'. The granting of marketing authorisation should therefore be made conditional on the putting in place of a risk management system, owing to the inherent nature of advanced therapy medicinal products.*

Amendment by Dagmar Roth-Behrendt

Amendment 78

ARTICLE 15, PARAGRAPH 2, SUBPARAGRAPH 1

2. Where there is particular cause for concern, the Commission *may*, on the advice of the Agency, require as part of the marketing authorisation that a risk management system designed to identify, prevent or minimise risks related to advanced therapy medicinal products, including an evaluation of the effectiveness of that system, be set up, or that specific post-marketing studies be carried out by the holder of the marketing authorisation and submitted for review to the Agency.

2. Where there is particular cause for concern, the Commission *shall*, on the advice of the Agency, require as part of the marketing authorisation that a risk management system designed to identify, prevent or minimise risks related to advanced therapy medicinal products, including an evaluation of the effectiveness of that system, be set up, or that specific post-marketing studies be carried out by the holder of the marketing authorisation and submitted for review to the Agency.

Or. en

*Justification*

*As in the regulation for medicines on paediatric use it appears appropriate to impose risk-management plans if there are grounds for concern.*

Amendment by Urszula Krupa

Amendment 79

ARTICLE 16, PARAGRAPH 7 A (new)

***(7a) Supervision of the tracking system should be entrusted to health care entities in the Member States.***

Or. pl

*Justification*

*Territorial entities should provide the Agency with permanent oversight of the tracking system.*

Amendment by Dagmar Roth-Behrendt

Amendment 80  
ARTICLE 17, PARAGRAPH 1

1. The applicant or holder of a marketing authorisation may request advice from the Agency on the design and conduct of pharmacovigilance and of the risk management system referred to in Article 15.

1. The applicant or holder of a marketing authorisation may request advice from the Agency on the design and conduct of pharmacovigilance and of the risk management system referred to in Article 15. ***Within 10 working days following the receipt of a request the Agency shall acknowledge the receipt to the applicant or holder of a marketing authorisation.***

Or. en

*Justification*

*Applicants or marketing authorisation holders shall receive an acknowledgement of the receipt of their request for scientific advice.*

Amendment by Anne Ferreira

Amendment 81  
ARTICLE 17, PARAGRAPH 2

2. By way of derogation from Article 8(1) of Regulation (EC) No 297/95, a 90% reduction shall apply to the fee payable to the Agency for any advice referred to in paragraph 1 and in Article 57(1)(n) of Regulation (EC) No 726/2004 in respect of advanced therapy medicinal products.

2. By way of derogation from Article 8(1) of Regulation (EC) No 297/95, a 90% reduction ***for SMEs and one of 65% for other applicants*** shall apply to the fee payable to the Agency for any advice referred to in paragraph 1 and in Article 57(1)(n) of Regulation (EC) No 726/2004 in respect of advanced therapy medicinal products.

Or. fr

*Justification*

*In order to assist and encourage SMEs to develop advanced therapy medicinal products, the reduction in the special fee should be adjusted on the basis of a company's size. A 65% decrease in the fee should also be envisaged so that a reduction can also be granted to non-SME applicants.*

Amendment 82  
ARTICLE 19 A (new)

***Article 19a***

***Technical support***

***Member States shall, with regard to the application of this Regulation, provide specific technical support for applicants and marketing authorisation holders. This support shall be made available through the competent national authorities and shall focus in particular on:***

***- support for enterprises which do not meet the criteria of Commission Recommendation 2003/361/EC to qualify as SMEs but have a similar need for support, e.g. if they are not considered as SMEs because they do not comply with the criterion of independence or exceed the maximum annual turnover due to high investments in research and development, and***

***- support for individual hospitals or other small-scale institutions, e.g. departments of universities, which do not fulfil the conditions of Article 3(7) of Directive 2001/83. Support shall be provided under the condition that advanced therapy medicinal products are prepared and used under the technical responsibility of a specialised physician and in accordance with a medical prescription for individual patients.***

Or. en

***Justification***

***Exemptions from the scope of the Directive shall be as limited as possible in order to bring the benefit of new medicines quickly to all patients in Europe. However, special support shall be given to groups of possible applicants with regard to the particularities of this highly innovative sector. This can be best achieved at the national level.***

Amendment by Peter Liese

Amendment 83  
ARTICLE 19 A (new)

***Article 19a***

***Incentives for small and medium-sized  
biotech enterprises***

***1. Manufacturers of advanced therapy medicinal products which employ not more than 500 persons and have a turnover not exceeding EUR 100 million, or a balance sheet total not exceeding EUR 70 million, shall be eligible for all incentives which are granted to small and medium-sized enterprises under Commission Recommendation 2003/361/EC.***

***2. The same shall apply to enterprises in which other enterprises have an interest of up to 50 %, if those enterprises invest more than 15 % of their annual turnover in research and development activities.***

Or. en

*Justification*

*For many young biotech enterprises it is difficult to meet the criteria for an SME. One of the reasons is that a purchase or sale of a patent or platform technology may generate a big one-off turnover which exceeds the current limitations. Another reason is that many enterprises don't comply with the current criteria of independence (interests below 25 %), since they built up alliances with other companies. These problems are likely to have the greatest relevance for biotech enterprises. These companies should nevertheless enjoy more favourable financial terms.*

Amendment by Peter Liese

Amendment 84  
ARTICLE 19 B (new)

***Article 19b***

***Reduction of the marketing authorisation  
fee***

**1. The marketing authorisation fee shall be reduced by 50% if the applicant can prove that there is a particular public interest in the Community in the advanced therapy medicinal product or if the return on investment to be expected from the marketing of such a product is small.**

**2. Paragraph 1 shall also apply to fees for post-authorisation activities carried out by the Agency in the first year following the granting of the marketing authorisation for the medicinal product.**

**3. In the case of small and medium-sized enterprises or enterprises which employ not more than 500 persons and have a turnover not exceeding EUR 100 million, or a balance sheet total not exceeding EUR 70 million, paragraph 1 shall also apply to the fees for post-authorisation activities carried out by the Agency without a time limit.**

**4. In the case of an enterprise in which other enterprises have an interest of up to 50% and if this enterprise invests more than 15% of its annual turnover in research and development activities, paragraph 1 shall also apply to the fees for post-authorisation activities carried out by the Agency without a time limit.**

Or. en

#### *Justification*

*Reductions of the fee for marketing authorisations is necessary in cases of ATMPs serving public interest like orphan drugs or where the applicant is an SME. For those products and enterprises the centralised procedure is a big administrative burden which should be eased by minimised fees. The stipulated cost reductions are also necessary in case of autologous ATMPs and those for intended use because these products can only be introduced into the market to a limited extent.*

Amendment by Dagmar Roth-Behrendt

Amendment 85

ARTICLE 21, PARAGRAPH 1, POINT (C)

(c) four members appointed by the Commission, on the basis of a public call for expressions of interest, two *of them to* represent *surgeons* and two *of them to* represent patients associations.

(c) four members *and four alternates* appointed by the Commission, on the basis of a public call for expressions of interest *and after consultation of the European Parliament, of which two members and two alternates shall* represent *health professionals* and two *members and two alternates shall* represent patients associations.

Or. en

*Justification*

*This amendment would ensure a better coherence with existing pharmaceutical legislation and a balanced composition of the Committee for Advanced Therapies.*

Amendment by Urszula Krupa

Amendment 86

ARTICLE 21, PARAGRAPH 1, POINT (C)

(c) *four* members appointed by the Commission, on the basis of a public call for expressions of interest, two of them to represent surgeons and two of them to represent patients associations.

(c) *six* members appointed by the Commission, on the basis of a public call for expressions of interest, two of them to represent surgeons, *two of them to represent bioethics experts* and two of them to represent patients associations..

Or. pl

*Justification*

*Bioethics experts should be included among the scientists on the Committee.*

Amendment by Cristina Gutiérrez-Cortines

Amendment 87

ARTICLE 21, PARAGRAPH 1, POINT (C)

(c) four members appointed by the Commission, on the basis of a public call for expressions of interest, two of them to represent *surgeons* and two of them to represent patients associations.

(c) four members appointed by the Commission, on the basis of a public call for expressions of interest, two of them to represent *physicians* and two of them to represent patients associations.

*Justification*

*Horizontal amendment that should apply to the whole document*

Amendment by Jorgo Chatzimarkakis

Amendment 88

ARTICLE 21, PARAGRAPH 1, POINT (C A) (new)

***(ca) four members and four alternates appointed by the Commission, on the basis of a public call for expressions of interest, who shall have expertise in respect of medical devices that contain or consist of, or are used in conjunction with, tissue engineered products.***

Or. en

*Justification*

*The CAT should be a body made up of experts being able to deliver the scientific expertise providing the basis for the final decision of the CHMP, its responsibility should therefore be increased. In order to ensure an appropriate level of expertise, it would be important to include experts as members that have a background in the evaluation of medical devices, as many of the products concerned share many characteristics of medical devices.*

Amendment by Anne Ferreira

Amendment 89

ARTICLE 21, PARAGRAPH 1, POINT (C A) (new)

***(ca) one member of the Agency's Working Party on pharmacovigilance.***

Or. fr

*Justification*

*In order to ensure that the Committee for Advanced Therapies awards special attention to the consideration of undesirable effects owing to the nature of advanced therapy medicinal products, a representative of the EMEA's Working Party on Pharmacovigilance should be a member of that Committee.*

Amendment by Dagmar Roth-Behrendt

Amendment 90  
ARTICLE 21, PARAGRAPH 2

2. All members of the Committee for Advanced Therapies shall be chosen for their scientific qualification or experience in respect of advanced therapy medicinal products. For the purposes of **point** (b) of paragraph 1, the Member States shall cooperate, under the coordination of the Executive Director of the Agency, in order to ensure that the final composition of the Committee for Advanced Therapies appropriately and in a balanced way covers the scientific areas relevant to advanced therapies, including medical devices, tissue-engineering, gene therapy, cell therapy, biotechnology, pharmacovigilance, risk management **and** ethics.

2. All members of the Committee for Advanced Therapies shall be chosen for their scientific qualification or experience in respect of advanced therapy medicinal products. For the purposes of **points (a) and (b)** of paragraph 1, the Member States shall cooperate, under the coordination of the Executive Director of the Agency, in order to ensure that the final composition of the Committee for Advanced Therapies appropriately and in a balanced way covers the scientific areas relevant to advanced therapies, including medical devices, tissue-engineering, gene therapy, cell therapy, biotechnology, pharmacovigilance, risk management, ethics **and public health**.

Or. en

*Justification*

*This amendment would ensure a better coherence with existing pharmaceutical legislation and a balanced composition of the Committee for Advanced Therapies.*

Amendment by Anne Ferreira

Amendment 91  
ARTICLE 21, PARAGRAPH 2

2. All members of the Committee for Advanced Therapies shall be chosen for their scientific qualification or experience in respect of advanced therapy medicinal products. For the purposes of point (b) of paragraph 1, the Member States shall cooperate, under the coordination of the Executive Director of the Agency, in order to ensure that the final composition of the Committee for Advanced Therapies appropriately and in a balanced way covers

2. All members of the Committee for Advanced Therapies shall be chosen for their scientific qualification or experience in respect of advanced therapy medicinal products, **or for their understanding of the diseases concerned**. For the purposes of point (b) of paragraph 1, the Member States shall cooperate, under the coordination of the Executive Director of the Agency, in order to ensure that the final composition of the Committee for Advanced Therapies

the scientific areas relevant to advanced therapies, including medical devices, tissue-engineering, gene therapy, cell therapy, biotechnology, pharmacovigilance, risk management and ethics.

appropriately and in a balanced way covers the scientific areas relevant to advanced therapies, including medical devices, tissue-engineering, gene therapy, cell therapy, biotechnology, pharmacovigilance, risk management and ethics.

Or. fr

*Justification*

*Article 21 of the proposal for a regulation provides for the committee to include two patients' representatives. However, the phrase 'All members of the Committee ... shall be chosen for their scientific qualification or experience in respect of advanced therapy medicinal products' raises fears that these requirements will exclude the majority of potential patients' representatives from the Committee, since they could not realistically claim to have any experience in respect of advanced therapy medicinal products.*

Amendment by Anne Ferreira

Amendment 92  
ARTICLE 21, PARAGRAPH 5

5. The names and scientific qualifications of the members shall be published **by the Agency**.

5. The names and scientific qualifications of the members shall be published **on the Agency's website at the earliest opportunity**.

Or. fr

*Justification*

*It seems essential for the information on the members of the Committee to be made public and disseminated via the Agency's website.*

Amendment by Dagmar Roth-Behrendt

Amendment 93  
ARTICLE 22, PARAGRAPH 1

1. Members of the Committee for Advanced Therapies and its experts shall undertake to act in the public interest and in an independent manner. They shall not have

1. Members of the Committee for Advanced Therapies and its experts shall undertake to act in the public interest and in an independent manner. They shall not have

financial or other interests in the pharmaceutical sector, medical device sector or biotechnology sector that could affect their impartiality.

financial or other interests in the pharmaceutical sector, medical device sector or biotechnology sector that could affect their impartiality. ***They shall make an annual declaration of their financial interests.***

Or. en

*Justification*

*This amendment clarifies that an identical level of transparency as for existing Committees within the EMEA applies for the new Committee for Advanced Therapies.*

Amendment by Dagmar Roth-Behrendt

Amendment 94

ARTICLE 22, PARAGRAPH 2 A (new)

***2a. Members of the Committee shall declare at each meeting any specific interest which could be considered to be prejudicial to their independence with respect to the items on the agenda. Those declarations shall be made available to the public.***

Or. en

*Justification*

*This amendment clarifies that an identical level of transparency as for existing Committees within the EMEA applies for the new Committee for Advanced Therapies.*

Amendment by Urszula Krupa

Amendment 95

ARTICLE 23, POINT (E A) (new)

***(ea) to ensure observance of bioethical principles in the sourcing, development and testing of advanced therapy medicinal products.***

Or. pl

*Justification*

*This should be one of the Committee's essential tasks.*

Amendment by Anne Ferreira

Amendment 96  
ARTICLE 24, PARAGRAPH 1 A (new)

***Each amendment proposed by the Commission shall be referred to the Committee for Advanced Therapies for its opinion. Each opinion shall be made public at the earliest opportunity.***

Or. fr

*Justification*

*The need to adapt the texts to scientific and technical developments, without their systematic passage before Parliament, must not lead to the interests of the patient being overlooked. Amendment of the rules governing clinical trials and the manufacture of advanced therapy medicinal products, as laid down in this proposal for a regulation, can only be envisaged if there is utmost transparency. The regulation should therefore set out very clearly that the Commission must justify any adaptations and the decision-making process, and that the Committee for Advanced Therapies should systematically be involved.*

Amendment by Miroslav Mikolášik

Amendment 97  
ARTICLE 25, TITLE

***Reporting***

***Report and review***

Or. en

*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 by Miroslav Mikolášik

Amendment 98

ARTICLE 25, PARAGRAPH 1 A (new)

***In this report, the Commission shall also assess the impact of technical progress on the application of this Regulation and, if necessary, make a legislative proposal to review its scope and to include novel therapies which involve neither gene therapy, cell therapy or tissue engineering.***

Or. en

*Justification*

*Scientific advances may make additional novel therapies possible which are neither gene therapy, cell therapy or 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 by Miroslav Mikolášik

Amendment 99

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.

Or. en

*Justification*

*This is a consequential amendment to Article 26A.*

Amendment by Miroslav Mikolášik

Amendment 100

ARTICLE 26 A (new)

***Article 26a***

***Specific provisions on committee procedure***

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

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

***2. The European Parliament, acting by a majority of its members, may object to the draft on the grounds that the Commission has exceeded the implementing powers provided for in this Regulation or on grounds of non-compatibility with the aim or content of this Regulation or of failure to respect the principles of subsidiarity or proportionality.***

***3. If, within a three-month period from the date of referral, the European Parliament opposes the draft measures, the Commission may abandon the measure, make a new proposal or propose new legislation under the legislative procedure.***

***4. If the European Parliament has not opposed the draft measures within the abovementioned period, the measures shall be adopted by the Commission.***

Or. en

*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 making a new agreement on the comitology procedure which is a step forward in balancing their powers. In the meantime, we are introducing the above mentioned procedure to strengthen the Parliament's role.*

Amendment by Dagmar Roth-Behrendt

Amendment 101

ARTICLE 27, POINT -1 (new)

Article 13, paragraph 1 (Regulation (EC) No 726/2004)

***(-1) In Article 13, the first sentence shall be***

*replaced by the following:*

***"Without prejudice to Article 4(4) and 4(5) of Directive 2001/83/EC, a marketing authorisation which has been granted in accordance with this Regulation shall be valid throughout the Community."***

Or. en

*Justification*

*Linked to amendment on Article 28, paragraph 2*

Amendment by Peter Liese

Amendment 102

ARTICLE 27, POINT 2

Annex, point 1 a (Regulation (EC) No 726/2994)

1a. Advanced therapy medicinal products, as defined in Regulation (EC) No [.../of the European Parliament and of the Council (Regulation on Advanced Therapy Medicinal Products)\*].

1a. Advanced therapy medicinal products, as defined in Regulation (EC) No [.../of the European Parliament and of the Council (Regulation on Advanced Therapy Medicinal Products)\*] ***except for advanced therapy medicinal products for autologous or intended use, which are exclusively manufactured and distributed in one Member State and for which this Member State has envisaged the national marketing authorisation procedure in accordance with the criteria of this Regulation as an alternative, for a period of five years subsequent to the granting of the marketing authorisation at national level. Thereafter an application for renewal within the centralised procedure shall be required, with the effect that after renewal the national marketing authorisation becomes a centralised marketing authorisation.***

Or. en

*Justification*

*In order to facilitate the stage of market entry for many SMEs wanting to market their product*

*only in one member state, a marketing authorisation at national level for products marketed at national level should be rendered possible. This national marketing authorisation should be limited to a period of five years. The renewal after this first period of five years can be conducted through a centralised marketing authorisation.*

Amendment by Miroslav Mikolášik

Amendment 103

ARTICLE 27, POINT 2 A (new)

Annex, point 3, subparagraph 2 (Regulation (EC) No. 726/2004)

***(2a) In the Annex, the second subparagraph of point 3 shall be replaced by the following:***

***"After 20 May 2008, the Commission, having consulted the Agency, may present any appropriate proposal modifying this point and the European Parliament and the Council shall take a decision thereon in accordance with the Treaty."***

Or. en

*Justification*

*This part of Regulation 726/2004 determines when a Community authorisation must be obtained. Under the present proposal, it may be that certain AT products will not require Community authorisation either because they do not involve one of the processes referred to in point 1 of the Annex to Reg. 726/2004, or because they are not used for the treatment of any of the diseases referred to in point 3 of that Annex. Currently, the list of diseases in point 3 can be extended by the Council on a Commission's proposal, without recourse to the EP. Decisions determining the scope of legislative acts must be dealt with by co-decision.*

Amendment by Dagmar Roth-Behrendt

Amendment 104

ARTICLE 27, POINT 2 A (new)

Annex, point 3, subparagraph 2 (Regulation (EC) No. 726/2004)

***(2a) In the Annex, the second subparagraph of point 3 shall be replaced by the following***

***"After 20 May 2008, the Commission, having consulted the Agency, may present any appropriate proposal modifying this***

***point and the European Parliament and the Council shall take a decision thereon in accordance with the Treaty."***

Or. en

*Justification*

*This amendment ensures Parliament's fair participation in accordance with the Treaty establishing the European Community with regard to changes to the list of pharmaceuticals for human use which fall under the centralised authorisation procedure.*

Amendment by Linda McAvan

Amendment 105

ARTICLE 28, POINT 1

Article 3, paragraph 7 (Directive 2001/83/EC)

***(1) In Article 3, the following paragraph 7 is added:*** ***deleted***

***"7. Any advanced therapy medicinal product, as defined in Regulation (EC) No [.../of the European Parliament and of the Council (Regulation on Advanced Therapy Medicinal Products\*)] which is both prepared in full and used in a hospital, in accordance with a medical prescription for an individual patient."***

Or. en

*Justification*

*The existing proposal is overly restrictive in that it does not cover the situation where more than one hospital co-operates, which is likely to be a frequent situation in this area of innovative healthcare. Neither does it cover a situation where another kind of institution, such as charity, co-operates with a hospital. Moreover, given the different legal and organisation arrangements of health services in Member States the legal effect of the provision is likely to vary arbitrarily. There is also a risk of creating a loophole where some hospitals could find ways of presenting large scale, fully commercial and standardised tissue engineering activity as meeting the criteria for this exemption. This would risk inconsistent standards and a reduction in public health protection.*

Amendment by Cristina Gutiérrez-Cortines

Amendment 106

ARTICLE 28, POINT 1

Article 3, paragraph 7 (Directive 2001/83/EC)

7. Any advanced therapy medicinal product, as defined in Regulation (EC) No [.../of the European Parliament and of the Council (Regulation on Advanced Therapy Medicinal Products)\*], which is both prepared in full and used in a hospital, **in accordance with a medical prescription for an individual patient.**

7. Any advanced therapy medicinal product, as defined in Regulation (EC) No [.../of the European Parliament and of the Council (Regulation on Advanced Therapy Medicinal Products)\*], which is both prepared in full and used in a hospital, **prepared in a non-profit manner and used at a national level.**

Or. en

*Justification*

*Advanced medical products manufactured by a non standardised procedure are to be excluded from this regulation, since they are not an industrial manufacturing as a consequences they should be excluded those products that are produced and used on a hospital setting.*

Amendment by Vittorio Prodi

Amendment 107

ARTICLE 28, POINT 1

Article 3, paragraph 7 (Directive 2001/83/EC)

7. Any advanced therapy medicinal product as defined in Regulation (EC) No (.../ of the European Parliament and of the Council (Regulation on Advanced therapy Medicinal products), which is both prepared in full and used in a hospital, in accordance with a medical prescription for an individual patient.

7. Any advanced therapy medicinal product as defined in Regulation (EC) No (.../ of the European Parliament and of the Council (Regulation on Advanced therapy Medicinal products), which is both prepared in full and used in a hospital **or in a network of public hospitals** in accordance with a medical prescription for an individual patient **or for non-profit clinical research.**

Or. en

Amendment by Dagmar Roth-Behrendt

Amendment 108

ARTICLE 28, POINT 1

Article 3, paragraph 7 (Directive 2001/83/EC)

7. Any advanced therapy medicinal product, as defined in Regulation (EC) No [...] of the European Parliament and of the Council (Regulation on Advanced Therapy Medicinal Products)\*], which is both prepared in full and used in a hospital, in accordance with a medical prescription for an individual patient.

7. Any advanced therapy medicinal product, as defined in Regulation (EC) No [...] of the European Parliament and of the Council (Regulation on Advanced Therapy Medicinal Products)\*], which is both prepared in full and used in a hospital, in accordance with a medical prescription for an individual patient ***under the exclusive professional responsibility of a medical practitioner.***

Or. en

*Justification*

*Any exclusion from the scope of this regulation shall be limited in order to ensure that patients in all Member States benefit quickly from innovations.*

Amendment by Dagmar Roth-Behrendt

Amendment 109

ARTICLE 28, POINT 2

Article 4, paragraph 5 (Directive 2001/83/EC)

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.

5. This Directive and all Regulations referred to therein shall not affect the application of ***non-discriminatory*** 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 ***on grounds not dealt with in the aforementioned Community legislation.*** The Member States shall communicate the national legislation concerned to the Commission. ***Information on such existing national legislation shall be listed in a register that is updated regularly and made publicly available.***

Or. en

*Justification*

*This amendment takes one of the solutions proposed by Parliament's legal service on legal problems identified with regard to the Commission's proposal. A register listing existing national legislation prohibiting or restricting the use of specific types of cells shall be set up in order to facilitate research and the authorisation of new advanced therapy products.*

Amendment by Linda McAvan

Amendment 110

ARTICLE 28, POINT 2 A (new)

Article 5, paragraph 1 a (new) (Directive 2001/83/EC)

***(2a) In Article 5, the following paragraph 1a is inserted:***

***"1a. Member States may exempt from the provisions of Article 6 advanced therapy medicinal products which are supplied in response to a bona fide unsolicited order, formulated in accordance with the specifications of an authorised health-care professional and for use by an individual patient under the direct personal responsibility of that healthcare professional."***

Or. en

*Justification*

*The existing proposal is overly restrictive in that it does not cover the situation where more than one hospital co-operates, which is likely to be a frequent situation in this area of innovative healthcare. Neither does it cover a situation where another kind of institution, such as charity, co-operates with a hospital. Moreover, given the different legal and organisation arrangements of health services in Member States the legal effect of the provision is likely to vary arbitrarily. There is also a risk of creating a loophole where some hospitals could find ways of presenting large scale, fully commercial and standardised tissue engineering activity as meeting the criteria for this exemption. This would risk inconsistent standards and a reduction in public health protection.*

Amendment by Vittorio Prodi

Amendment 111

ARTICLE 28 A (new)

*Article 28 a*

*Production for clinical trials*

*The Commission shall identify, in accordance with the procedure referred to in Decision 1999/468/EC, specific manufacturing requirements, among those foreseen by the guidelines of good manufacturing practice of investigational medicinal products, to be applied to the production of advanced therapy medicinal products for clinical trials to be performed in the same hospital where the production took place.*

Or. en

*Justification*

*No specific provision is foreseen in the Regulation as far as concerns the production of advanced medicinal products to be used in clinical trials is concerned.*

Amendment by Peter Liese

Amendment 112

ARTICLE 29, PARAGRAPH 1

1. Advanced therapy medicinal products which were legally on the Community market in accordance with national or Community legislation at the time of entry into force of this Regulation **shall comply with this Regulation** no later than **2 years** after *its* entry into force.

1. **For** advanced therapy medicinal products, **other than tissue engineered products**, which were legally on the Community market in accordance with national or Community legislation at the time of entry into force of this Regulation, **an application for a marketing authorisation shall be filed** no later than **five years** after **the** entry into force **of this Regulation**.

Or. en

*Justification*

*The envisaged transitional period of two years is too short, since the duration of the clinical trials alone will in many cases exceed the proposed time period. Furthermore the applicant should only be responsible for the date of filing the application and not for delays due to the Agency/national competent authorities or problems during the assessment phase. Otherwise, it could deprive patients from these important new medicinal products.*

Amendment by Dagmar Roth-Behrendt

Amendment 113  
ARTICLE 29, PARAGRAPH 1

1. Advanced therapy medicinal products which were legally on the Community market in accordance with national or Community legislation at the time of entry into force of this Regulation shall comply with this Regulation no later than **2 years** after its entry into force.

1. Advanced therapy medicinal products which were legally on the Community market in accordance with national or Community legislation at the time of entry into force of this Regulation shall comply with this Regulation no later than **5 years** after its entry into force.

Or. en

*Justification*

*The transitional period should be extended in order to enable the adjustment to the new legislation for products already legally on the market.*

Amendment by John Bowis

Amendment 114  
ARTICLE 29, PARAGRAPH 1

1. **Advanced** therapy medicinal products which were legally on the **Community** market in accordance with national or Community legislation at the time of entry into force of this Regulation **shall comply with this Regulation no later than 2 years** after **its** entry into force.

1. **Gene and cell** therapy medicinal products which were legally on the market **in the Community** in accordance with national or Community legislation at the time of entry into force of this Regulation **may remain on the market for a period of 2 years** after **the** entry into force **of this Regulation**.

Or. en

*Justification*

*Human tissue engineered products are currently unregulated. The transitional period should be sufficiently long to ensure that manufacturers have enough time to perform the necessary tests and applications in order not to stop on-going therapies unnecessarily. It is also important that this transition period starts when all specific technical requirements are available and applicable.*

Amendment by John Bowis

Amendment 115  
ARTICLE 29, PARAGRAPH 1 A (new)

***1a. Tissue engineered products which were legally on the market in the Community in accordance with national or Community legislation at the date of application specified in the second paragraph of Article 30 may remain on the market for a period of 5 years after the date specified in the first paragraph of Article 30.***

Or. en

*Justification*

*Human tissue engineered products are currently unregulated. The transitional period should be sufficiently long to ensure that manufacturers have enough time to perform the necessary tests and applications in order not to stop on-going therapies unnecessarily. It is also important that this transition period starts when all specific technical requirements are available and applicable.*

Amendment by Miroslav Mikolášik

Amendment 116  
ARTICLE 29, PARAGRAPH 1 A (new)

***1a. Tissue engineered products which are legally on the Community market in accordance with national or Community legislation at the date of application specified in the second paragraph of Article 30 must comply with this Regulation no later than 4 years after the date specified in that paragraph.***

Or. en

*Justification*

*Manufacturers will not be in a position to design development protocols until all the requirements specific to tissue engineering products are published. The transitional period for these products must therefore take into account the time to publish all these necessary requirements.*

Amendment by Peter Liese

Amendment 117

ARTICLE 29, PARAGRAPH 1 A (new)

***1a. For tissue engineered products which are legally on the Community market in accordance with national or Community legislation at the time of entry into force of the technical requirements referred to in Article 8, an application for a marketing authorisation shall be filed no later than five years after the entry into force of those technical requirements.***

Or. en

*Justification*

*The envisaged Transitional period of two years is too short, since the duration of the clinical trials alone will in many cases exceed the proposed time period. Furthermore the applicant should only be responsible for the date of filing the application and not for delays due to the Agency/national competent authorities or problems during the assessment phase. Otherwise, it could deprive patients from these important new medicinal products.*

Amendment by John Bowis

Amendment 118

ARTICLE 29, PARAGRAPH 2

2. By way of derogation from Article 3(1) of Regulation (EC) No 297/95, no fee shall be payable to the Agency in respect of applications submitted for the authorisation of the advanced therapy medicinal products mentioned in ***paragraph 1***.

2. By way of derogation from Article 3(1) of Regulation (EC) No 297/95, no fee shall be payable to the Agency in respect of applications submitted for the authorisation of the advanced therapy medicinal products mentioned in ***paragraphs 1 and 1a***.

Or. en

*Justification*

*Human tissue engineered products are currently unregulated. The transitional period should be sufficiently long to ensure that manufacturers have enough time to perform the necessary tests and applications in order not to stop on-going therapies unnecessarily. It is also important that this transition period starts when all specific technical requirements are available and applicable.*

Amendment by Miroslav Mikolášik

Amendment 119  
ARTICLE 30, PARAGRAPH 2

***The measures envisaged in Articles 4, 5 and 8 shall be presented to the European Parliament by [6 months after the publication of this Regulation in the Official Journal of the European Union].***

*It shall apply from [3 months after entry into force]*

***This Regulation shall apply from [3 months after entry into force].***

***For tissue engineered products this Regulation shall apply as of the entry into force of all the requirements referred to in Articles 4, 5 and 8.***

Or. en

*Justification*

*Manufacturers will not be in a position to design development protocols until the technical requirements are published and the adaptations of the Good Clinical Practice Directive and the Good Manufacturing Practice Directive are finalised. Therefore, we propose 6 months time limit for the Commission to adopt the necessary measures.*

Amendment by John Bowis

Amendment 120  
ARTICLE 30, PARAGRAPH 2

*It shall apply from [3 months after entry into force]*

*It shall apply from [3 months after entry into force], **except for tissue engineered products.***

***For tissue engineered products this Regulation shall apply from the date on which all the requirements referred to in Articles 4,5 and 8 have entered into force.***

Or. en

*Justification*

This is necessary to take into account the different timeframes necessary for the application of

Regulations and Directives. The proposal recognises that the pharmaceutical regime cannot be applied to Tissue Engineered Products as it currently stands. It is therefore important that the Regulation is applicable only when all the directives modified by it are also of application.