REPORT


Committee on the Environment, Public Health and Food Safety

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(*) Enhanced cooperation between committees - Rule 47 of the Rules of Procedure
Symbols for procedures

* Consultation procedure  
majority of the votes cast

**I Cooperation procedure (first reading)  
majority of the votes cast

**II Cooperation procedure (second reading)  
majority of the votes cast, to approve the common position
majority of Parliament’s component Members, to reject or amend the common position

*** Assent procedure  
minority of Parliament’s component Members except in cases covered by Articles 105, 107, 161 and 300 of the EC Treaty and Article 7 of the EU Treaty

***I Codecision procedure (first reading)  
majority of the votes cast

***II Codecision procedure (second reading)  
majority of the votes cast, to approve the common position
majority of Parliament’s component Members, to reject or amend the common position

***III Codecision procedure (third reading)  
majority of the votes cast, to approve the joint text

(The type of procedure depends on the legal basis proposed by the Commission.)

Amendments to a legislative text

In amendments by Parliament, amended text is highlighted in bold italics. Highlighting in normal italics is an indication for the relevant departments showing parts of the legislative text for which a correction is proposed, to assist preparation of the final text (for instance, obvious errors or omissions in a given language version). These suggested corrections are subject to the agreement of the departments concerned.
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(*) Enhanced cooperation between committees - Rule 47 of the Rules of Procedure
DRAFT EUROPEAN PARLIAMENT LEGISLATIVE RESOLUTION


(Codecision procedure: first reading)

The European Parliament,

– having regard to the Commission proposal to the European Parliament and the Council (COM(2005)0567)

– having regard to Article 251(2) and Article 95 of the EC Treaty, pursuant to which the Commission submitted the proposal to Parliament (C6-0401/2005),

– having regard to Rule 51 of its Rules of Procedure,

– having regard to the report of the Committee on the Environment, Public Health and Food Safety and the opinions of the Committee on Industry, Research and Energy and the Committee on Legal Affairs (A6-0031/2007),

1. Approves the Commission proposal as amended;

2. Calls on the Commission to refer the matter to Parliament again if it intends to amend its proposal substantially or replace it with another text;

3. Instructs its President to forward its position to the Council and Commission.

Text proposed by the Commission

Amendments by Parliament

Amendment 1

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

1 Not yet published in OJ.
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.

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 2

RECITAL 5

(5) Advanced therapy medicinal products should be regulated in so far as they are intended to be placed on the market in Member States and either prepared industrially or manufactured by a method involving an industrial process, within the meaning of Article 2(1) of Directive 2001/83/EC. Advanced therapy medicinal products which are both prepared in full and used in a hospital, in accordance with a medical prescription for an individual patient, should thus be excluded from the scope of the present Regulation.

(5) This Regulation is a lex specialis, which introduces additional provisions to those laid down in Directive 2001/83/EC. The scope of this Regulation should be to regulate advanced therapy medicinal products which are intended to be placed on the market in Member States and either prepared industrially or manufactured by a method involving an industrial process, in accordance with the general scope of the Community pharmaceutical legislation laid down in Title II of Directive 2001/83/EC. Advanced therapy medicinal products which are prepared in full in a hospital in a non-profit manner and on a one-off basis according to a specific, non-standardised and non-patented process, and used in a hospital, in order to comply with an individual medical prescription for an individual patient under the exclusive professional responsibility of a medical practitioner or for clinical research, should thus be excluded from the scope of this Regulation.
Justification

It should be clarified that this Regulation is a lex specialis in relation to Dir. 2001/83/EC, as it introduces additional requirements that are specific to ATMP. The scope of this Regulation is the general scope of the pharmaceutical legislation, as laid down in Dir. 2001/83/EC. Where hospitals or other institutions prepare products using an established process to create treatments for patients on a routine basis, they should have to comply with the provisions of this Regulation. However, when hospitals produce ATMP for research purposes or on an exceptional, one-off basis, they should not have to comply with the centralised authorisation procedure.

Amendment 3
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) Legislation in force in Member States concerning the use of certain types of cells, such as embryonic stem cells, varies 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 of 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 controversies.

Justification

JURI amendment, which was incorporated in the report without vote following Rule 47. 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 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 4

RECITAL 9

(9) The evaluation of advanced therapy medicinal products often requires very specific expertise, which goes beyond the traditional pharmaceutical field and covers areas on the borderline to other sectors such as biotechnology and medical devices. For this reason, it is appropriate to create, within the Agency, a Committee for Advanced Therapies, which the Committee for Medicinal Products for Human Use of the Agency should consult on the assessment of data related to advanced therapy medicinal products, before issuing its final scientific opinion. In addition, the Committee for Advanced Therapies may be consulted for the evaluation of any other medicinal product which requires specific expertise falling within its area of competence.

Justification

Due to a highly specific and unique character of the advanced therapy medicinal products, a new Committee for Advanced Therapies is established within EMEA and composed of experts having specific qualifications or experience in this highly innovative and quickly developing field. Therefore, the new structure should be responsible for drafting an opinion on the quality, safety, and efficacy of products for the final approval by the CHMP. Furthermore, the committee should be consulted for the evaluation of other products under its competence.

Amendment 5

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.

Justification

In order to cover all other medical fields which the advanced therapies may relate to, the Committee for Advanced Therapies should be represented by a more general medical expertise.

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.

Amendment 7
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.

Specific manufacturing requirements for investigational medicinal products to be applied to the production of advanced therapy medicinal products for clinical trials performed in the same hospital where the production took place should be laid down. Those rules should ensure an adequate time interval between single clinical trials (including multi-centre clinical trials) and a coordinated surveillance and information exchange.

Justification

No specific provision is foreseen in the regulation as far as the production of advanced therapy medicinal products to be used in clinical trials performed in the same hospital where the production took place is concerned. Moreover, clinical trials should be conducted in the safest possible manner (adequate time interval, etc).

Amendment 8
RECITAL 16

(16) The manufacture of advanced therapy medicinal products should be in compliance with the principles of good manufacturing practice, as set out in Commission Directive 2003/94/EC of 8 October 2003 laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use. Furthermore, guidelines specific to advanced therapy medicinal products should be drawn up, so as to properly reflect the particular nature of their
Advanced Therapy medicinal products have specific characteristics that differ greatly from traditional medicinal products. That leads to important differences in their manufacturing process (e.g. in Article 11.4, the GMP Directive requires that sample batches of finished products should be kept for 1 year after expiry date. It is, however, difficult to consider expiry dates for certain classes of ATMPs).

Amendment 9
RECITAL 17


Justification
In order to ensure the continuous utilisation of the vast experience and expertise of the notified bodies on the evaluation of medical devices or active implantable medical devices, the notified bodies may assess the medical device or the active implantable medical device part of the combined advanced therapy medicinal product. In that case, the Agency should take into account the results of these assessments in its final evaluation of the combined product.

Amendment 10
RECITAL 18

(18) Specific rules should be laid down, where available, the results of the assessment of the medical device or the active implantable medical device by a notified body in accordance with those Directives should be taken into account by the Agency in the evaluation of a combined product carried out under this Regulation.

Justification
In order to ensure the continuous utilisation of the vast experience and expertise of the notified bodies on the evaluation of medical devices or active implantable medical devices, the notified bodies may assess the medical device or the active implantable medical device part of the combined advanced therapy medicinal product. In that case, the Agency should take into account the results of these assessments in its final evaluation of the combined product.
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.

These rules should comply fully with the patient's right to know the origin of any cells or tissues used in the preparation of advanced therapy medicinal products, while respecting donor anonymity.

Amendment 11
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.

Justification

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

Amendment 12
RECITAL 19A (new)

(19a) The operation of this Regulation requires the establishment of guidelines, to be drawn up either by the Agency or by the Commission. In both cases, open consultation with all interested parties, in particular the industry, should be enacted in order to allow a pooling of the limited expertise in this area and ensure proportionality.

Justification

When drawing up guidelines for the implementation of this Regulation, principles of open
consultation with all interested parties, in particular the industry should be enacted in order to allow a pooling of the limited expertise in this area and ensure proportionality.

Amendment 13
RECITAL 21

(21) As science evolves very rapidly in this field, undertakings developing advanced therapy medicinal products should be enabled to request scientific advice from the Agency, including advice on post-authorisation activities. As an incentive, the fee for that scientific advice should be kept at a minimal level.

Amendments 13
RECITAL 21

(21) As science evolves very rapidly in this field, undertakings developing advanced therapy medicinal products should be enabled to request scientific advice from the Agency, including advice on post-authorisation activities. As an incentive, the fee for that scientific advice should be kept at a minimal level for small and medium-sized enterprises, and should also be reduced for other applicants.

Justification

This Regulation seeks to encourage and support SMEs in the development of ATMPs. Therefore, it is necessary to introduce special fee-waivers applicable to SMEs on scientific advice.

Amendment 14
RECITAL 22

(22) The Agency should be empowered to give scientific recommendations on whether a given product based on cells or tissues meets the scientific criteria which define advanced therapy medicinal products, in order to address, as early as possible, questions of borderline with other areas such as cosmetics or medical devices, which may arise as science develops.

Amendments 14
RECITAL 22

(22) The Agency should be empowered to give scientific recommendations on whether a given product based on genes, cells or tissues meets the scientific criteria which define advanced therapy medicinal products, in order to address, as early as possible, questions of borderline with other areas such as cosmetics or medical devices, which may arise as science develops. The Committee for Advanced Therapies, with its unique expertise, should have a prominent role in the provision of such advice.

Justification

Due to its specific expertise in advanced therapy medicinal products, the Committee for Advanced Therapies should be instrumental in providing advice to operators on whether a product is or is not an advanced therapy medicinal product.
(24) In order to take into account scientific and technical developments, the Commission should be empowered to adopt any necessary changes regarding the technical requirements for applications for marketing authorisation of advanced therapy medicinal products, the summary of product characteristics, labelling, and package leaflet. The Commission should ensure that relevant information on envisaged measures is made available to interested parties without delay.

Justification

*Better predictability of future regulations is of the greatest importance for industry in order to make well-planned and cost-effective investments in R&D and production. Therefore, relevant information about envisaged measures should be made known as quickly as possible.*

Amendment 16

RECITAL 27

(27) The measures necessary for the implementation of this Regulation should be adopted in accordance with Council Decision 1999/468/EC of 28 June 1999 laying down the procedures for the exercise of implementing powers conferred on the Commission. The regulatory procedure with scrutiny provided for in Article 5a of that Decision should apply to the adoption of amendments to Annexes II to IV to this Regulation and to Annex I to Directive 2001/83/EC. Since these measures are essential for the proper operation of the whole regulatory framework, they should be adopted swiftly, within 9 months after the entry into force of this Regulation.

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 9 months time limit for the Commission to adopt the necessary measures.*

Amendment 17

ARTICLE 1 A (new)

PE 380.740v02-00 14/93 RR\380740EN.doc
Article 1a

Exclusions

This Regulation shall not apply to advanced therapy medicinal products that contain or are derived from human embryonic or foetal cells, primordial germ cells or cells derived from those cells.

Justification

JURI amendment, which was incorporated in the report without vote following Rule 47. 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).

Amendment 18
ARTICLE 2, PARAGRAPH 1, POINT (B), INTRODUCTORY PART

(b) tissue engineered product means a product that:

Justification

Adding the term "medicinal" clarifies that products which do not meet the definition of a medicinal product cannot be covered by this regulation.

Amendment 19
ARTICLE 2, PARAGRAPH 1, POINT (B), SUBPARAGRAPH 2 A (new)

Products containing or made exclusively of non-viable human or animal cells and/or tissues, which do not contain any viable cells or tissues and 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 20
ARTICLE 2, PARAGRAPH 1, POINT (D), INDENT 1 A (new)

- its cellular or tissue part contains viable cells or tissues; or

Justification
For the purposes of this Regulation, the most important criterion when defining a combined advanced therapy medicinal product should be the viability of its cellular or tissue part. For the patient's safety and the high standards of the evaluation of a product, a combined product should be always classified as an advanced therapy medicinal product when it contains viable tissues or cells.

Amendment 21
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 containing non-viable cells or tissues must be liable to act upon the human body with action that can be considered as primary to that of the devices referred to.

Justification
A combined product should always be considered as advanced therapy medicinal product when it contains non-viable cells or tissues which act upon human body in a manner that is considered as primary to the action of the device part of the product concerned.

Amendment 22
ARTICLE 2, PARAGRAPH 1, SUBPARAGRAPH 1 A (new)

Where a product contains viable cells or tissues, the pharmacological, immunological or metabolic action of those cells or tissues shall be considered as the primary mode of action of the product.

Justification
This new provision clarifies the rule concerning products which contain viable cells or tissues, whilst maintaining in principle the criterion of “primary mode of action” for borderline classification. For the patient's safety and the high standards of the evaluation of a combined product, the most important criterion should be the viability of the cellular or tissue part of such a product.
Amendment 23
ARTICLE 4, PARAGRAPHS 2 AND 3

2. The Commission shall, in accordance with the procedure referred to in Article 26(2), amend Directive 2005/28/EC in order to take account of the specific characteristics of advanced therapy medicinal products.

3. The Commission shall draw up detailed guidelines on good clinical practice specific to advanced therapy medicinal products.

Justification

The Regulation should set out very clearly that the Commission must involve the EMEA, through the Committee for Advanced Therapies, whenever good clinical practice requirements need to be amended or guidelines related to advanced therapy medicinal products need to be drawn up.

Amendment 24
ARTICLE 5, PARAGRAPH -1 (new)

The Commission shall, in accordance with the procedure referred to in Article 26(2), amend Directive 2003/94/EC to take into account the specific characteristics of advanced therapy medicinal products and in particular tissue engineered products.

Justification

Advanced therapy medicinal products have specific characteristics that differ greatly from traditional medicinal products. That leads to important differences in their manufacturing process (e.g. Article 11.4. of the GMP Directive requires that sample batches of finished products should be kept for 1 year after the expiry date. It is, however, difficult to consider expiry dates for certain classes of ATMPs).
Detailed guidelines in line with the principles of good manufacturing practice and specific to advanced therapy medicinal products shall be published by the Commission.

The Commission shall draw up detailed guidelines in line with the principles of good manufacturing practice and specific to advanced therapy medicinal products.

**Justification**

For the sake of consistency, the wording should be put in line with the equivalent provision in Article 4(3).

**Amendment 26**

**ARTICLE 7**

Specific requirements for tissue engineered products

Specific requirements for advanced therapy medicinal products containing devices

In addition to the requirements laid down in Article 6(1) of Regulation (EC) No 726/2004, applications for the authorisation of a tissue engineered product shall include a description of the physical characteristics and performance of the product and a description of the product design methods, in accordance with Annex I to Directive 2001/83/EC.

In addition to the requirements laid down in Article 6(1) of Regulation (EC) No 726/2004, applications for the authorisation of an advanced therapy medicinal product containing medical devices, bio-materials, scaffolds or matrices shall include a description of the physical characteristics and performance of the product and a description of the product design methods, in accordance with Annex I to Directive 2001/83/EC.

**Justification**

The scope of this article should be clarified and amended to encompass all those products in need of these specific requirements. Restricting the requirements to tissue engineered products would exclude those advanced therapy medicinal products that also have special physical characteristics possibly affecting the performance of the product. However, extending these requirements to all advanced therapy products would create unnecessary work for enterprises; all advanced therapy products do not have special physical characteristics that could affect their performance.

**Amendment 27**

**ARTICLE 8**

The Commission shall, in accordance with the procedure referred to in Article 26(2) of

The Commission shall, after consultation of the Agency and in accordance with the
this Regulation, amend Annex I to Directive 2001/83/EC in order to lay down technical requirements that are specific to tissue engineered products, in particular those referred to in Article 7, with a view to taking account of scientific and technical evolution.  

procedure referred to in Article 26(2a) of this Regulation, amend Annex I to Directive 2001/83/EC in order to lay down technical requirements that are specific to tissue engineered products, in particular those referred to in Article 7, with a view to taking account of scientific and technical evolution.

Justification

_The Regulation should set out very clearly that the Commission must involve the EMEA, through the Committee for Advanced Therapies, whenever the technical requirements laid down in Annex I to Directive 2001/83/EC need to be amended._

Amendment 28

**ARTICLE 9, PARAGRAPH 2**

2. The rapporteur or co-rapporteur appointed by the Committee for Medicinal Products for Human Use pursuant to Article 62 of Regulation (EC) No 726/2004 shall be a member of the Committee for Advanced Therapies. This member shall also act as rapporteur or co-rapporteur for the Committee for Advanced Therapies.

2. The rapporteur or co-rapporteur appointed by the Committee for Medicinal Products for Human Use pursuant to Article 62 of Regulation (EC) No 726/2004 shall be a member of the Committee for Advanced Therapies, _proposed by the Committee for Advanced Therapies and having specific expertise for the product_. This member shall also act as rapporteur or co-rapporteur for the Committee for Advanced Therapies.

Justification

_In order to ensure the highest level of expertise, the rapporteur and co-rapporteur appointed by the CHMP should be proposed by the Committee for Advanced Therapies and should have specific expertise for the relevant product._

Amendment 29

**ARTICLE 9, PARAGRAPH 2 A (new)**

2a. _When preparing a draft opinion for final approval by the Committee for Medicinal Products for Human Use, the Committee for Advanced Therapies shall endeavour to reach a scientific consensus. If such consensus cannot be reached, the Committee for Advanced Therapies shall_
adopt the position of the majority of its members. The draft opinion shall mention the divergent positions and the grounds on which they are based.

Justification

In order to guarantee transparency in the process of preparation of a draft opinion, a clear decision procedure should be defined within Committee for Advanced Therapies. Consequently, we suggest that a scientific consensus should be reached by its members.

Amendment 30
ARTICLE 9, PARAGRAPH 2 B (new)

2b. 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.

In case of disagreement with the draft opinion of the Committee for Advanced Therapies, the applicant may submit, within 15 days of receipt of the draft opinion, written observations to the Committee for Medicinal Products for Human Use. The applicant shall be heard by the Committee for Medicinal Products for Human Use before it issues its opinion, if the applicant so requests in its written observations.

Justification

The amendment aims at enhancing a more transparent procedure. Due to Article 9 (2) of Regulation (EC) No 726/2004 where the applicant is given the opportunity to request a re-examination of the opinion of the Committee for Medicinal Products for Human Use in giving written notice to the agency, an applicant receiving an opinion from the Committee of Advanced Therapies shall also receive the opportunity of appeal in order to ensure consistency within the Agency.

Amendment 31
ARTICLE 9, PARAGRAPH 3

3. The advice given by the Committee for

3. The draft opinion given by the
Advanced Therapies under paragraph 1 shall be sent to the chairman of the Committee for Medicinal Products for Human Use in a timely manner so as to ensure that the deadline laid down in Article 6(3) of Regulation (EC) No 726/2004 can be met.

Committee for Advanced Therapies under paragraph 1 shall be sent to the chairman of the Committee for Medicinal Products for Human Use in a timely manner so as to ensure that the deadline laid down in Article 6(3) or 9(2) of Regulation (EC) No 726/2004 can be met.

**Justification**

*Due to the highly specific and unique character of the advanced therapy medicinal products, a new Committee for Advanced Therapies is established within EMEA, composed of experts having specific qualifications or experience in this highly innovative and quickly developing field. Therefore, this new structure should be responsible for drafting an opinion on the quality, safety, and efficacy of products for the final approval by the CHMP. The draft opinion should be given in a timely manner so the deadline laid down in Article 9(2) of Regulation (EC) No 726/2004 can also be met.*

**Amendment 32**

**ARTICLE 9, PARAGRAPH 4**

4. Where the scientific opinion on an advanced therapy medicinal product drawn up by the Committee for Medicinal Products for Human Use under Article 5, paragraphs 2 and 3 of Regulation (EC) No 726/2004 is not in accordance with the advice of the Committee for Advanced Therapies, the Committee for Medicinal Products for Human Use shall annex to its opinion a detailed explanation of the scientific grounds for the differences.

4. Where the scientific opinion on an advanced therapy medicinal product drawn up by the Committee for Medicinal Products for Human Use under Article 5(2) and (3) of Regulation (EC) No 726/2004 is not in accordance with the **draft opinion** of the Committee for Advanced Therapies, the Committee for Medicinal Products for Human Use shall annex to its opinion a detailed explanation of the scientific grounds for the differences.

**Justification**

*See the justification for the amendment of the Article 9, paragraph 3.*

**Amendment 33**

**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

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. be subject to final evaluation by the Agency.

Justification

According to paragraph 2, a medical device or the active implantable medical device part of a combined advanced therapy medicinal product have to be assessed by a notified body in order to benefit from its extensive specific experience. The final evaluation should be carried out by the Agency who should incorporate the assessment of a notified body in its final opinion.

Amendment 34
ARTICLE 10, PARAGRAPH 1 A (new)

1a. The application for a marketing authorisation for a combined advanced therapy medicinal product shall include evidence of conformity with the essential requirements referred to in Article 6.

Justification

In accordance with Article 6 of the proposed Regulation, the device part of a combined advanced therapy medicinal product must meet the relevant device essential requirements. Evidence of conformity with these requirements should be provided in the marketing authorisation application.

Amendment 35
ARTICLE 10, PARAGRAPH 2

2. Where the medical device or active implantable medical device which is part of a combined advanced therapy medicinal product has already been assessed by a notified body in accordance with Directive 93/42/EEC or Directive 90/385/EEC, the Agency shall take account of the results of that assessment in its evaluation of the medicinal product concerned.

The Agency may request the relevant notified body to transmit any information

2. The application for a marketing authorisation for a combined advanced therapy medicinal product shall include, where available, the results of the assessment by a notified body in accordance with Directive 93/42/EEC or Directive 90/385/EEC of the medical device or active implantable medical device part. The Agency shall take account of the results of that assessment in its evaluation of the medicinal product concerned.

The Agency may request the relevant notified body to transmit any information
related to the results of its assessment. The notified body shall transmit the information within a period of one month.

If the application does not include the results of the assessment, then the Agency may seek an opinion on the conformity of the device part with Annex I to Directive 93/42/EEC or Directive 90/385/EEC from a notified body identified in conjunction with the applicant.

Amendment 36
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 easy to use.

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 37
ARTICLE 15, TITLE

Post-authorisation Risk Management

Post-authorisation follow-up of efficacy and adverse reactions, and Risk Management

Justification

This is a consequential amendment to amendment 38 (Article 15, paragraph 1).
Amendment 38
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 authorisation application, the measures envisaged to ensure the follow-up of efficacy of advanced therapy medicinal products.

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 and of adverse reactions thereto.

Justification

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

Amendment 39
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, characterise, 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.

Justification

In order to ensure the effectiveness of the risk management system, the Commission should have an obligation to require necessary measures to be carried out when there is a cause for concern.

Amendment 40
ARTICLE 16, PARAGRAPH 1

1. The holder of a marketing authorisation

1. The holder of a marketing authorisation
for an advanced therapy medicinal product shall establish and maintain a system ensuring that the individual product and its starting and raw materials, including all substances coming into contact with the tissues or cells it may contain, can be traced through the sourcing, manufacturing, packaging, transport and delivery to the hospital, institution or private practice where the product is used.

Justification

Traceability during storing steps should also be ensured. Adding ‘storing’ establishes a coherent system of product traceability, and is in line with Directive 2004/23/EC.

Amendment 41
ARTICLE 16, PARAGRAPH 4

4. The marketing authorisation holder shall keep the data referred to in the first paragraph for a minimum of 30 years after placing the product on the market, or longer if required by the Commission as a term of the marketing authorisation.

Justification

The proposed wording is unambiguous, whereas “placing on the market” might create difficulties in interpretation. The proposed wording provides a pragmatic solution for the marketing authorisation holder to know exactly from when traceability data must be kept.

Amendment 42
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 small and medium-sized enterprises and 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.
Justification

This Regulation seeks to encourage and support SME's in the development of ATMPs. Therefore, it is necessary to introduce special fee-waivers applicable to SME's on scientific advice. The 10% of the basic fee which the SME's should cover themselves is a symbolic amount, in order to prevent any abuse of the totally gratis system. Moreover, to support the applicants which do not fall under the SME criteria and to ensure the competitiveness of the whole sector, a reduction of 65% should be applied to all companies irrespective of their size.

Amendment 43
ARTICLE 18, PARAGRAPH 1

1. Any applicant developing a product based on cells or tissues may request a scientific recommendation of the Agency with a view to determining whether the referred product falls, on scientific grounds, within the definition of an advanced therapy medicinal product. The Agency shall deliver this recommendation after consultation with the Commission.

Justification

It should be clarified that the procedure foreseen in this Article may apply to all types of advanced therapy medicinal products, including products based on genes. The proposed amendment also foresees that an applicant will get clarity on the classification of the concerned product in a timely manner, thus facilitating business planning and further development of the product.

Amendment 44
ARTICLE 19 A (new)

Article 19a
Incentives for small and medium-sized biotech enterprises

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 as defined in Commission Recommendation 2003/361/EC\(^1\).

\(^1\) OJ L 124, 20.5.2003, p. 36.

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. These companies should nevertheless enjoy more favourable financial terms.

Amendment 45
ARTICLE 19B (new)

**Article 19b**

Reduction of the fee for marketing authorisation

1. The fee for marketing authorisation 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 that product is small.

2. Paragraph 1 shall also apply to fees charged by the Agency for post-authorisation activities 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, without any time limit, to the fees charged by the Agency for post-authorisation activities.

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 46
ARTICLE 19 C (new)

Article 19c
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 focus in particular on 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/EC. 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.

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 47
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) two members and two alternates appointed by the Commission, on the basis of a public call for expressions of interest and after consultation of the European Parliament, to represent physicians;

(ca) two members and two alternates appointed by the Commission, on the basis of a public call for expressions of interest and after consultation of the
European Parliament, to represent patients associations.

Justification

In order to cover all medical fields which the advanced therapies may relate to, more general medical expertise, i.e. physicians with clinical expertise, should be represented in the Committee for Advanced Therapies. In addition, by introducing alternate members, we would like to ensure a permanent representation of the groups involved. The appointment of these members and their alternates should take place in consultation with the European Parliament.

Amendment 48
ARTICLE 21, PARAGRAPH 2

2. All members and alternates 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.

Justification

The alternate members of the Committee for Advanced therapies introduced in paragraph 1 shall comply with the same criteria of scientific qualification or experience in the field of advanced therapy medicinal products as its members. 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 49
ARTICLE 21, PARAGRAPH 5

At least two members and two alternates of the Committee for Advanced Therapies shall have scientific expertise in medical devices.

Justification

The alternate members of the Committee for Advanced therapies introduced in paragraph 1 shall comply with the same criteria of scientific qualification or experience in the field of advanced therapy medicinal products as its members. 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.
5. The names and scientific qualifications of the members shall be published by the Agency.

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 50
ARTICLE 22

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.

In addition to the requirements laid down in Article 63 of Regulation (EC) No 726/2004, members and alternates of the Committee for Advanced Therapies shall have no financial or other interests in the biotechnology sector and medical device sector that could affect their impartiality. All indirect interests that could relate to these sectors shall be entered in the register referred to in Article 63(2) of Regulation (EC) No 726/2004.

2. All indirect interests that could relate to the pharmaceutical sector, medical device sector or biotechnology sector shall be entered in the register referred to in Article 63(2) of Regulation (EC) No 726/2004.

Justification

It should be clarified that an identical level of transparency as for existing Committees within the EMEA (pursuant to Article 63 of Regulation (EC) No 726/2004) applies for the new Committee for Advanced Therapies. It should also be clarified that interests in the biotechnology or medical device sector are forbidden.

Amendment 51
ARTICLE 23, POINT (A)

(a) to advise the Committee for Medicinal Products for Human Use on any data generated in the development of an advanced therapy medicinal product, for

(a) to formulate a draft opinion on the quality, safety and efficacy of an advanced therapy medicinal product for final approval by the Committee for
the formulation of an opinion on its quality, safety and efficacy; Medicinal Products for Human Use and to advise the latter on any data generated in the development of such a product;

Justification

Due to the highly specific and unique character of the advanced therapy medicinal products, a new Committee for Advanced Therapies is established within EMEA, composed of experts having specific qualification or experience in this highly innovative and quickly developing field. Therefore, the new structure should be responsible for drafting an opinion on the quality, safety, and efficacy of products for the final approval by the CHMP. Furthermore, the committee should be consulted for the evaluation of other products under its competence.

Amendment 52
ARTICLE 23, POINT (A A) (new)

(aa) to provide advice, pursuant to Article 18, on whether a product falls within the definition of an advanced therapy medicinal product;

Justification

Having specific expertise in advanced therapy medicinal products, the Committee for Advanced Therapies should have a prominent role in the classification task of whether a product is or is not an advanced therapy medicinal product.

Amendment 53
ARTICLE 23, POINT (E A) (new)

(ea) to contribute to the scientific advice procedures referred to in Article 17 of this Regulation and in Article 57(1)(n) of Regulation (EC) No 726/2004;

Justification

The Committee on Advanced Therapies should consist of the best possible experts from Member States. Their expertise should therefore be drawn upon for any advice issued regarding an advanced therapy medicinal product.

Amendment 54
ARTICLE 24

RR\380740EN.doc 31/93 PE 380.740v02-00 EN
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.

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 co-decision, fully involving the European Parliament. The regulation should set out very clearly that the Commission must involve the EMEA, through the Committee for Advanced Therapies, whenever adaptation of the Annexes to technical progress is required. The adaptation of Annexes II to IV should fall under the new regulatory procedure with scrutiny.

Amendment 55
ARTICLE 25, TITLE

Reporting

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 interests of patients for these to be included at some future date in order to allow European authorisation of the resulting products.

Amendment 56
ARTICLE 25, PARAGRAPH 1 A (new)

In this report, the Commission shall assess the impact of technical progress on the application of this Regulation. It shall also, if necessary, make a legislative proposal to include novel therapies which involve neither gene therapy, cell therapy nor tissue engineering.

Justification

Scientific advances may make additional novel therapies possible which are neither gene therapy, cell therapy nor tissue engineering. It would be in the interests of patients for these to be included at some future date, in order to allow European authorisation of the resulting products.
Amendment 57
ARTICLE 26, PARAGRAPH 2 A (new)

2a. Where reference is made to this paragraph, Article 5a(1) to (4) and Article 7 of Decision 1999/468/EC shall apply, having regard to the provisions of Article 8 thereof.

Justification
This amendment is in line with the new comitology provisions (regulatory procedure with scrutiny).

Amendment 58
ARTICLE 27, POINT -1 (new)
Article 13, paragraph 1 (Regulation (EC) No 726/2004)

(-1) In Article 13, the first sentence of paragraph 1 is replaced by the following:

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

Justification
This is a consequential amendment to Article 28(2) to ensure legal coherence.

Amendment 59
ARTICLE 27, POINT 2 A (new)

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

"After 20 May 2008, the Commission, having consulted the Agency, may present any appropriate proposal to amend this point, and the European Parliament and the Council shall take a decision thereon in accordance with the Treaty."
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 proposal, without recourse to the EP. Decisions determining the scope of legislative acts must be dealt with by co-decision.

Amendment 60
ARTICLE 28, POINT -1 (new)
Article 1, point 4 a (new) (Directive 2001/83/EC)

(-1) In Article 1, the following point 4a is added:

"4a. Tissue engineered product:
A product as defined in Article 2 of Regulation (EC) No **/** on advanced therapy medicinal products."

Justification

For the sake of legal coherence and clarity, it is necessary to include a cross reference to the definition of a tissue engineered product in Directive 2001/83/EC on medicinal products, which already contains the definitions of a gene therapy medicinal product and a somatic cell therapy medicinal product.

Amendment 61
ARTICLE 28, POINT 1
Article 3, point 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 prepared in full in a hospital in a non-profit manner on a one-off basis according to a specific, non-standardised and non-patented process, and used in a hospital in order to comply with an individual medical prescription for an individual patient under the exclusive professional responsibility of a medical practitioner or
for clinical research.

Points 1 and 2 do not apply to advanced therapy medicinal products.

Justification

For the justification concerning hospitals, see amendment to Recital 5. Exceptions given in Directive 2001/83/EC (Article 3, points 1 and 2) allow pharmacies to prepare medicinal products in accordance with a medical prescription without complying with medicinal product legislation. This exception would also give the in-house pharmacies of hospitals the possibility of producing TEP using standardized methods and on a routine basis. Therefore this amendment is crucial to ensure that only one-off basis products are excluded from the scope of this Regulation.

Amendment 62
ARTICLE 28, POINT 2
Article 4, paragraphs 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.

Justification

The Commission’s proposal poses serious problems of compatibility with the legal base (Art. 95 ECT). The reason is that the current wording of Article 28(5) gives a too wide opportunity to restrict the free movement of certain advanced therapy products. Legislative acts based on Art. 95 are intended to improve the conditions of the establishment and functioning of the internal market. The Commission’s proposal does not and should certainly not cover or harmonise aspects of public morality and public policy aspects of advanced therapy. However, the current wording allows restrictions not only related to these subsidiary aspects and should, therefore, be amended in line with suggestions of Parliament’s legal service.
Amendment 63
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.

Amendment 64
ARTICLE 29, PARAGRAPH 1 A (new)

1a. Tissue engineered products which were 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 that date.

Amendment 65
ARTICLE 29, PARAGRAPH 2

2. By way of derogation from Article 3(1) of Regulation (EC) No 297/95, no fee shall

Justification

Today companies are already producing and marketing TEP at national level through national authorisation systems. In order for a company to obtain a centralised marketing authorisation (e.g. design the new trials together with the EMEA, to conduct the trials, to develop the dossier and to submit it to the EMEA for evaluation) the proposed timeframe of 2 years is too short. Taking into account the time required for the above-mentioned steps and in order to avoid products that have been safely treating patients up to now being removed from those patients during the transitional period, we suggest a period of 4 years.

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.

2. By way of derogation from Article 3(1) of Regulation (EC) No 297/95, no fee shall

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be payable to the Agency in respect of applications submitted for the authorisation of the advanced therapy medicinal products mentioned in paragraph 1.

Justification

See the amendment for Article 29, paragraph 1a (new).

Amendment 66
ARTICLE 29, PARAGRAPH 2 A (new)

2a. With regard to autologous products, on the reasoned request of a Member State and by way of derogation from Article 3 of Regulation (EC) No 726/2004, the Commission may in accordance with the procedure laid down in Article 26(2) and after consultation of the Committee on Advanced Therapies approve for a period of five years a national authorisation in accordance with the principles of this Regulation. The Commission may only take such a decision if it judges that:

- the regulatory authority of the Member State concerned has sufficient expertise in the field of advanced therapy medicinal products; and

- the marketing of the specific medicinal product outside the given Member State is not possible.

Detailed procedural rules for the application of this Article shall be laid down by the Commission and published in the Official Journal of the European Union.

Amendment 67
ARTICLE 30, PARAGRAPHS 2 A AND 2 B (new)

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.

The implementing measures envisaged in Articles 4, 5 and 8 shall be adopted as soon as possible and, in any event, no later than 9 months after the entry into force of this Regulation.

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 9 months time limit for the Commission to adopt the necessary measures.

Amendment 68
ANNEX II, POINT 2.2.

2.2. qualitative and quantitative composition 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.

Amendment 69
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;
Justification

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

Amendment 70
ANNEX IV, POINT (A) (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.
EXPLANATORY STATEMENT

Rapid development in the fields of biology, biotechnology and medicine and attempts to achieve sustainable growth of health protection within the European Union lead to the development of new treatments and highly innovative medicinal products.

In this context, products which involve intervention in gene therapy, cell therapy and tissue engineering are of great importance, having a high potential in the treatment of diseases such as cancer, cartilage or bone diseases or injuries, repair of genetic disorders, repair of post heart attack damage as well as skin replacement in burn victims.

Nowadays, the legal framework at the Community level related to these advanced therapies remains fragmented, as only gene therapy and somatic cell therapy medicinal products benefit from a legal definition. Tissue engineered products remain unregulated, which leads to the fragmentation of the market and which does not allow patients to have easy access to the necessary treatments.

The current proposal introduces a single harmonising regulatory framework for the evaluation, authorisation and supervision of advanced therapy medicinal products: marketing authorisation requirements and procedure, post-authorisation vigilance and traceability. The proposed Regulation should be seen within the wider perspective of the existing legislation in this field, such as Directive 2001/83/EC on medicinal products, Regulation (EC) No 726/2004 on the European Medicines Agency (EMEA) or Directive 2004/23/EC laying down quality and safety standards of human tissues and cells.

The proposal introduces a European centralised marketing authorisation procedure and creates a new Committee for Advanced Therapies within EMEA, composed of highly qualified and experienced experts in all fields related to these products. In addition, the proposed Regulation sets up a strengthened requirement for the post-authorisation monitoring system and for traceability of the patient and foresees specific technical requirements for tissue engineered products. Moreover, additional specific incentives for the applicants and especially for SMEs are introduced, in order to promote competitiveness within the EU.

The rapporteur welcomes this proposal for a Regulation and the introduction of a new coherent legal framework for these innovative, specific and complex medicinal products. He agrees on the necessity of a centralised authorisation procedure in order to facilitate the market access and to ensure the free movement of advanced therapy medicinal products within the Community. Priority should be given to the demonstration of quality, safety and efficacy of these products in order to ensure a high level of health protection within the EU. The highest possible level of legal certainty should be guaranteed while allowing sufficient flexibility at the technical level.

Nevertheless, the rapporteur would like to underline the importance of clear definitions in order to avoid a legal uncertainty or grey zones, particularly as regards the definition of combined advanced therapy medicinal products and their evaluation. It should also be made crystal clear that products prepared in a hospital, on a one-off basis for an individual patient, should not comply with the centralised authorisation procedure. Moreover, products applied in the production of advance therapy medicinal products for clinical trials and products for clinical research should not be forgotten.
In addition, the rapporteur would like to stress the important role of the Committee for Advanced Therapies within EMEA. This highly qualified body should play a vital role in the process of scientific evaluation of advanced therapy medicinal products and its internal decision procedure should be clearly defined.

Moreover, advanced therapy medicinal products could raise serious ethical concerns, as they are likely to contain human cells or tissues. The Commission's proposal should not have an impact on the national legislation prohibiting or restricting the use of certain type of human or animal cells (such as embryonic stem cells) or the sale, supply or use of medicinal products derived from these cells. According to Parliament's legal service, the original drafting of this provision raises serious concerns in the light of the legal basis of the proposal.

The development in biotechnology and biomedicine should be carried out while fully respecting fundamental rights. Rights such as the right to human dignity or to the integrity of the person laid down in the Oviedo Convention as well as in the Charter of fundamental rights should be entirely respected. Therefore, in his first draft report the rapporteur underlined that authorisation procedure should be carried out in accordance with the principle of non-commercialisation of the human body or its parts as such. Moreover, the rapporteur proposed amendments in order to exclude the European marketing authorization under this regulation for products modifying the germ line genetic identity of human beings and for products derived from human-animal hybrids or chimeras (but allowing the transplantation of somatic animal cells or tissues to the human body for therapeutic purposes, i.e. Xenotransplantation).

These amendments were adopted by the Committee on Legal Affairs. Even though these amendments were adopted by the majority in ENVI committee, the first draft report as amended was rejected in the final vote. The rapporteur is still convinced that the approach chosen by the JURI Committee is the most appropriate. Nevertheless, his intention is to find the broadest possible consensus in this area. Therefore, he does not propose any of these amendments in his new report. Two amendments, 3 and 17, were incorporated in the report without vote in the Environment Committee, following enhanced cooperation (Rule 47) with the Legal Affairs Committee.
OPINION OF THE COMMITTEE ON INDUSTRY, RESEARCH AND ENERGY

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


Draftsman: Giles Chichester

SHORT JUSTIFICATION

Advanced therapies are highly innovative medical products based on genes (gene therapy), cells (cell therapy) or tissues (tissue engineering). These advanced therapies enable revolutionary treatment of diseases and injuries, such as cancer, Parkinson's disease, skin in burn victims or serious cartilage damage, and are expected to change medical practice significantly.

Currently, the development of the field of advanced therapies is hampered by the lack of harmonised EU legislation. Especially tissue-engineered products are at the moment not regulated on Community level, which leads to divergent national legislation and authorisation. This hampers the internal market and negatively affects EU's innovative capacity and competitiveness.

This proposed Regulation intends to bridge the existing regulatory gap by addressing all advanced therapy products within a single, integrated legal framework. The Regulation builds on already-existing legislation (in particular Directive 2001/83/EC on medical products and Regulation (EC) No 726/2004 on the European Medicines Agency), and should therefore be seen in their totality.

The main elements of the Commission's proposal are:

- A centralised marketing authorisation procedure, to benefit from the pooling of expertise at European level and direct access to the EU market;
- A new and multidisciplinary expert Committee (Committee for Advanced Therapies), within the European Medicines Agency (EMEA), to assess advanced therapy products and follow scientific developments in the field;
- Tailor-made technical requirements, which are adapted to the particular characteristics of these products;
- Strengthened requirements for risk management and traceability;
- A system of low-cost, top-quality scientific advice provided by EMEA;
- Special incentives for small and medium-sized enterprises (SMEs).

The draftswoman welcomes the Commission's proposal. Tissue engineering is an emerging biotechnology sector at the interface between medicine, cellular and molecular biology, materials science and engineering. By developing products designed to replace, repair or regenerate human tissues, it could mean the end of organ shortage, saving every year thousands of people in Europe. The draftswoman therefore welcomes the creation of a robust and comprehensive regulatory framework, that will give the sector harmonised market access, while at the same time foster the competitiveness and guarantee a high level of health protection.

The draftswoman would like to emphasise the fact that the definitions should be precise enough to provide the necessary legal certainty, but at the same time sufficient flexible in order to keep the pace with the evolution of science and technology. Such a balance should also be sought for the marketing authorisation procedure. The draftswoman supports the creation of a fully centralised authorisation procedure to benefit from the pooling of expertise, but at the same time stresses the need to alleviate the regulatory burden that such a procedure might entail, especially on SMEs.

As certain advanced therapy products may be based on human cells, they can raise important ethical issues. Currently, decisions on the use or prohibition of any type of cells, including embryonic stem cells, are a national responsibility. In this proposal, this principle is kept, meaning that decisions on the development, use and/or sale of products based on any specific type of human or animal cells will remain a national responsibility. This is fully in line with the Directive on the quality and safety of human tissues and cells (Directive 2004/23/EC).

### AMENDMENTS

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

<table>
<thead>
<tr>
<th>Text proposed by the Commission¹</th>
<th>Amendments by Parliament</th>
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<td>(5) Advanced therapy medicinal products should be regulated in so far as they are</td>
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¹ Not yet published in OJ.

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intended to be placed on the market in Member States and either prepared industrially or manufactured by a method involving an industrial process, within the meaning of Article 2(1) of Directive 2001/83/EC. Advanced therapy medicinal products which are both prepared in full and used in a hospital, in accordance with a medical prescription for an individual patient, should thus be excluded from the scope of the present Regulation.

intended to be placed on the market in Member States and either prepared industrially or manufactured by a method involving an industrial process, within the meaning of Article 2(1) of Directive 2001/83/EC. Advanced therapy medicinal products which are prepared in full in a hospital on a one-off basis according to a specific, non-standardised and non-patented process, and used in a hospital, in order to comply with an individual medical prescription for an individual patient, should thus be excluded from the scope of this Regulation.

Justification

Where hospitals or other institutions prepare products using an established process to create treatments for patients on a serial and routine basis, they should have to comply with the provisions of this Regulation. However, when hospitals produce advanced therapy products for research purposes or on an exceptional, one-off basis, they should not have to comply with the centralised authorisation procedure.

Amendment 2
RECITAL 7 B (new)

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 3

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 from human-animal hybrids or chimeras. 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 4

RECITAL 9

(9) The evaluation of advanced therapy medicinal products often requires very specific expertise, which goes beyond the traditional pharmaceutical field and covers areas on the borderline to other sectors such as biotechnology and medical devices. For this reason, it is appropriate to create, within
the Agency, a Committee for Advanced Therapies, which the Committee for Medicinal Products for Human Use of the Agency should consult on the assessment of data related to advanced therapy medicinal products, before issuing its final scientific opinion. In addition, the Committee for Advanced Therapies may be consulted for the evaluation of any other medicinal product which requires specific expertise falling within its area of competence.

Justification

Due to a highly specific and unique character of the advanced therapy medicinal products, a new Committee for Advanced Therapies is established within EMEA and composed of experts having specific qualifications or experience in this highly innovative and quickly developing field. Therefore, the new structure should be responsible for drafting an opinion on the quality, safety, and efficacy of products for the final approval by the CHMP. Furthermore, the committee should be consulted for the evaluation of other products under its competence.

Amendment 5
RECITAL 9 A (new)

(9a) The Committee for Advanced Therapies should provide advice to the Committee for Medicinal Products for Human Use on whether a product falls within the definition of an advanced therapy medicinal product.

Justification

Due to its specific expertise in advanced therapy medicinal products, the Committee for Advanced Therapies should assist the CHMP in its classification task of whether a product is or is not an advanced therapy medicinal product.

Amendment 6
RECITAL 14

(14) As a matter of principle, human cells or tissues contained in advanced therapy medicinal products should be procured

deleted
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.

**Justification**

This recital can be deleted as a consequence to the introduction of a new recital 7a and new articles 3a and 28a.

**Amendment 7**

**RECITAL 16**

(16) The manufacture of advanced therapy medicinal products should be in compliance with the principles of good manufacturing practice, as set out in Commission Directive 2003/94/EC of 8 October 2003 laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use. Furthermore, guidelines specific to advanced therapy medicinal products should be drawn up, so as to properly reflect the particular nature of their manufacturing process.

**Justification**

The existing Good Manufacturing principles established by Directive 2003/94/EC may not be fully appropriate as regards to advanced therapy products. A new GMP Directive, especially focusing on Advanced Therapy products, would be appropriate, not just guidance on existing GMP.

**Amendment 8**

**RECITAL 24**

(24) In order to take into account scientific and technical developments, the Commission should be empowered to adopt

(24) In order to take into account scientific and technical developments, the Commission should be empowered to adopt
any necessary changes regarding the technical requirements for applications for marketing authorisation of advanced therapy medicinal products, the summary of product characteristics, labelling, and package leaflet.

The Commission should ensure that relevant information on envisaged measures is made available to interested parties without delay.

Justification

Better predictability of future regulations is of the greatest importance for industry in order to make well-planned and cost-effective investments in R&D and production. Therefore, relevant information about envisaged measures should be made known as quickly as possible.

Amendment 9

RECITAL 25

(25) Provisions should be laid down to report on the implementation of this Regulation after experience has been gained, with a particular attention to the different types of advanced therapy medicinal products authorised and the measures provided for in Chapter 6 and in Articles 9, 14(9) and 70(2) of Regulation (EC) No 726/2004.

Justification

The report on the implementation of this Regulation should cover the whole scope of the present regulation, including the incentive measures for SMEs, the 'fast-track' approvals and the appeal procedure.

Amendment 10

ARTICLE 1 A (new)

Article 1a

Exclusion from the scope

This Regulation shall not apply to any advanced therapy medicinal product which is prepared in full in a hospital on a one-off basis according to a specific, non-
standardised and non-patented process, and used in a hospital, in order to comply with an individual medical prescription for an individual patient.

Justification

Where hospitals or other institutions prepare products by using an established process to create treatments for patients on a serial and routine basis, they should have to comply with the provisions of this Regulation, ensuring quality, safety and efficacy of products. However, when hospitals produce ATPs for research purposes or on an exceptional, one-off basis, they should not have to comply with the centralised authorisation process. To ensure the coherence with the Article 28, paragraph 1 we introduce the exclusion from the scope in the present Regulation.

Amendment 11
ARTICLE 2, PARAGRAPH 1, POINT (D), INDENT 1 A (new)

- its cellular or tissue part contains viable cells or tissues; or

Justification

For the purposes of this Regulation, the most important criterion when defining a combined advanced therapy medicinal product should be the viability of its cellular or tissue part. For the patient’s safety and the high standards of the evaluation of a product, a combined product should be always classified as an advanced therapy medicinal product when it contains viable tissues or cells.

Amendment 12
ARTICLE 2, PARAGRAPH 1, POINT (D), INDENT 2

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

Justification

A combined product should always be considered as advanced therapy medicinal product when it contains non-viable cells or tissues which act upon human body in a manner that is considered as primary to the action of the device part of the product concerned.
Amendment 13
ARTICLE 3 A (new)

Article 3a
Ban on 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 this 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 shouldn’t compromise the protection of fundamental rights. These rights, including 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 if they are carefully observed at every stage of the authorisation process. Therefore, EMEA should be subject to this specific obligation. Member States should have an obligation to ensure voluntary and unpaid donation and to guarantee the procurement of tissues or cells on a non-profit basis.

Amendment 14
ARTICLE 3 B (new)

Article 3b
Ban on products modifying the human germ line

No authorisation shall be granted to products modifying 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 15
ARTICLE 4, PARAGRAPH 3

3. The Commission shall draw up detailed guidelines on good clinical practice specific to advanced therapy medicinal products.

3. The Commission shall draw up detailed guidelines on clinical trial authorization procedures and good clinical practice specific to advanced therapy medicinal and in particular tissue engineered products.

Justification

This amendment recognizes that in particular for tissue engineered products for which no legislation and hence no guidelines exist today, these need to be developed, not only with regard to Good Clinical Practice but also related to Clinical trial authorizations.

Amendment 16
ARTICLE 9, PARAGRAPH 3

3. The advice given by the Committee for Advanced Therapies under paragraph 1 shall be sent to the chairman of the Committee for Medicinal Products for Human Use in a timely manner so as to ensure that the deadline laid down in Article 6(3) of Regulation (EC) No 726/2004 can be met.

3. The draft opinion given by the Committee for Advanced Therapies under paragraph 1 shall be sent to the chairman of the Committee for Medicinal Products for Human Use in a timely manner so as to ensure that the deadline laid down in Article 6(3) or 9(2) of Regulation (EC) No 726/2004 can be met.

Justification

Due to the highly specific and unique character of the advanced therapy medicinal products, a new Committee for Advanced Therapies is established within EMEA, composed of experts having specific qualifications or experience in this highly innovative and quickly developing field. Therefore, this new structure should be responsible for drafting an opinion on the quality, safety, and efficacy of products for the final approval by the CHMP. The draft opinion should be given in a timely manner so the deadline laid down in Article 9(2) of Regulation (EC) No 726/2004 can also be met.
Amendment 17
ARTICLE 9, PARAGRAPH 4

4. Where the scientific opinion on an advanced therapy medicinal product drawn up by the Committee for Medicinal Products for Human Use under Article 5, paragraphs 2 and 3 of Regulation (EC) No 726/2004 is not in accordance with the advice of the Committee for Advanced Therapies, the Committee for Medicinal Products for Human Use shall annex to its opinion a detailed explanation of the scientific grounds for the differences.

Justification

See the justification for the amendment of the Article 9, paragraph 3.

Amendment 18
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.

Justification

According to paragraph 2, a medical device or the active implantable medical device part of a combined advanced therapy medicinal product have to be assessed by a notified body in order to benefit from its extensive specific experience. The final evaluation should be carried out by the Agency who should incorporate the assessment of a notified body in its final opinion.

Amendment 19
ARTICLE 10, PARAGRAPH 2

2. Where the medical device or active implantable medical device which is part of a combined advanced therapy medicinal product shall include an application for a marketing authorisation for a combined advanced therapy medicinal product shall include an
product **has already been assessed** by a notified body in accordance with Directive 93/42/EEC or Directive 90/385/EEC, the Agency shall **take account of** the results of that assessment in its evaluation of the medicinal product concerned.

**assessment** by a notified body identified in conjunction with the applicant in accordance with Directive 93/42/EEC or Directive 90/385/EEC **of the medical device or active implantable medical device which forms part of the combined advanced therapy medicinal product.** The Agency shall **incorporate** the results of that assessment in its evaluation of the medicinal product concerned.

**Justification**

In order to ensure the continuous utilisation of the vast experience and expert knowledge of the notified bodies concerning the evaluation of medical devices or active implantable medical devices, the notified bodies should assess the medical device or the active implantable medical device part of the combined advanced therapy medicinal product. The Agency should incorporate these assessments in its final evaluation of the combined product in accordance with paragraph 1.

**Amendment 20**
**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 easy to use.**

2. **Where products are exclusively applied to patients by medical practitioners, the summary of product characteristics pursuant to Article 11 of Directive 2001/83/EC can be used as package leaflet.**

**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 21**
**ARTICLE 15, PARAGRAPH 2, SUBPARAGRAPH 1**

2. Where there is particular cause for concern, the Commission **may,** on the advice of the
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.

Justification

In order to ensure the effectiveness of the risk management system, the Commission should have an obligation to require necessary measures to be carried out when there is a cause for concern.

Amendment 22
ARTICLE 15, PARAGRAPH 4

4. The Agency shall draw up detailed guidelines relating to the application of paragraphs 1, 2 and 3.

Justification

When drawing up post-authorisation risk management guidelines, principles of regulatory cooperation and dialogue with the marketing authorization holder should be enacted in order to allow a pooling of the limited expertise in this area.

Amendment 23
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 95% reduction for small and medium-sized enterprises and 80% 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.
Justification

This Regulation seeks to encourage and support SME's in the development of ATMPs. Therefore, special fee-waivers should be introduced for SME's on scientific advice. The 5% of the basic fee which the SME's should cover themselves is a symbolic amount, in order to prevent any abuse of the system. To support applicants which are not SMEs and to ensure the competitiveness of the whole sector, a reduction of 70% should be applied to all companies irrespective of their size.

Amendment 24
ARTICLE 18, PARAGRAPH 1

1. Any applicant developing a product based on cells or tissues may request a scientific recommendation of the Agency with a view to determining whether the referred product falls, on scientific grounds, within the definition of an advanced therapy medicinal product. The Agency shall deliver this recommendation after consultation with the Commission.

Justification

The proposed amendment foresees that an applicant will get clarity on the classification of the concerned product in a timely manner, thus facilitating business planning and further development of the product.

Amendment 25
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 granted to small and medium-sized enterprises under Commission Recommendation
2003/361/EC of 6 May 2003 concerning the definition of micro, small and medium-sized enterprises.\(^1\)

2. The same shall apply to an enterprise in which other enterprises have an interest up to 50% and which invests more than 15% of its annual turnover in research and development activities.

\(^1\) L 124, 20.5.2003, p. 36.

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 26
ARTICLE 19B (new)

Article 19b
Reduction of the fee for marketing authorisation

1. The fee for marketing authorisation shall be reduced to 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. The first paragraph shall also apply to fees for post-authorisation activities 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, the first paragraph shall also apply to the fees for post-authorisation activities by the Agency without a time limit.

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

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 27
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.

Justification

In order to cover all medical fields which the advanced therapies may relate to, more general medical expertise, i.e. medical doctors, should be represented in the Committee for Advanced Therapies. In addition, by introducing alternate members, we would like to ensure a permanent representation of the groups involved. The appointment of these members and their alternates should take place in consultation with the European Parliament.

Amendment 28
ARTICLE 21, PARAGRAPH 1, POINT (C A) (new)

(ca) two members and two alternates appointed by the Commission, on the basis of a public call for expressions of interest
and after consultation of the European Parliament, to represent patients associations.

Justification

By introducing alternate members, we would like to ensure a permanent representation of the groups involved. The appointment of these members and their alternates should take place in consultation with the European Parliament.

Amendment 29
ARTICLE 21, PARAGRAPH 2

2. All members and alternates 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.

Justification

The alternate members of the Committee for Advanced therapies introduced in paragraph 1 shall comply with the same criteria of scientific qualification or experience in the field of advanced therapy medicinal products as its members.

Amendment 30
ARTICLE 23, POINT (A)

(a) to advise the Committee for Medicinal Products for Human Use on any data generated in the development of an advanced therapy medicinal product, for the formulation of an opinion on its quality, safety and efficacy;

(a) to draw up a draft opinion on the quality, safety and efficacy of an advanced therapy medicinal product submitted for review; this draft opinion shall be transmitted to the Committee for Medicinal Products for Human Use for approval. The
Committee for Advanced Therapies shall advise the Committee for Medicinal Products for Human Use on any data generated in the product’s development.

Justification

The Committee on Advanced Therapies should consist of the best possible experts from Member States. Their expertise should therefore form the basis of any product opinion delivered by the CHMP.

Amendment 31
ARTICLE 23, POINT (A A) (new)

(aa) to advise the Committee for Medicinal Products for Human Use on the amendments provided for in Articles 4(2), 8, 19 and 24;

Justification

The assessment of advanced therapy medicinal products often requires very specific expertise, for which reason the specialised Committee for Advanced Therapies is created. Therefore, it is logical that this specialised committee should have an advisory role in the comitology procedure to amend the Annexes and other technical requirements.

Amendment 32
ARTICLE 23, POINT (E A) (new)

(ea) to provide advice on the scientific advice procedures referred to in Article 17;

Justification

The Committee on Advanced Therapies should consist of the best possible experts from Member States. Their expertise should therefore be drawn upon for any advice issued regarding an advanced therapy medicinal product.

Amendment 33
ARTICLE 23, POINT (E B) (new)

(eb) to provide advice on product classification as referred to in Article 18.
Justification

The Committee on Advanced Therapies should consist of the best possible experts from Member States. Their expertise should therefore be drawn upon for any advice issued regarding the classification of an advanced therapy medicinal product.

Amendment 34
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.

Justification

Annex I contains a fundamental and substantial definition. Therefore, 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 35
ARTICLE 25

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 and on the use and effect of the measures provided for in Chapter 6 of this Regulation and in Articles 9, 14(9) and 70(2) of Regulation (EC) No 726/2004. On the basis of that report, the Commission may propose amendments to this Regulation and Regulation (EC) No 726/2004.

Justification

The report on the implementation of this Regulation should cover the whole scope of the present regulation, including the incentive measures for SMEs, the 'fast-track' approvals and the appeal procedure. On the basis of this report, the Commission should re-evaluate the current provisions and propose amendments to improve them, also with a view of harmonizing the different provisions and procedures currently in use within the EMEA.
2a. The Commission shall ensure that relevant information about envisaged measures is made available to all interested parties in due time.

Justification

This is necessary to ensure that Industry and other stakeholders are involved from the very beginning in the elaboration of secondary legislation as well as of guidance documents. This is a concept already introduced in Community legislation (see art. 15.5 of Directive 2004/22/EC of 21 March 2004 on measuring instruments).

“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 that Member State has envisaged the national marketing authorisation procedure as an alternative, for a period of five years subsequent to the granting of the marketing authorisation at national level. Afterwards an application for renewal within the centralised procedure is necessary with the effect that after the renewal the national marketing authorisation becomes a centralised marketing authorisation.

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 38
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.

Justification

Exceptions given in Directive 2001/83/EC allow pharmacies to prepare medicinal products in accordance with a medical prescription without complying with medicinal product legislation. This exception would as well give the in-house pharmacies of hospitals the possibility producing TEP using standardized methods and on routinely basis. Therefore this amendment is crucial to ensure that only one-off basis products are excluded from the scope of this Regulation.

Amendment 39
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.”
Justification

Member States should retain the rights to prohibit or allow products on ethical grounds reflecting the views held by that Member State. The Commission should be informed in a transparent manner by the Member States of which products will be allowed to be placed on the market with a view to allowing manufacturers to consult an authoritative list.

Amendment 40

ARTICLE 29

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.

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.

3. 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.

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 41  
ARTICLE 30

This Regulation shall enter into force on the 20th day following that of its publication in the Official Journal of the European Union.

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

This Regulation shall be binding in its entirety and directly applicable in all Member States.

1. This Regulation shall enter into force on the 20th day following that of its publication in the Official Journal of the European Union.

2. It shall apply from *, except in relation to tissue engineered products.

3. In relation to 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.

4. This Regulation shall be binding in its entirety and directly applicable in all Member States.

* 3 months after the date of entry into force of this Directive.

Justification

This is necessary to take into account the different timeframes necessary for the application of Regulations and Directives. The proposal recognizes that the pharmaceutical regime cannot be applied to TEP 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.
| Committee responsible | ENVI |
| Opinion by | ITRE |
| Date announced in plenary | 30.11.2005 |
| Enhanced cooperation – date announced in plenary | no |
| Drafts(wo)man | Giles Chichester |
| Date appointed | 20.6.2006 |
| Previous drafts(wo)man | Pia Elda Locatelli |
| Discussed in committee | 20.3.2006 3.5.2006 20.6.2006 |
| Date adopted | 20.6.2006 |
| Result of final vote | +: 27 -: 17 0: 0 |
| Members present for the final vote | Šarūnas Birutis, Jan Březina, Renato Brunetta, Jerzy Buzek, Joan Calabuig Rull, Pilar del Castillo Vera, Jorgo Chatzimarkakis, Giles Chichester, Den Dover, Lena Ek, Nicole Fontaine, Adam Gierek, Norbert Glante, Umberto Guidoni, András Gyürk, Rebecca Harms, Erna Hennicot-Schoepges, Ján Hudacký, Romana Jordan Cizelj, Anne Laperrrouze, Vincenzo Lavarra, Pia Elda Locatelli, Eugenijus Maldeikis, Eluned Morgan, Angelika Niebler, Umberto Pirilli, Miloslav Ransdorf, Herbert Reul, Teresa Riera Madurell, Mechtild Rothe, Andres Tarand, Britta Thomsen, Patrizia Toia, Catherine Trautmann, Claude Turmes, Nikolaos Vakalis, Alejo Vidal-Quadras Roca, Dominique Vlasto |
| Substitute(s) present for the final vote | María del Pilar Ayuso González, Dorette Corbey, Peter Liese, Vittorio Prodi, John Purvis, Esko Seppänen |
| Substitute(s) under Rule 178(2) present for the final vote | |
| Comments (available in one language only) | Prior to taking the final vote, Pia Elda Locatelli stated that given the fact that the amendments adopted had changed her initial position on the subject, she therefore could not continue as draftsman. The Committee then appointed its chairman, Giles Chichester, draftsman. |
17.7.2006

OPINION OF THE COMMITTEE ON LEGAL AFFAIRS (*)

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


Draftswoman (*): Hiltrud Breyer

(*) Enhanced cooperation between committees - Rule 47 of the Rules of Procedure

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 the Committee on Legal Affairs 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 have just reached 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 Committee therefore proposes to exclude 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.


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

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## Amendments by Parliament

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### Justification

*The title of the proposal need to be changed, as Directive 2004/23/EC is also amended (see amendment 45).*

### Amendment 2

**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) Legislation in force in Member States concerning the use of certain types of cells, such as embryonic stem cells, varies 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 of 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 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 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 resolutions of 10 March 2005 on the trade in human egg cells and of 26 October 2005 on patents for biotechnological inventions. 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.


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/EC prohibits gene therapy trials that result in modifications to a subject's germ line genetic identity.
Directive 98/44/EC 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. By way of exception, the prohibition of authorisation should not apply to products intended to treat cancers of the gonads.

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 gonades should be permitted to have European marketing authorisation.

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 9

(9) The evaluation of advanced therapy medicinal products often requires very specific expertise, which goes beyond the traditional pharmaceutical field and covers areas on the borderline to other sectors such as biotechnology and medical devices. For this reason, it is appropriate to create, within the Agency, a Committee for Advanced Therapies, which the Committee for Medicinal Products for Human Use of the Agency should consult on the assessment of data related to advanced therapy medicinal products, before issuing its final scientific opinion. In addition, the Committee for Advanced Therapies may be consulted for the evaluation of any other medicinal product which requires specific expertise falling within its area of competence.

Justification

Due to a highly specific and unique character of the advanced therapy medicinal products, a new Committee for Advanced Therapies is established within EMEA and composed of experts having specific qualifications or experience in this highly innovative and quickly developing field. Therefore, the new structure should be responsible for drafting an opinion on the quality, safety, and efficacy of each advanced therapy medicinal product for final approval by the Committee for Medicinal Products for Human Use of the Agency. In addition, the Committee for Advanced Therapies should be consulted for the evaluation of any other medicinal product which requires specific expertise falling within its area of competence.

Amendment 7
RECITAL 9 A (new)

(9a) The Committee for Advanced Therapies should provide advice to the Committee for Medicinal Products for Human Use on whether a product falls within the definition of an advanced therapy medicinal product.
Due to its specific expertise in advanced therapy medicinal products, the Committee for Advanced Therapies should assist the CHMP in its classification task of whether a product is or is not an advanced therapy medicinal product.

Amendment 8
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.

Justification

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

Amendment 9
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.

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 10
RECITAL 16

(16) The manufacture of advanced therapy
medicinal products should be in compliance with the principles of good manufacturing practice, as set out in Commission Directive 2003/94/EC of 8 October 2003 laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use. Furthermore, guidelines specific to advanced therapy medicinal products should be drawn up, so as to properly reflect the particular nature of their manufacturing process.

Justification

Advanced Therapy medicinal products have specific characteristics that differ greatly from traditional medicinal products. That leads to important differences in their manufacturing process (e.g. in Article 11.4. the GMP Directive requires that sample batches of finished products should be kept for 1 year after expiry date. It is, however, difficult to consider expiry dates for certain classes of ATMPs).

Amendment 11

RECITAL 28


Justification

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

Amendment 12

ARTICLE 1 A (new)

Article 1a

Exclusions

This Regulation shall not apply to any advanced therapy medicinal products that
contain or are derived from human embryonic and foetal cells, primordial germ cells and cells derived from those cells.

**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).

Amendment 13

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

- its cellular or tissue part contains viable cells or tissues; or

**Justification**

For the purposes of this Regulation, the most important criterion when defining a combined advanced therapy medicinal product should be the viability of its cellular or tissue part. For the patient's safety and the high standards of the evaluation of a product, a combined product should be always classified as an advanced therapy medicinal product when it contains viable tissues or cells.

Amendment 14

**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 containing non-viable cells or tissues must be liable to act upon the human body with action that can be considered as primary to that of the devices referred to.

**Justification**

A combined product should always be considered as advanced therapy medicinal product when it contains non-viable cells or tissues which act upon human body in a manner that is considered as primary to the action of the device part of the product concerned.

Amendment 15

**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 of any non-human life form into which a human cell 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)(new) of the present Regulation.*

Amendment 16

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 17

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
Amendment 18
ARTICLE 3 A (new)

Article 3a
Prohibition of commercialisation of the human body and its parts as such

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 as such 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 a very important one is the person's integrity, are laid down in the the patenting directive, the Oviedo Convention and the Charter of Fundamental Rights.

Amendment 19
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, except for those intended to treat cancers of the gonads.

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, with the exclusion of cancer treatment.

Amendment 20
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 21
ARTICLE 5, PARAGRAPH -1 (new)

The Commission shall, in accordance with the procedure referred to in Article 26(2), amend Directive 2003/94/EC to take into account the specific characteristics of advanced therapy medicinal product and, especially, tissue engineered products.

Justification

Advanced therapy medicinal products have specific characteristics that differ greatly from traditional medicinal products. That leads to important differences in their manufacturing process (e.g. Article 11.4. of the GMP Directive requires that sample batches of finished products should be kept for 1 year after the expiry date. It is, however, difficult to consider
expiry dates for certain classes of ATMPs).

Amendment 22
ARTICLE 7 A (new)

Article 7a
Specific requirements for products containing animal cells

In addition to the requirements laid down in this Regulation and the Annexes hereto, products containing non-human cells or tissues shall be authorised only where it is guaranteed that they will not give rise to problems relating to the identification of endogenous retroviruses in the external cells and in the recipients, the possible creation of new viruses, possible immune reactions or the possible development of cancer.

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 23
ARTICLE 9, PARAGRAPH 2

2. The rapporteur or co-rapporteur appointed by the Committee for Medicinal Products for Human Use pursuant to Article 62 of Regulation (EC) No 726/2004 shall be a member of the Committee for Advanced Therapies. This member shall also act as rapporteur or co-rapporteur for the Committee for Advanced Therapies.

2. The rapporteur or co-rapporteur appointed by the Committee for Medicinal Products for Human Use pursuant to Article 62 of Regulation (EC) No 726/2004 shall be a member of the Committee for Advanced Therapies, shall be proposed by the Committee for Advanced Therapies and shall possess specific expertise in relation to the product concerned. This member shall also act as rapporteur or co-rapporteur for the Committee for Advanced Therapies.

Justification

In order to ensure the highest level of expertise, the rapporteur and co-rapporteur appointed by the CHMP should be proposed by the Committee for Advanced Therapies and should have
specific expertise for the relevant product.

Amendment 24
ARTICLE 9, PARAGRAPH 3

3. The advice given by the Committee for Advanced Therapies under paragraph 1 shall be sent to the chairman of the Committee for Medicinal Products for Human Use in a timely manner so as to ensure that the deadline laid down in Article 6(3) of Regulation (EC) No 726/2004 can be met.

Justification

Due to the highly specific and unique character of the advanced therapy medicinal products, a new Committee for Advanced Therapies is established within EMEA, composed of experts having specific qualifications or experience in this highly innovative and quickly developing field. Therefore, this new structure should be responsible for drafting an opinion on the quality, safety, and efficacy of products for the final approval by the CHMP. The draft opinion should be given in a timely manner so the deadline laid down in Article 9(2) of Regulation (EC) No 726/2004 can also be met.

Amendment 25
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 easy to use.

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 26
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.

**Justification**

*In order to ensure the effectiveness of the risk management system, the Commission should have an obligation to require necessary measures to be carried out when there is a cause for concern.*

**Amendment 27**

**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.

**Justification**

*This Regulation seeks to encourage and support SME's in the development of ATMPs. Therefore, it is necessary to introduce special fee-waivers applicable to SME's on scientific advice. The 5% of the basic fee which the SME's should cover themselves is a symbolic amount, in order to prevent any abuse of the totally gratis system. Moreover, to support the applicants which do not fall under the SME criteria and to ensure the competitiveness of the whole sector, a reduction of 70% should be applied to all companies irrespective of their size.*

**Amendment 28**

**ARTICLE 18, PARAGRAPH 1**

1. Any applicant developing a product based on cells or tissues may request a scientific recommendation of the Agency with a view to determining whether the referred product falls, on scientific grounds, within the definition of an advanced therapy medicinal product. The Agency shall deliver this recommendation after consultation with the Commission.

1. Any applicant developing a product based on cells or tissues may request a scientific recommendation of the Agency with a view to determining whether the referred product falls, on scientific grounds, within the definition of an advanced therapy medicinal product. The Agency shall deliver this recommendation, after consultation with the **Committee for Advanced Therapies and the**
Commission, **within 60 days after receipt of the request.**

**Justification**

The proposed amendment foresees that an applicant will get clarity on the classification of the concerned product in a timely manner, thus facilitating business planning and further development of the product.

Amendment 29
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 as defined in Commission Recommendation 2003/361/EC.

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


**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 oneoff 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 30
ARTICLE 19 B (new)

**Article 19b**
Reduction of the fee for marketing authorisation
1. The fee for marketing authorisation 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 that product is small.

2. Paragraph 1 shall also apply to fees charged by the Agency for post-authorisation activities 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, without any time limit, to the fees charged by the Agency for post-authorisation activities.

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

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 31

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

(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.

represent physicians and two of them to represent patients associations.

Justification

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

Amendment 32
ARTICLE 21, PARAGRAPH 1, POINT (C) AND POINT (C A) (new)

(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) two members and two alternates appointed by the Commission, on the basis of a public call for expressions of interest and after consultation of the European Parliament, to represent physicians;

(ca) two members and two alternates appointed by the Commission, on the basis of a public call for expressions of interest and after consultation of the European Parliament, to represent patients associations.

Justification

In order to cover all medical fields which the advanced therapies may relate to, more general medical expertise, i.e. medical doctors, should be represented in the Committee for Advanced Therapies. In addition, by introducing alternate members, we would like to ensure a permanent representation of the groups involved. The appointment of these members and their alternates should take place in consultation with the European Parliament.

Amendment 33
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

2. All members and alternates 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. management and ethics.

Justification

The alternate members of the Committee for Advanced therapies introduced in paragraph 1 shall comply with the same criteria of scientific qualification or experience in the field of advanced therapy medicinal products as its members.

Amendment 34
ARTICLE 23, POINT (A)

(a) to advise the Committee for Medicinal Products for Human Use on any data generated in the development of an advanced therapy medicinal product, for the formulation of an opinion on its quality, safety and efficacy;

Justification

Due to the highly specific and unique character of the advanced therapy medicinal products, a new Committee for Advanced Therapies is established within EMEA, composed of experts having specific qualification or experience in this highly innovative and quickly developing field. Therefore, the new structure should be responsible for drafting an opinion on the quality, safety, and efficacy of products for the final approval by the CHMP. Furthermore, the committee should be consulted for the evaluation of other products under its competence.

Amendment 35
ARTICLE 23, POINT (A A) (new)

(aa) to provide advice, pursuant to Article 18, to the Committee for Medicinal Products for Human Use on whether a product falls within the definition of an advanced therapy medicinal product;

Justification

Having specific expertise in advanced therapy medicinal products, the Committee for Advanced Therapies should assist the CHMP in its classification task of whether a product is or is not an advanced therapy medicinal product.

Amendment 36
ARTICLE 23, PARAGRAPH 1 A (new)

When preparing a draft opinion for final approval by the Committee for Medicinal Products for Human Use, the Committee
for Advanced Therapies shall endeavour to reach a scientific consensus. If such consensus cannot be reached, the Committee for Advanced Therapies shall adopt the position of the majority of its members. The draft opinion shall mention the divergent positions and the grounds on which they are based.

Justification

In order to guarantee transparency in the process of preparation of a draft opinion, a clear decision procedure should be defined within Committee for Advanced Therapies. Consequently, we suggest that a scientific consensus should be reached by its members.

Amendment 37

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.

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 38

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,
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 39
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 40
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.

Justification

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

Amendment 41
ARTICLE 26 A (new)

Article 26a

Without prejudice to the implementing measures already adopted, on 1 April 2008
at the latest, the application of the provisions of this Regulation requiring the adoption of technical rules, amendments and decisions shall be suspended. Acting on a proposal from the Commission, the European Parliament and the Council may renew the provisions concerned in accordance with the procedure laid down in Article 251 of the Treaty and, to that end, they shall review them prior to the expiry of the date referred to above.

The first paragraph shall apply until such time as it is superseded by a new agreement on comitology.

Justification

This amendment is preliminary tabled until the new comitology procedure is adopted which ensures more control by the Parliament.

Amendment 42
ARTICLE 27, POINT 2
Annex, point 1 a (Regulation (EC) No 726/2004)

“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)*].

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 43
ARTICLE 28, POINT 2

“As 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.”

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 44
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 45

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.

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 46

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 the technical requirements referred to in Article 8.

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 47
ANNEX II, POINT 2.2.

2.2. qualitative and quantitative composition 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.

Amendments
ANNEX II, POINT 2.2.

2.2. qualitative and quantitative composition 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, 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 48
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 49
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, including the

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

Justification

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

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<td>13.7.2006</td>
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| Result of final vote | +: 13  
-: 8  
0: 1 |
<p>| Members present for the final vote | Maria Berger, Carlo Casini, Monica Frassoni, Giuseppe Gargani, Pia-Noora Kauppi, Katalin Lévai, Hans-Peter Mayer, Aloyzas Sakalas, Daniel Strož, Diana Wallis, Rainer Wieland, Tadeusz Zwiefka |
| Substitute(s) present for the final vote | Hiltrud Breyer, Manuel Medina Ortega, Marie Panayotopoulou-Cassiotou, Michel Rocard |
| Substitute(s) under Rule 178(2) present for the final vote | Sharon Bowles, Esther Herranz García, Mieczysław Edmund Janowski, Peter Liese, Maria Martens, Miroslav Mikolášik |
| Comments (available in one language only) | |</p>
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| Date submitted to Parliament | 1 |
| Committee responsible | ENVI |
| Date announced in plenary | 30.11.2005 |

| Committee(s) asked for opinion(s) | ITRE | IMCO | JURI |
| Date announced in plenary | 30.11.2006 | 30.11.2006 | 23.3.2006 |
| Date of decision | IMCO | 30.1.2006 |

| Enhanced cooperation | JURI |
| Date announced in plenary | 18.5.2006 |

| Rapporteur(s) | Miroslav Mikolášik |
| Date appointed | 14.12.2005 |

| Legal basis disputed | |
| Date of JURI opinion | |

| Financial endowment amended | |
| Date of BUDG opinion | |

| Date adopted | 30.1.2007 |
| Result of final vote | + 55 | - 6 | 0 | 3 |


| Substitute(s) present for the final vote | Pilar Ayuso, Niels Busk, Philippe Busquin, Hélène Goudin, Umberto Guidoni, Karin Jöns, Henrik Lax, Caroline Lucas, Jiří Maštálka, Miroslav Mikolášik, Bart Staes |

| Substitute(s) under Rule 178(2) present for the final vote | Iles Braghetto, Ioannis Gklavakis, Mieczyslaw Janowski, Maria Petre, Zita Plestinska, Konrad Szymanski |

| Date tabled | 7.2.2007 |

| Comments (available in one language only) | |