# ЕВРОПЕЙСКИ ПАРЛАМЕНТ

*2004* *2009*

*Документ за разглеждане в заседание*

ОКОНЧАТЕЛЕН
**A6-0031/2007**

7.2.2007

# ***I
# ДОКЛАД

относно предложението за регламент на Европейския парламент и на Съвета относно лекарствените продукти за съвременно лечение и за изменение на Директива 2001/83/ЕО и Регламент (ЕО) № 726/2004
(COM(2005)0567 – C6-0401/2005 – 2005/0227(COD))

Комисия по околна среда, обществено здраве и безопасност на храните

Докладчик: Miroslav Mikolášik

Докладчик по становище (*): Hiltrud Breyer, Комисия по правни въпроси

(*) Засилено сътрудничество между комисиите – член 47 от Правилника за дейността

## *Легенда на използваните знаци*

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| * | Процедура на консултация<br>*мнозинство от подадените гласове* |
| **I | Процедура на сътрудничество (първо четене)<br>*мнозинство от подадените гласове* |
| **II | Процедура на сътрудничество (второ четене)<br>*мнозинство от подадените гласове за одобряване на общата позиция*<br>*мнозинство от всички членове на Парламента за отхвърляне или изменение на общата позиция* |
| *** | Одобрение<br>*мнозинство от всички членове на Парламента, освен в случаите по членове 105, 107, 161 и 300 от Договора за ЕО и член 7 от Договора за ЕС* |
| ***I | Процедура на съвместно вземане на решение (първо четене)<br>*мнозинство от подадените гласове* |
| ***II | Процедура на съвместно вземане на решение (второ четене)<br>*мнозинство от подадените гласове за одобряване на общата позиция*<br>*мнозинство от всички членове на Парламента за отхвърляне или изменение на общата позиция* |
| ***III | Процедура на съвместно вземане на решение (трето четене)<br>*мнозинство от подадените гласове за одобрение на съвместния проект* |

(Посочената процедура се базира на правната основа, предложена от Комисията.)

## *Изменения на законодателен текст*

Измененията, внесени от Парламента, са отбелязани с ***потъмняване и курсив***. Отбелязването с *курсив без потъмняване* е предназначено за техническите служби и се отнася до частите от законодателния текст, за които е предложена поправка с оглед изготвяне на окончателния текст (например очевидни грешни или липсващи части в дадена езикова версия). Предложенията за поправка подлежат на съгласуване със засегнатите технически служби.

**СЪДЪРЖАНИЕ**

**Страница**



(*) Засилено сътрудничество между комисиите - член 47 от Правилника за дейността

## ЗАКОНОДАТЕЛНА ПРОЕКТОРЕЗОЛЮЦИЯ НА ЕВРОПЕЙСКИЯ ПАРЛАМЕНТ

**относно предложението за регламент на Европейския парламент и на Съвета относно лекарствените продукти за съвременно лечение и за изменение на Директива 2001/83/ЕО и Регламент (ЕО) № 726/2004**
**(COM(2005)0567 – C6-0401/2005 – 2005/0227(COD))**

**(Процедура на съвместно вземане на решение: първо четене)**

*Европейският парламент*,

– като взе предвид предложението на Комисията до Европейския парламент и до Съвета (COM(2005)0567)[1],

– като взе предвид член 251, параграф 2 и член 95 от Договора за ЕО, съгласно които предложението му е представено от Комисията (C6-0401/2005),

– като взе предвид член 51 от своя правилник,

– като взе предвид доклада на Комисията по околна среда, обществено здраве и безопасност на храните и становищата на Комисията по промишленост, изследвания и енергетика и на Комисията по правни въпроси (A6-0031/2007)

1. одобрява предложението на Комисията във вида, в който е изменено;

2. призовава Комисията да се отнесе до него отново, в случай че възнамерява да внесе съществени изменения в своето предложение или да го замени с друг текст;

3. възлага на своя председател да предаде позицията на Парламента на Съвета и на Комисията.

| Текст, предложен от Комисията | Изменения, внесени от Парламента |
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| Изменение 1<br>СЪОБРАЖЕНИЕ 2 | |
| 2) Доколкото за тези продукти за съвременно лечение се твърди, че притежават свойства за лечение или профилактика на заболявания при хора, или че могат да се използват при хора с цел възстановяване, коригиране или изменение на физиологични функции чрез упражняване на фармакологично, имунологично или метаболично | 2) Доколкото за тези продукти за съвременно лечение се твърди, че притежават свойства за лечение или профилактика на заболявания при хора, или че могат да се използват при хора с цел възстановяване, коригиране или изменение на физиологични функции чрез упражняване ***главно*** на фармакологично, имунологично или |

[1] Все още непубликувано в ОВ.

действие, те са биологични лекарствени продукти по смисъла на член 1, параграф 2 от Директива 2001/83/ЕО на Европейския парламент и на Съвета от 6 ноември 2001 г. за утвърждаване на кодекс на Общността относно лекарствени продукти за хуманна употреба и на приложение I към нея. Поради това, основната цел на всички норми, уреждащи тяхното производство, разпространение и употреба, трябва да бъде защитата на общественото здраве.

метаболично действие, те са биологични лекарствени продукти по смисъла на член 1, параграф 2 от Директива 2001/83/ЕО на Европейския парламент и на Съвета от 6 ноември 2001 г. за утвърждаване на кодекс на Общността относно лекарствени продукти за хуманна употреба и на приложение I към нея. Поради това, основната цел на всички норми, уреждащи тяхното производство, разпространение и употреба, трябва да бъде защитата на общественото здраве.

*Обосновка*

*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.*

Изменение 2
СЪОБРАЖЕНИЕ 5

5) Лекарствените продукти за съвременно лечение ***следва да се регулират, доколкото*** са предназначени за пускане на пазара в държавите-членки и се приготвят по промишлен способ или се произвеждат по метод, предполагащ промишлен процес ***по смисъла на член 2, параграф 1*** от Директива 2001/83/ЕО. Следователно, лекарствените продукти за съвременно лечение, които изцяло се приготвят и използват в болнично заведение ***по*** лекарско предписание за отделен пациент, следва да бъдат изключени от приложното поле на настоящия регламент.

5) ***Настоящият регламент е специален законов акт, чрез който се въвеждат допълнителни разпоредби към посочените в Директива 2001/83/ЕО. Приложното поле на настоящия регламент е да регламентира*** лекарствените продукти за съвременно лечение***, които*** са предназначени за пускане на пазара в държавите-членки и се приготвят по промишлен способ или се произвеждат по метод, предполагащ промишлен процес ***в съответствие с общото приложно поле на законодателството на Общността в областта на фармацевтиката по дял II*** от Директива 2001/83/ЕО. Следователно, лекарствените продукти за съвременно лечение, които изцяло се приготвят ***в болнично заведение, с нестопанска цел и еднократно, съгласно специфичен,***

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| | ***нестандартизиран и непатентован процес*** и се използват в болнично заведение ***с цел изпълнение на отделно*** лекарско предписание за отделен пациент ***на изключителната професионална отговорност на медицинско лице или за клинични изследвания***, следва да бъдат изключени от приложното поле на настоящия регламент. |

*Обосновка*

*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.*

Изменение 3
СЪОБРАЖЕНИЕ 6

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| 6) Регулирането на лекарствените продукти за съвременно лечение на общностно равнище не следва да съставлява вмешателство в решения на държавите-членки относно даването на разрешения за употреба на специфичен тип ***човешки*** клетки, ***като например ембрионални стволови клетки или животински клетки.*** То не следва да засяга и прилагането на националното законодателство, което забранява или ограничава продажбата, доставката или употребата на лекарствени продукти, съдържащи, състоящи се или получени от такива клетки. | 6) ***Действащото законодателство в държавите-членки относно употребата на определени типове клетки, като например ембрионални стволови клетки, значително се различава.*** Регулирането на лекарствените продукти за съвременно лечение на общностно равнище не следва да съставлява вмешателство в решения на държавите-членки относно даването на разрешения за употреба на специфичен тип клетки. То не следва да засяга и прилагането на националното законодателство, което забранява или ограничава продажбата, доставката или употребата на лекарствени продукти, съдържащи, състоящи се или получени от такива клетки. ***Освен това, невъзможно е да се прецени кога, ако изобщо някога, изследванията за тези клетки ще достигнат етапа, на който търговските продукти, получени от тези клетки, могат да бъдат пуснати на пазара. С цел спазване на основните*** |

***принципи и правилното функциониране на вътрешния пазар и за да се гарантира правна сигурност, настоящият регламент би следвало да се прилага само по отношение на продукти, получени от клетки, за които пускането на пазара е реалистично в близко бъдеще и които не предизвикват значими спорове.***

*Обосновка*

*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.*

Изменение 4
СЪОБРАЖЕНИЕ 9

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| 9) Оценката на лекарствени продукти за съвременно лечение често изисква много специфични експертни познания, които излизат извън рамките на традиционната фармацевтична област и обхващат области на границата с други области, като например биотехнология и медицински изделия. Поради това е целесъобразно в рамките на Агенцията да се създаде Комитет за съвременни лечения, до който Комитетът за лекарствени продукти за хуманна употреба ***да се допитва относно оценката на данни, свързани с лекарствени продукти за съвременно лечение, преди да издаде окончателното си научно становище.*** В допълнение, допитване до Комитета за съвременни лечения ***може*** да се извършва и за оценката на всеки друг лекарствен продукт, която изисква специфични експертни познания в кръга | 9) Оценката на лекарствени продукти за съвременно лечение често изисква много специфични експертни познания, които излизат извън рамките на традиционната фармацевтична област и обхващат области на границата с други области, като например биотехнология и медицински изделия. Поради това е целесъобразно в рамките на Агенцията да се създаде Комитет за съвременни лечения, ***който би следвало да отговаря за подготовката на проектостановище относно качеството, безопасността и ефикасността на всеки лекарствен продукт за съвременно лечение за окончателно одобрение от*** Комитета за лекарствени продукти за хуманна употреба на Агенцията. В допълнение, допитване до Комитета за съвременни лечения ***би следвало*** да се извършва и за оценката на всеки друг лекарствен продукт, която изисква |

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| на неговата компетентност. | специфични експертни познания в кръга на неговата компетентност. |

*Обосновка*

*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.*

Изменение 5
СЪОБРАЖЕНИЕ 10

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| 10) Комитетът за съвременни лечения следва да обединява най-добрите налични експертни познания в Общността относно лекарствените продукти за съвременно лечение. Съставът на Комитета за съвременни лечения следва да гарантира подходящо обхващане на научните области, които са относими към съвременните лечения, в т.ч. генно лечение, клетъчно лечение, тъканно инженерство, медицински изделия, фармакологична бдителност и етика. Следва да са представени и сдружения на пациенти и ***хирурзи*** с научни експертни познания за лекарствени продукти за съвременно лечение. | 10) Комитетът за съвременни лечения следва да обединява най-добрите налични експертни познания в Общността относно лекарствените продукти за съвременно лечение. Съставът на Комитета за съвременни лечения следва да гарантира подходящо обхващане на научните области, които са относими към съвременните лечения, в т.ч. генно лечение, клетъчно лечение, тъканно инженерство, медицински изделия, фармакологична бдителност и етика. Следва да са представени и сдружения на пациенти и ***лекари*** с научни експертни познания за лекарствени продукти за съвременно лечение. |

*Обосновка*

*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.*

Изменение 6
СЪОБРАЖЕНИЕ 14

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| 14) По правило, човешките клетки или тъкани, съдържащи се в лекарствени продукти за съвременно лечение, следва | 14) ***По отношение на даренията на човешки клетки или тъкани, следва да бъдат спазвани европейски принципи, като например анонимност както на*** |

да са плод на доброволно и безвъзмездно дарение. Доброволните и безвъзмездни дарения на тъкани и клетки ***са фактор, който може*** да способства за гарантирането на високи стандарти на безопасност за тъкани и клетки, а оттам и за защита на човешкото здраве.

***донора, така и на реципиента, алтруизъм на донора и солидарност между донор и реципиент.*** По правило, човешките клетки или тъкани, съдържащи се в лекарствени продукти за съвременно лечение, следва да са плод на доброволно и безвъзмездно дарение. ***Държавите-членки се приканват да вземат всички необходими мерки за насърчаване на силно участие на публичния и нестопанския сектор в осигуряването на човешки клетки или тъкани, тъй като*** доброволните и безвъзмездни дарения на тъкани и клетки ***могат*** да способстват за гарантирането на високи стандарти на безопасност за тъкани и клетки, а оттам и за защита на човешкото здраве.

Изменение 7
СЪОБРАЖЕНИЕ 15

15) Клиничните изпитвания на лекарствени продукти за съвременно лечение следва да се провеждат в съответствие с общите принципи и етични изисквания, определени в Директива 2001/20/ЕО на Европейския парламент и на Съвета от 4 април 2001 г. относно сближаване на законовите, подзаконовите и административните разпоредби на държавите-членки относно прилагането на добрата клинична практика при провеждане на клинични изпитвания на лекарствени продукти за хуманна употреба . Въпреки това, следва да се определят специфични правила, като се адаптира Директива 2005/28/ЕО от 8 април 2005 г. относно определяне на принципи и подробни насоки за добра клинична практика по отношение на лекарствените продукти за хуманна употреба, предназначени за изследване, както и изискванията относно издаването на разрешителни за производство или

15) Клиничните изпитвания на лекарствени продукти за съвременно лечение следва да се провеждат в съответствие с общите принципи и етични изисквания, определени в Директива 2001/20/ЕО на Европейския парламент и на Съвета от 4 април 2001 г. относно сближаване на законовите, подзаконовите и административните разпоредби на държавите-членки относно прилагането на добрата клинична практика при провеждане на клинични изпитвания на лекарствени продукти за хуманна употреба . Въпреки това, следва да се определят специфични правила, като се адаптира Директива 2005/28/ЕО от 8 април 2005 г. относно определяне на принципи и подробни насоки за добра клинична практика по отношение на лекарствените продукти за хуманна употреба, предназначени за изследване, както и изискванията относно издаването на разрешителни за производство или

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| внос на такива продукти, за да се отчетат напълно специфичните технически характеристики на лекарствените продукти за съвременно лечение. | внос на такива продукти, за да се отчетат напълно специфичните технически характеристики на лекарствените продукти за съвременно лечение. ***Трябва да се определят специфични производствени изисквания за лекарствените продукти, предназначени за изследване, които следва да се прилагат при производството на лекарствени продукти за съвременно лечение за клинични изпитвания, провеждани в същото болнично заведение, където е осъществено производството. Тези правила би трябвало да осигурят достатъчен период от време между единичните клинични изпитвания(в т.ч. многоцентрови клинични изпитвания) и координираното наблюдение и обмен на информация.*** |

*Обосновка*

*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).*

Изменение 8
СЪОБРАЖЕНИЕ 16

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| 16) Производството на лекарствени продукти за съвременно лечение следва да съответства на принципите за добра производствена практика, определени в Директива 2003/94/ЕО на Комисията от 8 октомври 2003 г. относно установяването на принципи и насоки за добра производствена практика по отношение на лекарствените продукти за хуманна употреба и изпитваните лекарствени продукти за хуманна употреба. Освен това, следва да се изготвят специфични насоки за лекарствените продукти за съвременно лечение, за да се отрази правилно особеното естество на техния | 16) Производството на лекарствени продукти за съвременно лечение следва да съответства на принципите за добра производствена практика, определени в Директива 2003/94/ЕО на Комисията от 8 октомври 2003 г. относно установяването на принципи и насоки за добра производствена практика по отношение на лекарствените продукти за хуманна употреба и изпитваните лекарствени продукти за хуманна употреба, ***и при необходимост да се приспособява, така че да отразява специфичния характер на продуктите.*** Освен това, следва да се изготвят специфични насоки за |

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| производствен процес. | лекарствените продукти за съвременно лечение, за да се отрази правилно особеното естество на техния производствен процес. |

*Обосновка*

*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)*.

Изменение 9
СЪОБРАЖЕНИЕ 17

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| 17) Лекарствените продукти за съвременно лечение могат да включват медицински изделия или активни имплантируеми медицински изделия. Тези изделия следва да отговарят на съществените изисквания, определени съответно в Директива 93/42/ЕИО на Съвета от 14 юни 1993 г. относно медицинските изделия и Директива 90/385/ЕИО на Съвета от 20 юни 1990 г. относно сближаване на законодателството на държавите-членки, свързано с активните имплантируеми медицински изделия, за да се гарантира достатъчно равнище на качество и безопасност. | 17) Лекарствените продукти за съвременно лечение могат да включват медицински изделия или активни имплантируеми медицински изделия. Тези изделия следва да отговарят на съществените изисквания, определени съответно в Директива 93/42/ЕИО на Съвета от 14 юни 1993 г. относно медицинските изделия и Директива 90/385/ЕИО на Съвета от 20 юни 1990 г. относно сближаване на законодателството на държавите-членки, свързано с активните имплантируеми медицински изделия, за да се гарантира достатъчно равнище на качество и безопасност. ***Когато е възможно, резултатите от оценката на медицинското изделие или на активното имплантируемо медицинско изделие от оправомощен орган в съответствие с посочените директиви би следвало да бъдат взети под внимание от Агенцията при оценката на даден комбиниран продукт, която се прави съгласно настоящия регламент.*** |

*Обосновка*

*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.*

Изменение 10
СЪОБРАЖЕНИЕ 18

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| 18) Следва да се определят специфични правила, за да се приспособят изискванията, определени в Директива 2001/83/ЕО по отношение на обобщението на характеристиките, етикетирането и листовката на продукта, към специфичните технически характеристики на лекарствените продукти за съвременно лечение. | 18) Следва да се определят специфични правила, за да се приспособят изискванията, определени в Директива 2001/83/ЕО по отношение на обобщението на характеристиките, етикетирането и листовката на продукта, към специфичните технически характеристики на лекарствените продукти за съвременно лечение. ***Тези правила би следвало да спазват напълно правото на пациента да бъде информиран за произхода на каквито и да е клетки или тъкани, използвани в подготовката на лекарствени продукти за съвременно лечение, като в същото време се зачита анонимността на донора.*** |

Изменение 11
СЪОБРАЖЕНИЕ 19

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| 19) ***Дългосрочното проследяване на състоянието на пациентите и фармакологичната бдителност*** са ключови аспекти на лекарствените продукти за съвременно лечение. ***Следователно***, когато това е обосновано от съображения за обществено здраве, от притежателя на разрешението за пускане на пазара следва да се изисква да установи подходяща система за управление на риска, с оглед отчитане на ***тези аспекти.*** | 19) ***Проследяването на ефикасността и на отрицателните реакции*** са ключови аспекти на лекарствените продукти за съвременно лечение. ***Следователно, в своето заявление за разрешение за пускане на пазара заявителят посочва точно какви мерки, ако има такива, са предвидени за осигуряване на такова проследяване.*** Когато това е обосновано от съображения за обществено здраве, от притежателя на разрешението за пускане на пазара следва да се изисква ***също*** да установи подходяща система за управление на риска, с оглед отчитане на ***рисковете, свързани с лекарствените продукти за съвременно лечение.*** |

*Обосновка*

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

Изменение 12
СЪОБРАЖЕНИЕ 19А (ново)

***19a) За прилагането на настоящия регламент е необходимо създаването на насоки, които следва да се съставят или от Агенцията, или от Комисията. И в двата случая би следвало да се проведат открити консултации с всички заинтересувани страни, по-специално с промишления сектор, за да се обедини ограниченият експертен опит в областта и да се осигури пропорционалност.***

*Обосновка*

*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.*

Изменение 13
СЪОБРАЖЕНИЕ 21

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| 21) Тъй като науката се развива много бързо в тази област, предприятията, разработващи лекарствени продукти за съвременно лечение, следва да могат да се обръщат към Агенцията за научни консултации, включително такива, които са свързани с дейности след издаването на разрешение. Като стимул, таксата за такива консултации следва да бъде минимална. | 21) Тъй като науката се развива много бързо в тази област, предприятията, разработващи лекарствени продукти за съвременно лечение, следва да могат да се обръщат към Агенцията за научни консултации, включително такива, които са свързани с дейности след издаването на разрешение. Като стимул, таксата за такива консултации следва да бъде минимална ***за малки и средни предприятия и следва също да бъде понижена за други заявители.*** |

*Обосновка*

*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.*

Изменение 14
СЪОБРАЖЕНИЕ 22

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| 22) Агенцията следва да е оправомощена да издава научни препоръки относно това дали определен продукт на основата на клетки или тъкани отговаря на научните критерии, които определят лекарствените продукти за съвременно лечение, за да може на възможно най-ранен етап да се решават въпроси на граничната линия с други области, като например козметични продукти или медицински изделия, които могат да възникнат с развитието на науката. | 22) Агенцията следва да е оправомощена да издава научни препоръки относно това дали определен продукт на основата на ***гени***, клетки или тъкани отговаря на научните критерии, които определят лекарствените продукти за съвременно лечение, за да може на възможно най-ранен етап да се решават въпроси на граничната линия с други области, като например козметични продукти или медицински изделия, които могат да възникнат с развитието на науката. ***Комитетът за съвременни лечения, със своя единствен по рода си експертен опит, би следвало да има важна роля при предоставянето на такива съвети.*** |

*Обосновка*

*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.*

Изменение 15
СЪОБРАЖЕНИЕ 24

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| 24) С оглед отчитане на развитието в областта на науката и техниката, Комисията следва да е оправомощена да приема всички необходими мерки във връзка с техническите изисквания за заявленията за издаване на разрешения за пускане на пазара на лекарствени продукти за съвременно лечение, обобщението на характеристиките, етикетирането и листовката на продукта. | 24) С оглед отчитане на развитието в областта на науката и техниката, Комисията следва да е оправомощена да приема всички необходими мерки във връзка с техническите изисквания за заявленията за издаване на разрешения за пускане на пазара на лекарствени продукти за съвременно лечение, обобщението на характеристиките, етикетирането и листовката на продукта. ***Комисията би следвало да следи за своевременното предоставяне на необходимата информация относно предвидените мерки на заинтересуваните страни.*** |

*Обосновка*

*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.*

Изменение 16
СЪОБРАЖЕНИЕ 27

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| 27) Необходимите мерки за прилагане на настоящия регламент следва да се приемат в съответствие с Решение 1999/468/ЕО на Съвета от 28 юни 1999 г. за определяне на условията и реда за упражняване на изпълнителните правомощия, предоставени на Комисията. | 27) Необходимите мерки за прилагане на настоящия регламент следва да се приемат в съответствие с Решение 1999/468/ЕО на Съвета от 28 юни 1999 г. за определяне на условията и реда за упражняване на изпълнителните правомощия, предоставени на Комисията. ***Процедурата по регулиране с контрол, предвидена в член 5а от посоченото решение, би следвало да се прилага за приемането на изменения на приложения от II до IV към настоящия регламент и на приложение I към Директива 2001/83/ЕО. Понеже тези мерки са от основно значение за правилното функциониране на цялата регулаторна рамка, те би следвало да се приемат бързо, в срок от 9 месеца след влизането в сила на настоящия регламент.*** |

*Обосновка*

*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.*

Изменение 17
ЧЛЕН 1 А (нов)

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| | ***Член 1а*** |
| | ***Изключения*** |
| | ***Настоящият регламент не се прилага за лекарствени продукти за съвременно лечение, които съдържат или са*** |

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| | ***получени от човешки ембрионални или зародишни клетки, първични зародишни клетки или от клетки, получени от такива клетки.*** |

*Обосновка*

*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).*

Изменение 18
ЧЛЕН 2, ПАРАГРАФ 1, БУКВА Б), УВОДНА ЧАСТ

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| б) продукт, получен чрез тъканно инженерство, означава продукт, който: | б) продукт, получен чрез тъканно инженерство, означава ***лекарствен*** продукт, който: |

*Обосновка*

Изменение 19
ЧЛЕН 2, ПАРАГРАФ 1, БУКВА Б), АЛИНЕЯ 2 А (нова)

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| | ***Продукти, които съдържат или са произведени от нежизнеспособни човешки или животински клетки и/или тъкани, които не съдържат никакви жизнеспособни клетки или тъкани и чието основно действие не е фармакологично, имунологично или метаболично, са изключени от това определение.*** |

*Обосновка*

*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.*

Изменение 20
ЧЛЕН 2, ПАРАГРАФ 1, БУКВА Г), ТИРЕ 1 А (ново)

***- клетъчната или тъканната му част съдържа жизнеспособни клетки или тъкани; или***

*Обосновка*

*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.*

Изменение 21
ЧЛЕН 2, ПАРАГРАФ 1, БУКВА Г), ТИРЕ 2

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| – клетъчната или тъканната му част трябва да може да упражнява върху човешкото тяло действие, което ***не може*** да се счита за ***спомагателно на*** действието на посочените изделия. | – клетъчната или тъканната му част, ***която съдържа нежизнеспособни клетки или тъкани***, трябва да може да упражнява върху човешкото тяло действие, което ***може*** да се счита за ***основно спрямо*** действието на посочените изделия. |

*Обосновка*

*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.*

Изменение 22
ЧЛЕН 2, ПАРАГРАФ 1, АЛИНЕЯ 1 А (нова)

***Когато даден продукт съдържа жизнеспособни клетки или тъкани, фармакологичното, имунологично или метаболично действие на тези клетки или тъкани се счита за основен способ на действие на продукта.***

*Обосновка*

*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.*

Изменение 23
ЧЛЕН 4, ПАРАГРАФИ 2 И 3

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| 2. Комисията, в съответствие с процедурата, посочена в член 26, параграф 2, изменя Директива 2005/28/ЕО с цел да се отчетат специфичните характеристики на лекарствените продукти за съвременно лечение. | 2. Комисията, ***след консултиране с Агенцията и*** в съответствие с процедурата, посочена в член 26, параграф 2, изменя Директива 2005/28/ЕО с цел да се отчетат специфичните характеристики на лекарствените продукти за съвременно лечение. |
| 3. Комисията изготвя подробни насоки за добра клинична практика, която е специфична за лекарствените продукти за съвременно лечение. | 3. Комисията, ***след консултиране с Агенцията***, изготвя подробни насоки за добра клинична практика, която е специфична за лекарствените продукти за съвременно лечение. |

*Обосновка*

*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.*

Изменение 24
ЧЛЕН 5, ПАРАГРАФ -1 (нов)

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| | ***Комисията, в съответствие с процедурата, посочена в член 26, параграф 2, изменя Директива 2003/94/ЕО с цел да се отчетат специфичните характеристики на лекарствените продукти за съвременно лечение и по-специално на продукти, получени чрез тъканно инженерство.*** |

*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).*

Изменение 25
ЧЛЕН 5

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| Комисията ***публикува*** подробни насоки, които са в съответствие с принципите на добрата производствена практика и са специфични за лекарствените продукти за съвременно лечение. | Комисията ***съставя*** подробни насоки, които са в съответствие с принципите на добрата производствена практика и са специфични за лекарствените продукти за съвременно лечение. |

*Обосновка*

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

Изменение 26
ЧЛЕН 7

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| Специфични изисквания за ***продуктите, получени чрез тъканно инженерство*** | Специфични изисквания за ***лекарствените продукти за съвременно лечение, които съдържат изделия*** |
| В допълнение към изискванията, предвидени в член 6, параграф 1 от Регламент (ЕО) № 726/2004, заявленията за разрешаване на продукт, ***получен чрез тъканно инженерство***, включват описание на физичните характеристики и действието на продукта, както и описание на методите за създаване на продукта, в съответствие с приложение I към Директива 2001/83/ЕО. | В допълнение към изискванията, предвидени в член 6, параграф 1 от Регламент (ЕО) № 726/2004, заявленията за разрешаване на ***лекарствен*** продукт ***за съвременно лечение, който съдържа медицински изделия, био-материали, структури или матрици***, включват описание на физичните характеристики и действието на продукта, както и описание на методите за създаване на продукта, в съответствие с приложение I към Директива 2001/83/ЕО. |

*Обосновка*

*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.*

Изменение 27
ЧЛЕН 8

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| Комисията, в съответствие с процедурата, посочена в ***член 26, параграф 2*** от настоящия регламент, изменя приложение I към Директива 2001/83/ЕО, за да се определят специфични технически изисквания за продуктите, получени чрез тъканно инженерство, по-конкретно посочените в член 7, с оглед отчитане на еволюцията в областта на науката и техниката. | Комисията, ***след консултиране с Агенцията и*** в съответствие с процедурата, посочена в ***член 26, параграф 2а*** от настоящия регламент, изменя приложение I към Директива 2001/83/ЕО, за да се определят специфични технически изисквания за продуктите, получени чрез тъканно инженерство, по-конкретно посочените в член 7, с оглед отчитане на еволюцията в областта на науката и техниката. |

*Обосновка*

*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.*

Изменение 28
ЧЛЕН 9, ПАРАГРАФ 2

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| 2. Докладчикът или съдокладчикът, определен от Комитета за лекарствени продукти за хуманна употреба съгласно член 62 от Регламент (ЕО) № 726/2004, е член на Комитета за съвременни лечения. Този член действа и в качеството на докладчик или съдокладчик за Комитета за съвременни лечения. | 2. Докладчикът или съдокладчикът, определен от Комитета за лекарствени продукти за хуманна употреба съгласно член 62 от Регламент (ЕО) № 726/2004, е член на Комитета за съвременни лечения, ***който се предлага от Комитета за съвременни лечения и притежава специални експертни познания за продукта.*** Този член действа и в качеството на докладчик или |

съдокладчик за Комитета за съвременни лечения.

*Обосновка*

*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.*

Изменение 29
ЧЛЕН 9, ПАРАГРАФ 2 А (нов)

***2а. Когато подготвя проектостановище за окончателно одобрение от Комитета за лекарствени продукти за хуманна употреба, Комитетът за съвременни лечения се стреми да постигне научно единодушие. В случай че такова единодушие не може да се постигне, Комитетът за съвременни лечения приема позицията на мнозинството от членовете си. В проектостановището се посочват различните позиции и основанията за тях.***

*Обосновка*

*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.*

Изменение 30
ЧЛЕН 9, ПАРАГРАФ 2 Б (нов)

***2б. Докладчикът и съдокладчикът имат право да задават въпроси директно на заявителя. Заявителят също може да предложи да му бъдат задавани въпроси. Докладчикът и съдокладчикът информират незабавно заинтересуваните комитети в писмена форма за подробностите за контактите със заявителя.***

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| | ***В случай на несъгласие с проектостановището на Комитета за съвременни лечения, в срок от 15 дни от получаване на проектостановището заявителят може да представи писмени бележки пред Комитета за лекарствени продукти за хуманна употреба. Преди да издаде становището си, Комитетът за лекарствени продукти за хуманна употреба изслушва заявителя, в случай че в своите писмени бележки заявителят пожелае така.*** |

*Обосновка*

*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.*

Изменение 31
ЧЛЕН 9, ПАРАГРАФ 3

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| 3. ***Съветът*** на Комитета за съвременни лечения по параграф 1 се изпраща своевременно на председателя на Комитета за лекарствени продукти за хуманна употреба, така че да се гарантира, че може да бъде спазен срокът, определен в член 6, параграф 3 от Регламент (ЕО) № 726/2004. | 3. ***Проектостановището*** на Комитета за съвременни лечения по параграф 1 се изпраща своевременно на председателя на Комитета за лекарствени продукти за хуманна употреба, така че да се гарантира, че може да бъде спазен срокът, определен в член 6, параграф 3 ***или член 9, параграф 2*** от Регламент (ЕО) № 726/2004. |

*Обосновка*

*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.*

Изменение 32
ЧЛЕН 9, ПАРАГРАФ 4

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| 4. Когато научното становище относно лекарствен продукт за съвременно лечение, изготвено от Комитета за лекарствени продукти за хуманна употреба съгласно член 5, параграфи 2 и 3 от Регламент (ЕО) № 726/2004, не съответства на ***съвета*** на Комитета за съвременни лечения, Комитетът за лекарствени продукти за хуманна употреба прилага към становището си подробно обяснение на научните основания за различията. | 4. Когато научното становище относно лекарствен продукт за съвременно лечение, изготвено от Комитета за лекарствени продукти за хуманна употреба съгласно член 5, параграфи 2 и 3 от Регламент (ЕО) № 726/2004, не съответства на ***проектостановището*** на Комитета за съвременни лечения, Комитетът за лекарствени продукти за хуманна употреба прилага към становището си подробно обяснение на научните основания за различията. |

*Обосновка*

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

Изменение 33
ЧЛЕН 10, ПАРАГРАФ 1

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| 1. Когато се касае за лекарствен продукт за комбинирано съвременно лечение, Агенцията ***оценява*** целия продукт, в т.ч. всички включени в него медицински изделия или активни имплантируеми медицински изделия. | 1. Когато се касае за лекарствен продукт за комбинирано съвременно лечение, Агенцията ***дава окончателна оценка за*** целия продукт, в т.ч. всички включени в него медицински изделия или активни имплантируеми медицински изделия. |

*Обосновка*

*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.*

Изменение 34
ЧЛЕН 10, ПАРАГРАФ 1 А (нов)

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| | ***1а. Заявлението за разрешение за пускане на пазара на лекарствен продукт за комбинирано съвременно лечение включва доказателство за съвместимост с основните изисквания, посочени в член 6.*** |

*Обосновка*

*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.*

Изменение 35
ЧЛЕН 10, ПАРАГРАФ 2

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| 2. ***Когато медицинското изделие или активното имплантируемо медицинско изделие, съставляващо част от лекарствен продукт за комбинирано съвременно лечение, вече е оценено*** от нотифициран орган в съответствие с Директива 93/42/ЕИО или Директива 90/385/ЕИО, при оценяване на съответния лекарствен продукт Агенцията взема под внимание резултатите от тази оценка. | 2. ***Заявлението за разрешение за пускане на пазара на лекарствен продукт за комбинирано съвременно лечение включва, по възможност, резултатите от оценката*** от нотифициран орган в съответствие с Директива 93/42/ЕИО или Директива 90/385/ЕИО, ***на медицинското изделие или частта на активното имплантируемо медицинско изделие.*** При оценяване на съответния лекарствен продукт Агенцията взема под внимание резултатите от тази оценка. |
| Агенцията може да изисква от съответния нотифициран орган да изпраща всякаква информация, свързана с резултатите от извършената от него оценка. Нотифицираният орган изпраща информацията в едномесечен срок. | Агенцията може да изисква от съответния нотифициран орган да изпраща всякаква информация, свързана с резултатите от извършената от него оценка. Нотифицираният орган изпраща информацията в едномесечен срок. |
| | ***Ако заявлението не включва резултатите от оценката, тогава Агенцията може да потърси становище относно съвместимостта на частта на изделието с приложение I към Директива 93/42/ЕИО или Директива 90/385/ЕИО, от нотифициран орган, определен заедно*** |

***със заявителя.***

Изменение 36
ЧЛЕН 14, ПАРАГРАФ 2

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| 2. ***Листовката на продукта отразява резултатите от допитвания до целеви групи от пациенти, за да се гарантира, че тя е четлива, ясна и разбираема.*** | 2. ***Когато продукти се прилагат на пациенти изключително от практикуващи лекари, обобщението на характеристиките на продукта съгласно член 11 от Директива 2001/83/ЕО може да се използва като листовка на продукта.*** |

*Обосновка*

*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.*

Изменение 37
ЧЛЕН 15, ЗАГЛАВИЕ

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| Управление на риска след издаване на разрешение | ***Проследяване на ефикасността и отрицателните реакции*** след издаване на разрешение ***и*** управление на риска |

*Обосновка*

*This is a consequential amendment to amendment 38 (Article 15, paragraph 1).*

Изменение 38
ЧЛЕН 15, ПАРАГРАФ 1

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| 1. В допълнение към изискванията за фармакологична бдителност, установени в членове от 21 до 29 от Регламент (ЕО) № 726/2004, в заявлението за издаване на | 1. В допълнение към изискванията за фармакологична бдителност, установени в членове от 21 до 29 от Регламент (ЕО) № 726/2004, в заявлението за издаване на |

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| разрешение за пускане на пазара заявителят подробно излага мерките, предвидени да гарантират проследяване на ефикасността на лекарствените продукти за съвременно лечение. | разрешение за пускане на пазара заявителят подробно излага мерките, предвидени да гарантират проследяване на ефикасността на лекарствените продукти за съвременно лечение ***и на отрицателните реакции към тях.*** |

*Обосновка*

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

Изменение 39
ЧЛЕН 15, ПАРАГРАФ 2, АЛИНЕЯ 1

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| 2. При наличие на конкретна причина за загриженост, по препоръка на Агенцията, Комисията ***може да постави*** изискване в рамките на заявлението за разрешение за пускане на пазара да се създаде система за управление на риска, предназначена да се установяват, предотвратяват или свеждат до минимум рисковете, свързани с лекарствените продукти за съвременно лечение, включително оценка на ефективността на тази система, или да се провеждат специфични изследвания от страна на притежателя на разрешението след пускането на пазара, които да се представят за разглеждане от Агенцията. | 2. При наличие на конкретна причина за загриженост, по препоръка на Агенцията, Комисията ***поставя*** изискване в рамките на заявлението за разрешение за пускане на пазара да се създаде система за управление на риска, предназначена да се установяват, ***характеризират***, предотвратяват или свеждат до минимум рисковете, свързани с лекарствените продукти за съвременно лечение, включително оценка на ефективността на тази система, или да се провеждат специфични изследвания от страна на притежателя на разрешението след пускането на пазара, които да се представят за разглеждане от Агенцията. |

*Обосновка*

*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.*

Изменение 40
ЧЛЕН 16, ПАРАГРАФ 1

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|---|---|
| 1. Притежателят на разрешение за пускане на пазара на лекарствен | 1. Притежателят на разрешение за пускане на пазара на лекарствен |

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| продукт за съвременно лечение създава и поддържа система, която гарантира, че всеки отделен продукт и неговите изходни материали и суровини, в т.ч. всички вещества, които влизат в контакт с тъканите или клетките, които може да се съдържат в него, могат да бъдат проследени по време на доставката на материали, производството, опаковането, превоза и доставката до лечебното заведение, институция или частен кабинет, където се използва продуктът. | продукт за съвременно лечение създава и поддържа система, която гарантира, че всеки отделен продукт и неговите изходни материали и суровини, в т.ч. всички вещества, които влизат в контакт с тъканите или клетките, които може да се съдържат в него, могат да бъде проследени по време на доставката на материали, производството, опаковането, ***складирането***, превоза и доставката до лечебното заведение, институция или частен кабинет, където се използва продуктът. |

*Обосновка*

*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.*

Изменение 41
ЧЛЕН 16, ПАРАГРАФ 4

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| 4. Притежателят на разрешение за пускане на пазара съхранява данните, посочени в параграф първи, в срок от най-малко 30 години от ***пускането на продукта на пазара***, или в по-дълъг срок, ако това се изисква от Комисията като условие за издаване на разрешение за пускане на пазара. | 4. Притежателят на разрешение за пускане на пазара съхранява данните, посочени в *параграф 1*, в срок от най-малко 30 години от ***датата на изтичане на срока на годност на продукта***, или в по-дълъг срок, ако това се изисква от Комисията като условие за издаване на разрешение за пускане на пазара. |

*Обосновка*

*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.*

Изменение 42
ЧЛЕН 17, ПАРАГРАФ 2

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| 2. В отклонение от разпоредбите на член 8, параграф 1 от Регламент (ЕО) № 297/95, се прилага намаление с 90% от | 2. В отклонение от разпоредбите на член 8, параграф 1 от Регламент (ЕО) № 297/95, се прилага намаление с 90% от |

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| таксата, която се заплаща на Агенцията за всяка консултация по параграф 1 и член 57, параграф 1, буква н) от Регламент (ЕО) № 726/2004 по отношение на лекарствени продукти за съвременно лечение. | таксата ***за малки и средни предприятия и с 65% за други заявители***, която се заплаща на Агенцията за всяка консултация по параграф 1 и член 57, параграф 1, буква н) от Регламент (ЕО) № 726/2004 по отношение на лекарствени продукти за съвременно лечение. |

*Обосновка*

*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.*

Изменение 43
ЧЛЕН 18, ПАРАГРАФ 1

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| 1. Всеки заявител, разработващ продукт въз основа на клетки или тъкани, може да се обърне към Агенцията за научна препоръка с цел да се определи дали даденият продукт спада от научна гледна точка към определението за лекарствен продукт за съвременно лечение. Агенцията предоставя такава препоръка след консултация с Комисията. | 1. Всеки заявител, разработващ продукт въз основа на ***гени,*** клетки или тъкани, може да се обърне към Агенцията за научна препоръка с цел да се определи дали даденият продукт спада от научна гледна точка към определението за лекарствен продукт за съвременно лечение. Агенцията предоставя такава препоръка след консултация с Комисията ***и в срок от 60 дни след получаване на искането.*** |

*Обосновка*

*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.*

Изменение 44
ЧЛЕН 19 А (нов)

***Член 19а***
***Стимули за малки и средни биотехнологични предприятия***

***Производителите на лекарствени продукти за съвременно лечение, които имат не повече от 500 служители и оборот до 100 милиона евро или обща сума на баланса до 70 милиона евро, имат право на всички стимули, които се предоставят на малки и средни предприятия, както са определени в Препоръка 2003/361/ЕО[1].***

***[1] ОВ L 124, 20.05.2003 г., стр. 36.***

*Обосновка*

*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. These companies should nevertheless enjoy more favourable financial terms.*

Изменение 45
ЧЛЕН 19 Б (нов)

***Член 19б***
***Намаляване на таксата за разрешение за пускане на пазара***

***1. Таксата за разрешение за пускане на пазара се намалява с 50%, ако заявителят може да докаже, че съществува особен обществен интерес в Общността по отношение на лекарствения продукт за съвременно лечение или ако очакваната възвращаемост на инвестицията от пускането на пазара на този продукт е ниска.***

***2. Параграф 1 се прилага също за такси, събирани от Агенцията за дейности след издаването на разрешение, през първата година след издаването на разрешение за пускане на пазара на лекарствения продукт.***

***3. В случаите на малки и средни предприятия или предприятия, които имат не повече от 500 служители и оборот до 100 милиона евро или обща сума на баланса до 70 милиона евро, се прилага също параграф 1, без ограничения на срока, по отношение на таксите, събирани от Агенцията за дейности след издаването на разрешение.***

*Обосновка*

*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.*

Изменение 46
ЧЛЕН 19 В (нов)

***Член 19в***

***Техническа подкрепа***

***Държавите-членки предоставят, с оглед на прилагането на настоящия регламент, специфична техническа подкрепа на заявителите и притежателите на разрешение за пускане на пазара. Тази подкрепа се предоставя посредством компетентните национални органи и е съсредоточена по-специално върху подкрепа на индивидуални болнични заведения или други малки институции, например университетски катедри, които не отговарят на условията по член 3, параграф 7 на Директива 2001/83/ЕО. Подкрепата се предоставя, при условие че лекарствените продукти за съвременно лечение се приготвят и използват на техническата отговорност на лекар специалист и по лекарско предписание за отделни***

***пациенти.***

*Обосновка*

*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.*

Изменение 47
ЧЛЕН 21, ПАРАГРАФ 1, БУКВА В)

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| в) ***четирима*** членове, назначени от Комисията въз основа на публична покана за изразяване на интерес, ***двама от които*** представляват ***сдружения на хирурзи и двама*** - сдружения на пациенти. | в) ***двама*** членове ***и двама заместници***, назначени от Комисията въз основа на публична покана за изразяване на интерес ***и след консултация с Европейския парламент***, които представляват ***лекарски сдружения***;<br><br>***ва) двама членове и двама заместници, назначени от Комисията въз основа на публична покана за изразяване на интерес и след консултация с Европейския парламент,*** които представляват сдружения на пациенти. |

*Обосновка*

*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.*

Изменение 48
ЧЛЕН 21, ПАРАГРАФ 2

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| 2. Всички членове на Комитета за съвременни лечения се избират с оглед на тяхната научна квалификация или опит по отношение на лекарствени продукти за съвременно лечение. По смисъла на параграф 1, буква б), държавите-членки си сътрудничат под координацията на изпълнителния директор на Агенцията, с цел да се гарантира, че окончателният | 2. Всички членове ***и заместник-членове*** на Комитета за съвременни лечения се избират с оглед на тяхната научна квалификация или опит по отношение на лекарствени продукти за съвременно лечение. По смисъла на параграф 1, буква б), държавите-членки си сътрудничат под координацията на изпълнителния директор на Агенцията, с |

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| състав на Комитета за съвременни лечения целесъобразно и балансирано обхваща научните области, които са относими към съвременните лечения, в т.ч. медицински изделия, тъканно инженерство, генно лечение, клетъчно лечение, биотехнологии, фармакологична бдителност, управление на риска и етика. | цел да се гарантира, че окончателният състав на Комитета за съвременни лечения целесъобразно и балансирано обхваща научните области, които са относими към съвременните лечения, в т.ч. медицински изделия, тъканно инженерство, генно лечение, клетъчно лечение, биотехнологии, фармакологична бдителност, управление на риска и етика.<br>***Поне двама членове и двама заместник-членове на Комитета по съвременно лечение притежават научни познания в областта на медицинските изделия.*** |

*Обосновка*

*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.*

Изменение 49
ЧЛЕН 21, ПАРАГРАФ 5

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| 5. ***Агенцията публикува*** имената и научните квалификации на членовете. | 5. Имената и научните квалификации на членовете ***се публикуват на Интернет страницата на Агенцията при първа възможност***. |

*Обосновка*

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

Изменение 50
ЧЛЕН 22

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| ***1. Членовете на Комитета за съвременни лечения и неговите експерти се задължават да изпълняват функциите си независимо и в полза на обществото. Те нямат*** финансови или други интереси във ***фармацевтичния сектор***, ***сектора на медицинските изделия или биотехнологичния сектор***, | ***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*** |

които биха могли да се отразят на тяхната безпристрастност.

***sectors*** shall be entered in the register referred to in Article 63(2) of Regulation (EC) No 726/2004.

***2.*** Всички косвени интереси, които биха могли да са свързани с ***фармацевтичния сектор, сектора на медицинските изделия или биотехнологичния сектор***, се вписват в регистъра по член 63, параграф 2 от Регламент (ЕО) № 726/2004.

*Обосновка*

*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.*

Изменение 51
ЧЛЕН 23, БУКВА А)

а) ***предоставяне на консултации*** на Комитета за лекарствени продукти за хуманна употреба относно всички данни, събрани при разработване на ***даден медицински*** продукт ***за съвременно лечение***, ***с оглед формулиране на становище относно неговото качество, безопасност и ефикасност***;

а) ***да изготви проектостановище относно качеството, безопасността и ефикасността на даден лекарствен продукт за съвременно лечение, което да представи за окончателно одобрение*** на Комитета за лекарствени продукти за хуманна употреба ***и да информира Комитета*** относно всички данни, събрани при разработване на ***такъв*** продукт;

*Обосновка*

*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.*

Изменение 52
ЧЛЕН 23, БУКВА А А) (нова)

***аа) да предостави консултация, съгласно член 18, относно това дали продуктът отговаря на определението за лекарствен продукт за съвременно лечение;***

*Обосновка*

*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.*

Изменение 53
ЧЛЕН 23, БУКВА Д А) (нова)

***да) да подпомага процедурите за научни консултации, посочени в член 17 на настоящия регламент и в член 57, параграф 1, буква н) на Регламент (ЕО) No 726/2004;***

*Обосновка*

*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.*

Изменение 54
ЧЛЕН 24

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| В съответствие с процедурата по ***член 26, параграф 2***, Комисията изменя ***приложения от I до IV***, за да ги адаптира към научно-техническото развитие. | В съответствие с процедурата по ***член 26, параграф 2а***, Комисията, ***след консултация с Агенцията***, изменя ***приложения от II до IV***, за да ги адаптира към научно-техническото развитие. |

*Обосновка*

*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.*

Изменение 55
ЧЛЕН 25, ЗАГЛАВИЕ

***Доклад*** ***Доклад и преразглеждане***

*Обосновка*

*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.*

Изменение 56
ЧЛЕН 25, ПАРАГРАФ 1 А (нов)

***В този доклад Комисията оценява влиянието на техническия напредък върху приложението на настоящия регламент. Тя също така изготвя, ако е необходимо, законодателно предложение за включване на нови лечения, които не включват нито генно лечение, нито клетъчно лечение, нито тъканно инженерство.***

*Обосновка*

*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.*

Изменение 57
ЧЛЕН 26, ПАРАГРАФ 2 А (нов)

***2а. Когато се прави позоваване на настоящия параграф, се прилагат член 5а, параграфи 1-4 и член 7 от Решение 1999/468 ЕО, като се вземат предвид разпоредбите на член 8 от него.***

*Обосновка*

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

Изменение 58
ЧЛЕН 27, ТОЧКА -1 (нова)
Член 13, параграф 1 (Регламент (ЕО) No 726/2004)

***(-1) В член 13, първото изречение на параграф 1 се заменя със следния текст:***

***"Без да накърнява разпоредбите на член 4, параграфи 4 и 5 на Директива 2001/83/ЕО, разрешението за пускане на пазара, което е предоставено съгласно настоящия регламент, е валидно за цялата Общност."***

*Обосновка*

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

Изменение 59
ЧЛЕН 27, ТОЧКА 2 А (нова)
Приложение, точка 3, алинея 2 (Регламент (ЕО) No 726/2004)

***2а) В приложението алинея втора от точка 3 се заменя, както следва:***

***"След 20 май 2008 г. Комисията, след като се консултира с Агенцията, може да представи всякакво подходящо предложение за изменение на настоящата точка и Европейският парламент и Съветът вземат решение за него съгласно Договора."***

*Обосновка*

*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.*

Изменение 60
ЧЛЕН 28, ТОЧКА -1 (нова)
Член 1, точка 4 а (нова) (Директива 2001/83/ЕО)

***(-1) Към член 1 се добавя следната точка 4а:***

***"4а. Продукт, получен от тъканно инженерство:***

***продукт, както е определен в член 2 от Регламент (ЕО) No **/** относно лекарствените продукти за съвременно лечение."***

*Обосновка*

*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.*

Изменение 61
ЧЛЕН 28, ТОЧКА 1
Член 3, точка 7, (Директива 2001/83/ЕО)

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| 7. Всеки лекарствен продукт за съвременно лечение, определен в Регламент (ЕО) № [.../на Европейския парламент и на Съвета (Регламент относно лекарствените продукти за съвременно лечение)*], който изцяло се изготвя и използва в лечебно заведение ***по*** лекарско предписание за отделен пациент. | 7. Всеки лекарствен продукт за съвременно лечение, определен в Регламент (ЕО) № [.../на Европейския парламент и на Съвета (Регламент относно лекарствените продукти за съвременно лечение)*], който изцяло се изготвя ***в болнично заведение, с нестопанска цел***, ***еднократно, съобразно специфичен, нестандартизиран и непатентован процес*** и се използва в лечебно заведение, ***за изпълнение на индивидуално*** лекарско предписание за отделен пациент ***на изключителната професионална отговорност на медицинско лице или за клинични изследвания***. |

***Точки 1 и2 не се прилагат за лекарствени продукти за съвременно лечение.***

*Обосновка*

*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.*

Изменение 62
ЧЛЕН 28, ТОЧКА 2Член 4, параграф 5 (Директива 2001/83/ЕО)

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| 5. Настоящата директива и всички регламенти, посочени в нея, не засягат прилагането на националното законодателство, забраняващо или ограничаващо употребата на който и да е конкретен вид човешки или животински клетки, или продажбата, доставката или използването на лекарствени продукти, съдържащи, състоящи се или получени от такива клетки. Държавите-членки съобщават на Комисията текстовете на съответните актове от националното законодателство. | 5. Настоящата директива и всички регламенти, посочени в нея, не засягат прилагането на ***недискриминиращо*** национално законодателство, забраняващо или ограничаващо употребата на който и да е конкретен вид човешки или животински клетки, или продажбата, доставката или използването на лекарствени продукти, съдържащи, състоящи се или получени от такива клетки ***поради причини, които не са споменати в горепосоченото законодателство на Общността***. Държавите-членки съобщават на Комисията текстовете на съответните актове от националното законодателство. ***Комисията прави тази информация обществено достъпна в регистър.*** |

*Обосновка*

*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.*

Изменение 63
ЧЛЕН 29, ПАРАГРАФ 1

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| 1. Лекарствените продукти за съвременно лечение, които са законосъобразно пуснати на общностния пазар в съответствие с националното или общностното законодателство към датата на влизане в сила на настоящия регламент, се привеждат в съответствие с настоящия регламент не по-късно от ***2 години*** след влизането му в сила. | 1. Лекарствените продукти за съвременно лечение, които ***не са получени от тъканно инженерство и*** са законосъобразно пуснати на общностния пазар в съответствие с националното или общностното законодателство към датата на влизане в сила на настоящия регламент, се привеждат в съответствие с настоящия регламент не по-късно от ***4 години*** след влизането му в сила. |

*Обосновка*

*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.*

Изменение 64
ЧЛЕН 29, ПАРАГРАФ 1 А (нов)

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| | ***1а. Продуктите, получени от тъканно инженерство, които са били законно на пазара на Общността в съответствие с националното или общностното законодателство към датата на прилагане, определена във втория параграф на член 30, трябва да се приведат в съответствие с настоящия регламент не по-късно от 4 години след тази дата.*** |

*Обосновка*

*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.*

Изменение 65
ЧЛЕН 29, ПАРАГРАФ 2

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| 2. В отклонение от разпоредбите на член 3, параграф 1 от Регламент (ЕО) № 297/95, не се заплащат такси на Агенцията за подадени заявления за издаване на разрешение за лекарствените продукти за съвременно лечение по ***параграф*** 1. | 2. В отклонение от разпоредбите на член 3, параграф 1 от Регламент (ЕО) № 297/95, не се заплащат такси на Агенцията за подадени заявления за издаване на разрешение за лекарствените продукти за съвременно лечение по ***параграфи*** 1 ***и 1а***. |

*Обосновка*

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

Изменение 66
ЧЛЕН 29, ПАРАГРАФ 2 А (нов)

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| | ***2а. По отношение на автологичните продукти, при обосновано искане на дадена държава-членка и в отклонение от разпоредбите на член 3 от Регламент (ЕО) No 726/2004, Комисията може, в съответствие с процедурата, установена в член 26, параграф 2, и след консултация с Комитета за съвременни лечения, да одобри за период от пет години национално разрешение в съответствие с принципите на настоящия регламент. Комисията може да вземе такова решение само ако сметне, че:*** |
| | ***- регулаторният орган на съответната държава-членка притежава достатъчно познания в областта на лекарствените продукти за съвременно лечение; и*** |

***- пускането на пазара на специфичния лекарствен продукт извън дадената държава-членка е невъзможно.***

***Подробните процедурни правила за приложение на настоящия член се установяват от Комисията и се публикуват в Официален вестник на Европейския съюз.***

Изменение 67
ЧЛЕН 30, ПАРАГРАФИ 2 А И 2 Б (нови)

***За продукти, получени от тъканно инженерство, настоящият регламент се прилага от влизането в сила на всички изисквания, посочени в членове 4, 5 и8.***

***Изпълнителните мерки, предвидени в членове 4, 5 и 8, се приемат възможно най-скоро и, във всеки случай, не по-късно от 9 месеца след влизането в сила на настоящия регламент.***

*Обосновка*

*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.*

Изменение 68
ПРИЛОЖЕНИЕ II, ТОЧКА 2.2.

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| 2.2. качествен и количествен състав на активните вещества и другите съставки на продукта, чието познаване е от съществено значение за правилната употреба, прием или имплантиране на продукта. Когато продуктът съдържа клетки или тъкани, се предоставя подробно описание на тези клетки или тъкани и на техния точен произход. | 2.2. качествен и количествен състав на активните вещества и другите съставки на продукта, чието познаване е от съществено значение за правилната употреба, прием или имплантиране на продукта. Когато продуктът съдържа клетки или тъкани, се предоставя подробно описание на тези клетки или тъкани и на техния точен произход, |

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| | ***включително на животинските видове в случаите на нечовешки произход***. |

*Обосновка*

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

Изменение 69
ПРИЛОЖЕНИЕ III, БУКВА Б)

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| б) Описание на активното(ите) вещество(а), изразени качествено и количествено, включително, когато продуктът съдържа клетки или тъкани, текстът „Този продукт съдържа клетки от човешки/животински [в зависимост от случая] произход“, заедно с кратко описание на тези клетки или тъкани и на техния специфичен произход; | б) Описание на активното(ите) вещество(а), изразени качествено и количествено, включително, когато продуктът съдържа клетки или тъкани, текстът „Този продукт съдържа клетки от човешки/животински [в зависимост от случая] произход“, заедно с кратко описание на тези клетки или тъкани и на техния специфичен произход, ***включително на животинските видове в случаите на нечовешки произход***. |

*Обосновка*

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

Изменение 70
ПРИЛОЖЕНИЕ IV, БУКВА А), ПОДТОЧКА (III)

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| (iii) когато продуктът съдържа клетки или тъкани, описание на тези клетки или тъкани и на техния специфичен произход; | (iii) когато продуктът съдържа клетки или тъкани, описание на тези клетки или тъкани и на техния специфичен произход, ***включително на животинските видове в случаите на нечовешки произход.*** |

*Обосновка*

*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.

20.6.2006

## OPINION OF THE COMMITTEE ON INDUSTRY, RESEARCH AND ENERGY

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

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

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:

| Text proposed by the Commission[1] | Amendments by Parliament |
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| Amendment 1<br>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) 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 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. |

[1] Not yet published in OJ.

*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)

***(7b) 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[1] prohibits gene therapy trials that result in modifications to a subject's germ line genetic identity. Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions[2] considers processes for modifying the human germ line genetic identity non-patentable. To ensure legal coherence, this Regulation should prohibit any authorisation of products that modify the germ line genetic identity of human beings.***

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***[1] L 121, 1.5.2001, p. 34.***
***[2] L 213, 30.7.1998, p. 13.***

*Justification*

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

Amendment 3
RECITAL 7 C (new)

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| | ***(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

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| (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. | (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 ***should be responsible for preparing a draft 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. |

*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)

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| | ***(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

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

*Justification*

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

Amendment 7
RECITAL 16

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| (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. | (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***, adapted where appropriate to take account of specific characteristics of advanced therapy medicinal products, especially tissue engineered products***. Furthermore, guidelines specific to advanced therapy medicinal products should be drawn up, so as properly to 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

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| (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. | (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

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| (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. | (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)

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| | ***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

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| – 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 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

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| 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

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| 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

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| 4. Where the scientific opinion on an advanced therapy medicinal product drawn up by the Committee for Medicinal Products | 4. Where the scientific opinion on an advanced therapy medicinal product drawn up by the Committee for Medicinal Products |

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| 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. | 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 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. | 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 ***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 19
ARTICLE 10, PARAGRAPH 2

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| 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. | 2. ***The application for a marketing authorisation for*** a combined advanced therapy medicinal product ***shall include an 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*** |

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| | ***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

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| 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

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|---|---|
| 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, | 2. Where there is particular cause for concern, the Commission ***shall***, on the advice of the Agency, require as part of the marketing authorisation that a risk management system designed to identify, prevent or minimise risks related to advanced therapy medicinal products, |

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| 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. | 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

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| 4. The Agency shall draw up detailed guidelines relating to the application of paragraphs 1, 2 and 3. | 4. The Agency shall draw up detailed guidelines relating to the application of paragraphs 1, 2 and 3. ***They shall be based on the principles of regulatory cooperation and dialogue with the marketing authorisation holder.*** |

*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

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| 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. | 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 of 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 25
ARTICLE 19 A (new)

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|---|---|
| | ***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.***

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***[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 19 B (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***

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| | ***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)

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| (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 ***medical doctors;*** |

*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)

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| | ***(ca) two members and two alternates appointed by the Commission, on the basis of a public call for expressions of interest*** |

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| | ***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

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

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| (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*** | (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 |

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| ***quality, safety and efficacy***; | 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)

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| | ***(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)

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| | ***(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)

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| | ***(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

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

*Justification*

*Annex I contains a fundamental and substantial definition. 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

| | |
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| 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. | 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.*

Amendment 36
ARTICLE 26, PARAGRAPH 2 A (new)

***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).*

Amendment 37
ARTICLE 27, POINT 2
Annex, point 1 a (Regulation (EC) No. 726/2004)

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| "1a. Advanced therapy medicinal products, as defined in Regulation (EC) No […/of the European Parliament and of the Council (Regulation on Advanced Therapy Medicinal Products)]. | "1a. Advanced therapy medicinal products, as defined in Regulation (EC) No […/of the European Parliament and of the Council (Regulation on Advanced Therapy Medicinal Products)]***, except for advanced therapy medicinal products for autologous or intended use which are exclusively manufactured and distributed in one Member State and for which 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)

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| *"*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 ***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.<br><br>***Paragraphs 1 and 2 do not apply to advanced therapy medicinal products.*** |

*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)

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| "5. This Directive and all Regulations referred to therein shall not affect the application of national legislation prohibiting or restricting the use of any | "5. This Directive and all Regulations referred to therein shall not affect the application of national legislation prohibiting or restricting the use of any |

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| 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." | specific type of human or animal cells, or the sale, supply or use of medicinal products containing, consisting of or derived from these cells***, on ethical grounds***. The Member States shall communicate the national legislation concerned to the Commission***. The Commission shall publish the results in a public register."*** |

*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

| | |
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| 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***. |
| | ***2. 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.*** |
| ***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

| | |
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| This Regulation shall enter into force on the 20th day following that of its publication in the Official Journal of the European Union. | ***1.*** 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]* | ***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.*** |
| This Regulation shall be binding in its entirety and directly applicable in all Member States. | ***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.*

## PROCEDURE

| | |
|---|---|
| **Title** | Proposal for a regulation of the European Parliament and of the Council on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004 |
| **References** | COM(2005)0567 – C6-0401/2005 – 2005/0227(COD) |
| **Committee responsible** | ENVI |
| **Opinion by**<br>Date announced in plenary | ITRE<br>30.11.2005 |
| **Enhanced cooperation – date announced in plenary** | no |
| **Drafts(wo)man**<br>Date appointed | Giles Chichester<br>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<br>–: 17<br>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 Laperrouze, 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 draftswoman. 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

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

Draftswoman (*): Hiltrud Breyer

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

## 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.

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

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

## AMENDMENTS

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

its report:

| Text proposed by the Commission | Amendments by Parliament |
|---|---|
| Amendment 1<br>TITLE | |
| Proposal for a Regulation of the European Parliament and of the Council on advanced therapy medicinal products and amending Directive 2001/83/EC ***and*** Regulation (EC) No 726/2004 | Proposal for a Regulation of the European Parliament and of the Council on advanced therapy medicinal products and amending Directive 2001/83/EC***,*** Regulation (EC) No 726/2004 ***and Directive 2004/23/EC*** |
| *Justification* | |
| *The title of the proposal need to be changed, as Directive 2004/23/EC is also amended (see amendment 45).* | |
| Amendment 2<br>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 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.*

Amendment3
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[1] and of 26 October 2005 on patents for biotechnological inventions[2]. To that end, it is necessary to ensure that the donation of tissues and cells is voluntary and unpaid and that their procurement is carried out on a non-profit basis. Voluntary and unpaid tissue and cell donations also contribute to high safety standards for tissues and cells and therefore to the protection of human health.***

***[1] OJ C 320 E, 15.12.2005, p. 251.***
***[2] Texts Adopted of that date, P6_TA(2005)0407.***

*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[1] prohibits gene therapy trials that result in modifications to a subject's germ line genetic identity. Directive 98/44/EC[2] 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.***

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***[1] Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (OJ L 121, 1.5.2001, p. 34).***
***[2] Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions (OJ L 213, 30.7.1998, p. 13).***

*Justification*

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

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| (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. | (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 ***should be responsible for preparing a draft 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. |

*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 7
RECITAL 9 A (new)

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| | ***(9a) The Committee for Advanced Therapies should provide advice to the*** |

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| | ***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 8
RECITAL 10

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| (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

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

*Justification*

*This recital shall be deleted as a consequence to the introduction of a new recital 7(a) and*

*new Articles 3(a) and 28(a).*

Amendment 10
RECITAL 16

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| (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. | (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***, and adapted, where necessary, to reflect the specific nature of the products***. 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

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

*Justification*

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

Amendment 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

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| – 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

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| Where an advanced therapy medicinal product contains human cells or tissues, the | Where an advanced therapy medicinal product contains human cells or tissues, the |

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

Amendment 18
ARTICLE 3 A (new)

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| | ***Article 3a***<br>***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:***<br>***- 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***<br>***- 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)

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| | ***Article 3b***<br>***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 endogen 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

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|---|---|
| 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 | 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 |

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| member of the Committee for Advanced Therapies. This member shall also act as rapporteur or co-rapporteur for the Committee for Advanced Therapies. | 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

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| 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 ***deadlines*** laid down in ***Articles*** 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 25
ARTICLE 14, PARAGRAPH 2

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| 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 may be used as the 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 26
ARTICLE 15, PARAGRAPH 2, SUBPARAGRAPH 1

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

*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

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| 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 SMEs and 70% 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 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

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| 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)

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| | ***Article 19a***<br>***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[1].*** |
| | ***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.*** |

[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 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***

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| | ***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)

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

*Justification*

*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)

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|---|---|
| (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***;<br>***(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

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| 2. All members of the Committee for Advanced Therapies shall be chosen for their scientific qualification or experience in respect of advanced therapy medicinal products. For the purposes of point (b) of paragraph 1, the Member States shall cooperate, under the coordination of the Executive Director of the Agency, in order to ensure that the final composition of the Committee for Advanced Therapies appropriately and in a balanced way covers the scientific areas relevant to advanced therapies, including medical devices, tissue-engineering, gene therapy, cell therapy, biotechnology, pharmacovigilance, risk management and ethics. | 2. All members ***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 34
ARTICLE 23, POINT (A)

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| (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 ***formulate a draft opinion on the quality, safety and efficacy of an advanced therapy medicinal product for final approval by*** the Committee for Medicinal Products for Human Use ***and to advise it*** 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 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

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

*Justification*

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

Amendment 38
ARTICLE 25

| | |
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| ***Reporting*** | ***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. | 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.<br>***In that report, the Commission shall also assess the impact of technical progress on the application of this Regulation and, if necessary, submit a legislative proposal for a review of its scope to include novel therapies which are neither gene therapy, nor cell therapy nor tissue engineering.*** |

*Justification*

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

Amendment 39
ARTICLE 25 A (new)

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| ***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

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

*Justification*

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

Amendment 41
ARTICLE 26 A (new)

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| | ***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)

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| "1a. Advanced therapy medicinal products, as defined in Regulation (EC) No […/of the European Parliament and of the Council (Regulation on Advanced Therapy | "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*** |

| | |
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| Medicinal Products)*]. | ***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 in accordance with the criteria of this Regulation as an alternative, for a period of five years subsequent to the granting of the marketing authorisation at national level. Afterwards an application for a single renewal within the centralised procedure shall be necessary, with the effect that, after the renewal, the national marketing authorisation will become 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 43
ARTICLE 28, POINT 2

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| "5. This Directive and all Regulations referred to therein shall not affect the application of national legislation prohibiting or restricting the use of any specific type of human or animal cells, or the sale, supply or use of medicinal products containing, consisting of or derived from these cells***. The Member States shall communicate the national legislation concerned to the Commission***." | "5. This Directive and all Regulations referred to therein shall not affect the application of 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***, by virtue of the Article 30 of the Treaty establishing the European Community***." |

*Justification*

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

Amendment 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

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| 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)

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| | ***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.

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| 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. | 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)

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| (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)

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| (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.*

## PROCEDURE

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|---|---|
| **Title** | Proposal for a regulation of the European Parliament and of the Council on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004 |
| **References** | COM(2005)0567 – C6-0401/2005 – 2005/0227(COD) |
| **Committee responsible** | ENVI |
| **Opinion by**<br>Date announced in plenary | JURI<br>23.3.2006 |
| **Enhanced cooperation – date announced in plenary** | 18.5.2006 |
| **Drafts(wo)man**<br>Date appointed | Hiltrud Breyer<br>19.4.2006 |
| **Previous drafts(wo)man** | |
| **Discussed in committee** | 30.5.2006 22.6.2006 |
| **Date adopted** | 13.7.2006 |
| **Result of final vote** | +: 13<br>–: 8<br>0: 1 |
| **Members present for the final vote** | Maria Berger, Carlo Casini, Monica Frassoni, Giuseppe Gargani, Piia-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 Panayotopoulos-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)** | |

## PROCEDURE

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|---|---|---|---|---|---|
| **Title** | Proposal for a regulation of the European Parliament and of the Council on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004 | | | | |
| **References** | COM(2005)0567 – C6 0401/2005 – 2005/0227(COD) | | | | |
| **Date submitted to Parliament** | 16.11.2005 | | | | |
| **Committee responsible**<br>Date announced in plenary | ENVI<br>30.11.2005 | | | | |
| **Committee(s) asked for opinion(s)**<br>Date announced in plenary | ITRE<br>30.11.2006 | IMCO<br>30.11.2006 | JURI<br>23.3.2006 | | |
| **Not delivering opinion(s)**<br>Date of decision | IMCO<br>30.1.2006 | | | | |
| **Enhanced cooperation**<br>Date announced in plenary | JURI<br>18.5.2006 | | | | |
| **Rapporteur(s)**<br>Date appointed | Miroslav Mikolášik<br>14.12.2005 | | | | |
| **Legal basis disputed**<br>Date of JURI opinion | | | | | |
| **Financial endowment amended**<br>Date of BUDG opinion | | | | | |
| **Discussed in committee** | 30.5.2006 | 13.9.2006 | 14.9.2006 | 20.11.2006 | 23.1.2007 |
| **Date adopted** | 30.1.2007 | | | | |
| **Result of final vote** | +<br>–<br>0 | 55<br>6<br>3 | | | |
| **Members present for the final vote** | Adamos Adamou, Georgs Andrejevs, Liam Aylward, Tiberiu Barbuletiu, Irena Belohorská, Johannes Blokland, John Bowis, Frieda Brepoels, Hiltrud Breyer, Martin Callanan, Dorette Corbey, Chris Davies, Avril Doyle, Edite Estrela, Anne Ferreira, Matthias Groote, Françoise Grossetête, Cristina Gutiérrez-Cortines, Satu Hassi, Gyula Hegyi, Mary Honeyball, Caroline Jackson, Dan Jørgensen, Christa Klaß, Eija-Riitta Korhola, Urszula Krupa, Marie-Noëlle Lienemann, Peter Liese, Jules Maaten, Linda McAvan, Miroslav Ouzký, Antonyia Parvanova, Vittorio Prodi, Frédérique Ries, Dagmar Roth-Behrendt, Guido Sacconi, Karin Scheele, Carl Schlyter, Horst Schnellhardt, Richard Seeber, Kathy Sinnott, Bogusław Sonik, Evangelia Tzampazi, Thomas Ulmer, Anja Weisgerber, Åsa Westlund, Anders Wijkman | | | | |
| **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 Plestinská, Konrad Szymanski | | | | |
| **Date tabled** | 7.2.2007 | | | | |
| **Comments**<br>**(available in one language only)** | | | | | |