
COM(2005) 567 final — 2005/0227 (COD)

(2006/C 309/03)

On 10 January 2006 the Council decided to consult the European Economic and Social Committee, under Article 95 of the Treaty establishing the European Community, on the abovementioned proposal. The Section for the Single Market, Production and Consumption, which was responsible for preparing the Committee’s work on the subject, adopted its opinion on 31 May 2006. The rapporteur was Mr Bedossa. At its 428th plenary session, held on 5 and 6 July 2006 (meeting of 5 July), the European Economic and Social Committee adopted the following opinion by 150 votes, with one abstention.

1. Summary


1.2 Against a backdrop of accelerating scientific progress, especially in the field of biotechnology, there is a real need for clarification, rigour and expertise.

1.3 The aim of the proposal is to provide a coherent picture of the various advanced therapies, to fill the existing regulatory gap and to bolster specific evaluation by the European Medicines Agency in these new disciplines. This will secure:

— a swift response to the demands of patients and expectations in the industry with regard to research into and the development of regenerative medicine;

— a high level of health protection for European patients;

— overall legal certainty, while allowing for sufficient flexibility at technical level in order to keep pace with the evolution of science and technology.

1.4 Given the particularities of advanced therapy products, it is essential to provide a robust and comprehensive regulatory framework that is applicable in all Member States.

1.5 A regulation is therefore considered as being the most appropriate legal instrument. This is all the more important given that current public health issues regarding advanced therapy medicinal products will remain unresolved in the EU until a specific legislative system is put in place.

1.6 However, some aspects of this draft regulation may give rise to implementing problems, in view of the definitions used, with the draft directive on medical devices. Care must be taken to ensure that the final text clears up outstanding questions and possible doubts. For instance:

— What is the point in this new regulation given that advanced gene and cell therapy medicinal products are already governed by specific directives on pharmaceutical products?

— The definitions given in Article 2b, in particular, appear complicated and are rather superfluous.

— It is also clear that national pharmaceutical legislation might stand in the way of European legislation.

— It would have been preferable in this case to use a more flexible approach and begin with mutual recognition.

— The question of autologous products of non-industrial origin in the hospital sector also raises the issues of ‘border line’ products of other origins and of rules applying at European level.

2. General comments

2.1 An article by article examination of the regulation raises a number of comments, questions and recommendations. With regard to Article 2: ‘Definitions’ (1):

2.2 The definitions concerning gene therapy and somatic cell therapy do not generally pose any problems given that reflection and experience have led to a consensus. These products are classed as medicines and are already regulated as such within the Community.

2.2.1 The definition of a tissue engineered product seems more complex however. As currently worded, the first indent of Article 2(1)(b) states that a tissue engineered product ‘contains or consists of engineered cells or tissues’, without specifying ‘as an integral part’. In practice, therefore, medical devices which contain tissue engineered products ‘with an ancillary function’ are also included among innovative medicinal products. This makes the provisions of the proposed directive on medical devices meaningless.

2.2.2 The wording of the second indent of Article 2(1)(b) could also give rise to implementing difficulties and, in particular, overlap with the medical device directive. As tissue engineered products are covered by legislation on medicinal products, it would be desirable to mention their primary activity of disease treatment or prevention, or of altering physiological functions through pharmacological, immunological or metabolic action, rather than just referring to their properties for ‘regenerating, repairing or replacing a human tissue’, as these properties are also shared by some types of medical device.

2.3 An effort has been made to narrow down the exact definition of a ‘tissue engineered product’ as much as possible. Nevertheless, the difference from cell therapy (bone marrow transplants, stem cell transplants, umbilical cord blood transplants, adult or embryonic stem cells, etc.) is not entirely clear.

2.4 The Committee proposes that examples of products currently considered to have been generated by tissue engineering be used as a starting point for attempts to clarify the definition. This would assist understanding, particularly since it is no secret that the subject is the focus of debate and controversy, particularly regarding embryonic stem cells.

2.5 At this point, there are no ethical problems apart from those surrounding human embryonic stem cells (HESC).

2.6 The controversy centres on the means of producing stem cells. More specifically, the production of these cells by nuclear transfer (in other words cloning) raises major ethical questions, and no real consensus has been found within the European Union to this day. Current concerns focus on the risks of reproductive cloning, egg trafficking and the commercialisation of human body parts.

2.7 Such practices are explicitly condemned by the European Convention on Bioethics (Oviedo Convention, 1998) and by the International Bioethics Committee (UNESCO, 1997).

2.8 In the absence of a consensus between EU Member States, HESC use falls within national responsibility.

2.9 The detail given in the recitals (3) is therefore essential, as it gives clear consideration to the reality of the debate and states that this text regulating advanced therapy medicinal products at Community level is not designed to ‘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’.

2.10 Neither is it designed to ‘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’.

3. Specific comments

3.1 The harmonisation of the principles governing other modern biotechnological medicines currently covered by Community-level regulations involves a centralised authorisation procedure, i.e. a single scientific evaluation of the quality, safety and effectiveness of advanced therapy medicinal products.

3.2 However, unlike traditional medical treatments, these therapies by their very nature require specific pre-clinical and clinical procedures, with particular emphasis on expertise, risk management and post-marketing authorisation (MA) pharmacovigilance.

3.3 The present draft regulation is right to stress the need to develop specific expertise in the evaluation of these products within the European Medicines Agency’s Committee for Medicinal Products for Human Use (CHMP (4)), also involving patient associations in the evaluation groups.

3.4 The proposal to set up a Committee for Advanced Therapies (CAT (4)) which the CHMP would consult on everything concerning the evaluation of data regarding advanced therapy medicinal products before issuing its final scientific opinion, is key.

3.5 This committee will bring together the few top experts currently working in the Community in the area of advanced therapy medicinal products and selected representatives of the parties concerned.

3.6 It is wholly justified as it will provide a means of defining not only scientific procedures but also standards for good clinical and manufacturing practice and will follow evaluation through to marketing authorisation (MA) and beyond to post-marketing authorisation.

3.7 The mention of the principle whereby ‘human cells or tissues contained in advanced therapy medicinal products should be procured from voluntary and unpaid donation’ is important. It responds to the constant concern to raise safety standards for tissue and cells, remove the risk of commercialising human body parts, and protect human health.

3.8 The proposal confirms the advisory role of the European Medicines Agency. This role will be critical on all kinds of issue that may arise as science evolves, be it the production of advanced therapy medicines, good manufacturing practice or rules relating to the summary of product characteristics, labelling or the package leaflet stating technical specificities, or when it is necessary to define the dividing line with other fields (such as cosmetics or certain medical devices).

(3) COM(2005) 567 final, 6th recital.

(4) It should be noted, when it comes to the membership of the CAT, that some language versions of COM(2003)567 final — 2005/0222 — (COD) use the term ‘surgeons’, whereas others refer to ‘doctors’. This opinion refers to doctors not surgeons.
3.8.1 Some have pointed out that the procedures used might be expensive, whereas national authorisation procedures are by nature more economical. There is also the problem of national transition periods being longer than EU transition periods (five years as opposed to two). The political risk posed by decentralised national procedures may hinder access to advanced therapy medicinal products, as some Member States have access and others do not.

3.9 Lastly, the proposal takes a useful look at the economic dimension (5). In the context of global competition in the health industry, the European Union must claim its rightful place on both the internal and global markets.

3.10 The economic risks linked with uncertainty or rapid changes in science, and the considerable cost of studies, hold back major and lasting investment in the field of medicine and advanced therapy medicinal products in particular.

3.11 Furthermore, it is frequently small and medium-sized companies that carry out the studies necessary to demonstrate the quality and non-clinical safety of advanced therapy medicinal products, and these do not always originate from previous experience in the pharmaceutical field (typically taking the form of spin-offs from biotech laboratories or manufacturers of medical devices).

3.12 The Commission proposes a ‘system of early evaluation and certification of quality and non-clinical safety data by the Agency, independently of any marketing authorisation application’ in order to support and encourage SMEs carrying out studies. This seems appropriate.

3.12.1 Meanwhile, in tissue engineering, products are often developed by SMEs, with the generation of start-ups and spin-offs, rather than by major pharmaceutical companies. This gives rise to a number of comments:

— What must this regulation cover in order for it to become operational? It will surely engender a heated debate, although the technologies used are full of promise.

— The membership of the CAT also poses a problem owing to its dependence on the CHMP (which is made up of one representative per Member State).

— The legislative framework used is inadequate, as these are unconventional pharmaceutical products that will require changes to other texts.

— The precautions taken regarding the use of stem cells may provoke a veto in the countries concerned, as the wording must be acceptable to avoid problems with the small print.

3.13 The aim of facilitating the evaluation of any subsequent request for marketing authorisation using the same data, should be supported and encouraged.

3.14 However, care should be taken and the provision altered if necessary in order to take account of rapid developments in scientific data (e.g. duration of data validity, data storage conditions), to provide permanent protection for patient health and, more generally, to abide by ethical standards.

3.15 The planned report on the ‘implementation of this Regulation after experience has been gained’ should provide an opportunity for debate within the bodies concerned (in particular the Committee for Advanced Therapies (CAT) and the Committee for Medicinal Products for Human Use (CHMP)).

3.15.1 However, the subordination of the CAT to the CHMP (the original mechanism for providing expertise) will weigh procedures down considerably and may give rise to unnecessary contradictions.

3.16 More generally, the planned publication of the report (Chapter 8, Article 25) could include not only ‘comprehensive information on the different types of advanced therapy medicinal products authorised pursuant to this Regulation’ but also information and results concerning the incentive measures provided for in Chapter 6 (Articles 17-18 and 19): ‘Scientific Advice’, ‘Scientific recommendation on advanced therapy classification’ and ‘Certification of quality and non-clinical data’.

4. Conclusions

4.1 On the whole, this draft regulation is relevant and useful. It provides a means of keeping up with scientific developments and deciding on definitions and the conditions for using advanced therapy medicinal products, thus serving patients’ interests.

4.1.1 These new technologies offer patients great hopes in terms of overcoming human suffering. However, if they are to respond to legitimate expectations, especially in the field of regenerative medicine, research must be supervised using essential tests, and the protocols for these must offer an absolute guarantee of patient safety. With this aim in view, the main objectives set out in the Justification of the Commission’s proposal for a Regulation (point 2.1) should be to guarantee not just a high level of health protection but also to give a guarantee of medicinal quality assurance. The issue of non-used waste — a rarely-discussed environmental aspect — must also not be overlooked.

4.2 The regulation is important, especially in the realms of gene therapy and somatic cell therapy. The caution exercised with regard to both definitions and the use of the products of tissue engineering clearly shows that the draft regulation is not intended to settle the debate once and for all or to pre-empt the deliberations of each Member State, since the ethical debate is not yet resolved and since it depends on varying interpretations of humanist values.

4.2.1 This draft regulation creates the preconditions for closing the regulatory gap that exists between its subject matter and the draft directive on medical devices. The general principle of risk evaluation applies to both advanced therapy medicinal products and medical devices. Complications may arise with combination products (i.e. medical devices containing tissue engineered elements). In such cases, both quality and safety must be guaranteed, and the evaluation must also cover the efficacy in use of an innovative medicinal product in a specific medical device.

4.3 In conclusion, the Committee endorses the proposed regulation while also stressing certain areas of concern for which clear solutions will be needed in order for the directive to be implemented successfully.

Brussels, 5 July 2006.

The President
of the European Economic and Social Committee
Anne-Marie SIGMUND