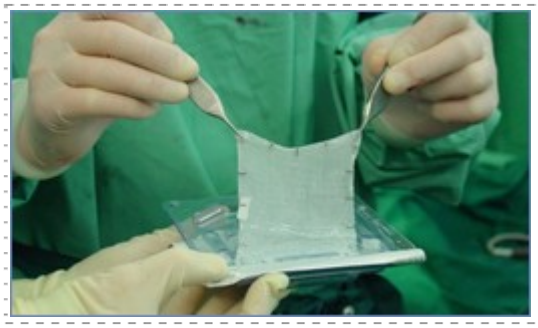
# Advanced therapy medicinal products backgrounder

## Summary

The draft Regulation on Advanced Therapy Products aims to establish harmonized rules for marketing human tissue engineering products, gene therapy products and somatic cell therapy products, based on the existing medicinal products legislation.

Eucomed has made some suggestions in relation to the following aspects of the proposal: products manufactured within the hospital; expertise within the European Medicines Evaluation Agency; transitional period for implementing the new regulation; national ethical standards; technical requirements; and product coverage.

## Introduction to the proposed Advanced Therapy Medicinal Products Regulation



Human tissue engineered skin (viable)

The draft Regulation on Advanced Therapy Medicinal Products published by the European Commission in November 2005 will establish harmonized rules for marketing human tissue engineering products as well as gene therapy products and somatic cell therapy products in the European Union.

The aim is to close the current regulatory gap. Whereas gene therapy and somatic cell therapy products are classified as 'medicinal products' and already regulated under the Medicinal Products Directive (2003/63/EC), there is at the moment no harmonized EU regulatory framework for human tissue engineering products.

**Tissue engineering** is the regeneration of biological tissue through the use of cells, with the aid of supporting structures and/or biomolecules (see examples on last page).

The development of human tissue engineering, and, in a wider sense, regenerative medicine, will change medical practice profoundly, offering better more cost-effective treatment, enhanced quality of life of patients and, in the future, a solution to overcome the shortage of donor organs for transplantation. The potential world-wide market for this cutting-edge sector has been evaluated at up to €400 billion[1].

The Commission proposal is to regulate the evaluation and authorization of these products by building on the existing medicinal products legislation. Detailed technical guidelines will be drawn up to assist.

## Proposed Advanced Therapy Products Regulation: Eucomed recommendations

### Scope of the regulation

**Patients should be assured that the treatments they receive are safe, are of high-quality, and perform as intended, no matter who prepares the treatment.**

The text needs to be amended to ensure that this is the case. Currently the proposal is worded in such a way that hospitals might be able to avoid complying with the provisions of the regulation, whereas industrial manufacturers of similar products would bear the obligations of compliance.

Obviously, products that are prepared for research purposes or on an exceptional, one-off basis should not have to comply with the authorisation process because this would be unworkable and not in the interests of patients. However, where hospitals are preparing products routinely, using an established process to create treatments for patients on a serial and routine basis, they too should have to comply with the provisions of the regulation.

This will ensure patients are always sure that their product is safe and of high-quality. It will secure public confidence in this emerging field of technology, will also ensure a "level playing field" and allow for continued investment in the field.

## EMEA Committee on advanced therapies

**It should be the European experts in this highly specialized and innovative field that are responsible for evaluating the new treatments and making scientific recommendations for a marketing authorisation.**

The text needs to be amended to clarify the role and responsibilities of the Committee for Advanced Therapies (CAT). Currently the CAT is foreseen only to have an advisory role and the decision regarding the recommendation of a Marketing Authorisation is left to the committee responsible for evaluating pharmaceutical products (CHMP). The products covered by this new regulation are highly specialised and should be evaluated and assessed by the top experts in the field.

We believe that, provided the CAT is appropriately constituted, there is no need to replicate the review process again at the CHMP level. The top experts in the field that constitute the CAT should be responsible for making a recommendation on the granting of a Marketing Authorisation, as is the case, for example, for herbal medicinal products and veterinary medicinal products. This would ensure that these products are evaluated and recommended by the highest expertise available in the field.

On a practical level, a mechanism for reaching agreement within the CAT and between the CAT and the CHMP needs to be outlined. This can be based on existing mechanisms in related fields. There should also be an opportunity for transparent appeal either to the CAT and/or the CHMP. Again, this can be modelled on existing mechanisms (e.g. as it is done for paediatrics).

## Transition period

**Patients that are currently being treated by products that will in future be covered by this Regulation should not have their treatment interrupted.**

The text currently proposes an unworkably short transition period (2 years) that could deprive patients of treatments they are currently receiving. This needs to be amended to a more realistic timeline.

There are already products available to patients on a national basis in certain member states, e.g. Germany. These have been authorised for use by the national authorisation systems. Patients should be assured that the treatment they are currently receiving will not be taken away from them during the process of implementing this new legislation. The current proposal foresees a transition period of just 2 years for these existing products to comply with the new provisions.

This is unworkably short to design and carry out all the necessary procedures 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 CAT for evaluation.

This could then mean that products that have been safely treating patients up to now might suddenly be removed from those patients while this whole process takes place, should it last longer than 2 years.

Companies are going to want to comply with the new regulation because of the support and incentives it offers.Forcing them to do so in an unrealistic timetable will not be good for patients. We would suggest a more realistic transition period for existing products of 5 years, which is in line with the "renewal" system normally foreseen for products evaluated by the EMEA. New products will, of course, have to comply with the provisions of the regulation from day one.

## Ethical issues

**Countries must retain the right to follow national ethical standards established by their own national laws. This should be done in a transparent and open manner.**

The proposed text quite correctly and understandably aims to allow Member States to opt out of offering treatments on their national markets where those treatments are based on human or animal cells that are ethically unacceptable in that country. This respects the right of each member state to make an ethical judgement in the interests of its own population regarding certain technologies where opinions differ, e. g. embryonic stem cells.

However, the text as it is currently worded would appear to remove any degree of certainty that a company might have. Therefore, we would propose that the text be amended to include a provision stating that the member states must give notice of the human or animal cells that will be prohibited. This will assist in commercial planning.

## Technical annexes

**The new legal framework should be developed with the highest level of technical expertise to ensure it is appropriate and workable, taking into account the specific characteristics of advanced therapy medicinal products and, in particular, tissue engineered products.**

The text proposes that a series of technical requirements be developed, as well as a series of amendments to existing legislation and guidelines be drawn up. Such elements are vital components of the whole legislative framework in this emerging field. However, for tissue engineered products in particular, modifying the Clinical Practice Directive (2005/28/EC) will be insufficient. The Clinical Trials Directive (2001/20/EC) and the Good Manufacturing Practices Directive (2003/94/EC) should also be amended.

Because expertise is so scarce, it will be crucial to ensure that the process is as inclusive as possible of stakeholder input. Eucomed and its members would welcome the opportunity to play an active role in developing these elements of the legal framework.

## Potentional regulatory gap for some human tissue engineered products

Eucomed has noted that as it stands, the draft Regulation on Advanced Therapy Medicinal Products will leave a number human tissue engineered products unregulated (those that do not act as medicines, i.e. whose principal mode of action is neither pharmaceutical, nor metabolic, nor immunologic). Eucomed is happy to share its expertise and experience in the area of human tissue engineering in view of helping to bridge this regulatory gap.

# Examples of human tissue engineered products

The Eucomed human tissue engineering vademecum provides examples of human tissue engineered products available to patients today and future prospects.

Click here to download this leaflet.

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[1] Report from the Institute for Prospective Technological Studies and Joint Research Centre of the European Commission, EUR 21000, October 2003