

# The new regulation on advanced therapy medicinal products in EU law: What are the main contributions?

Regulation (EC) No 1394/2007 on advanced therapy medicinal products,  
amending directive 2001/83/EC and regulation (EC) No 726/2004



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## INTRODUCTION

- Before 2007** { -As medicinal products, gene therapy medicinal products and cell therapy medicinal products were submitted to the Community general pharmaceutical legislation.  
-Nothing for Tissue engineered products at Community level → Divergent national approaches.
- Since 2007** { -One single and coherent legal framework at Community level, including Tissue engineered products  
-Novelty, complexity and technical specificity of Advanced Therapy Medicinal Products (ATMP) → setting up of a judicial system stricter than the one applicable to medicinal products in general.  
-New regulation= "lex specialis" : it introduces additional provisions to those laid down in the Community general pharmaceutical legislation.

## DEFINITIONS

Gene Therapy Medicinal Product (GTMP)	(Somatic) Cell Therapy Medicinal Product (CTMP)	Tissue Engineered Product (TEP): Article 2. 1. (b) of the Regulation (EC) 1394/2007
<ul style="list-style-type: none"> <li>•set of manufacturing processes</li> <li>• gene transfer by a vector (of viral or non-viral origin, included in a human or animal cell), either <i>in vivo</i> or <i>ex vivo</i>, to human/animal cells and its subsequent expression <i>in vivo</i>.</li> </ul> <p>(Part IV of Annex I to Directive 2001/83/EC)</p>	<ul style="list-style-type: none"> <li>▪use in humans of autologous, allogeneic or xenogeneic somatic living cells</li> <li>▪Substantial alteration of their biological characteristics to obtain a therapeutic, diagnostic or preventive effect.</li> </ul> <p>(Part IV of Annex I to Directive 2001/83/EC)</p>	<ul style="list-style-type: none"> <li>•Contains or consists of engineered cells or tissues (of human or animal origin or both, viable or non viable), AND</li> <li>▪ Is presented as having properties for human beings to regenerate, repair or replace a human tissue.</li> <li>▪If no any viable cells or tissues AND no pharmacological, immunological or metabolic principal action= NOT TEP.</li> </ul>

## MARKETING AUTHORISATION PROCEDURE AND POST- AUTHORISATION REQUIREMENTS

Marketing authorisation procedure	Post-authorisation follow- up of efficacy and adverse reactions, and risk management:	Traceability
<p><u>Unique and centralised marketing authorisation procedure by EMEA</u></p> <ul style="list-style-type: none"> <li>•Creation of the Committee for Advanced Therapy (CAT) within EMEA.</li> <li>•Compulsory consultation of the CAT by the Committee for medicinal Products for Human Use (CMHU): for marketing authorisation and pharmacovigilance.</li> <li>•Recommendation of the CAT: <ul style="list-style-type: none"> <li>-In principle by consensus</li> <li>-If no consensus: majority of members with mention of divergent opinions</li> <li>-Non- binding for CMHU.</li> </ul> </li> </ul>	<p><u>Strengthened post-authorisation requirements :</u></p> <ul style="list-style-type: none"> <li>•<u>Applicant</u>: Details the measures envisaged to ensure the follow-up of efficacy of ATMP and of adverse reactions.</li> <li>•<u>Commission</u> : requires, where there is specific cause for concern, on the advice of the EMEA: <ul style="list-style-type: none"> <li>- The setting up of a risk management system, including an evaluation of the effectiveness of that system</li> <li>- Or, specific marketing studies carried out by the holder of the marketing authorisation, and submitted for review to the Agency.</li> </ul> </li> <li>•<u>EMEA</u>: <ul style="list-style-type: none"> <li>- Requests submission of additional reports;</li> <li>-Informs the Commission of any failure to comply with the post-authorisation requirements. (Guidelines expected)</li> </ul> </li> </ul>	<p><u>Reinforced traceability</u></p> <ul style="list-style-type: none"> <li>•<u>Decentralised system</u>: <ul style="list-style-type: none"> <li>-keeping the data for at least 30 years after the expiry date of the product or longer if required by the Commission</li> <li>-transmission of the data to the EMEA or to another legal entity in case of bankruptcy or liquidation,</li> <li>- guidelines expected.</li> </ul> </li> <li>•<u>Complete system</u>: <ul style="list-style-type: none"> <li>-Traceability of the individual product, its starting and raw materials</li> <li>-Traceability system to link patient and product.</li> </ul> </li> </ul>

## SOLVED DIFFICULTIES AND ISSUES TO BE DISCUSSED

Difficulties solved by the ATMP regulation	Issues to be discussed
<ul style="list-style-type: none"> <li>• <u>Delimitation between medical devices and ATMP</u> → New category: Combined advanced therapy medicinal products: Specific marketing authorisation procedure.</li> <li>• <u>Conflict of qualification</u>: products which fall within two definitions: <ul style="list-style-type: none"> <li>-CTMP or TEP + GTMP → GTMP</li> <li>-TEP + CTMP → TEP</li> </ul> </li> <li>-Possibility for the applicant to ask a scientific recommendation of the Agency.</li> </ul>	<ul style="list-style-type: none"> <li>• <u>Exclusion of ethical concerns</u>: <ul style="list-style-type: none"> <li>-Embryonic stem cells uses</li> <li>-Possibility for the Member States to prohibit or restrict the use of medicinal products containing, consisting or derived from specific type of human or animal cells appealing Article 30 EC Treaty.</li> </ul> </li> <li>• <u>Exclusion of ATMP prepared in a hospital</u> on a non-routine basis under the exclusive medical responsibility of a medical practitioner, in order to comply with an individual medical prescription for a custom-made product for an individual patient : Incoherence with the practice at date.</li> </ul>

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