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Supplemental Information

EU Regulatory Pathways for ATMPs: Standard, Accelerated and Adaptive Pathways to Marketing Authorisation

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Table S2: Definitions of ATMPs according to Directive 2009/120/EC and Regulation (EC) No. 1394/2007
Directive 2009/120/EC further clarifies the definitions of GTMPs and SCTMPs with respect to Regulation (EC) 1394/2007 (the ATMP Regulation). Definitions for Tissue-engineered Products (TEPs) and Combined ATMPs are provided in the ATMP Regulation only.

GTMP	• it contains an active substance which contains or consists of a recombinant nucleic acid used in or administered to human beings with a view to regulating, repairing, replacing, adding or deleting a genetic sequence
	• its therapeutic, prophylactic or diagnostic effect relates directly to the recombinant nucleic acid sequence it contains, or to the product of genetic expression of this sequence
SCTMP	• it contains or consists of cells or tissues that have been subject to substantial manipulation so that biological characteristics, physiological functions or structural properties relevant for the intended clinical use have been altered, or of cells or tissues that are not intended to be used for the same essential function(s) in the recipient and the donor
	• it is presented as having properties for, or is used in or administered to human beings with a view to treating, preventing or diagnosing a disease through the pharmacological, immunological or metabolic action of its cells or tissues
TEP	• contains or consists of engineered cells or tissues
	• it is presented as having properties for, or is used in or administered to human beings with a view to regenerating, repairing or replacing a human tissue
	• it may contain cells or tissues of human or animal origin, or both
	• it may also contain additional substances, such as cellular products, bio-molecules, biomaterials, chemical substances, scaffolds or matrices
Combined ATMP	• it must incorporate, as an integral part of the product at least one medical device
	• its cellular or tissue part must contain viable cells or tissues, or
	• 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

Table S4: Definitions of non-similarity for ATMPs

Incentives provided to developers of EU OMPs include market exclusivity for 10 years following the granting of a Marketing Authorisation. Market exclusivity is protected by a requirement for applicants submitting an MAA to indicate in the application if any medicinal product has been designated as an OMP for a condition relating to the proposed therapeutic indication. If it has, and the competitor OMP is still under market exclusivity, the applicant is further required to submit a report on the similarity of the active substances, with significant differences being needed to demonstrate non-similarity and allow the new product to be marketed. Definitions of medicinal product similarity were initially established in 2000 in Commission Regulation (EC) No 847/2000, but did not at the time include ATMPs. Definitions of similarity for ATMP have now been published in Commission Regulation (EU) 2018/781 of 29 May 2018 amending Regulation (EC) No 847/2000 as regards the definition of the concept 'similar medicinal product'. These definitions for ATMPs are shown.

SCTMPs, TEPs and cell-based GTMPs (Cell-based ATMPs)	Non-cell–based GTMPs
Two related cell-based medicinal products are not similar if: • There are differences in starting materials or the final composition of the product which have significant impact on the biological characteristics and/or biological activity relevant for the intended therapeutic effect and/or safety attributes of the product. The different source of the starting materials (e.g. as in the case of autologous ATMPs) is not sufficient to support a claim that two products are non-similar; or • there are differences in the manufacturing technology having a significant impact on the biological characteristics and/or biological activity relevant for the intended therapeutic effect and/or safety attributes of the product.	Two gene therapy medicinal products shall not be considered similar when there are differences in the therapeutic sequence, viral vector, transfer system, regulatory sequences or manufacturing technology that significantly affect the biological characteristics and/or biological activity relevant for the intended therapeutic effect and/or safety attributes of the product. Differences in the therapeutic sequence without a significant impact on the intended therapeutic effect are not sufficient to support the claim that two gene therapy medicinal products are non-similar.