THE EU REVISION OF THE PHARMACEUTICAL LEGISLATION : WHAT CHANGES TO EXPECT FOR ATMP?

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BACKGROUND & METHOD

After more than 5 years of preparatory works, the European Union (EU) is about to adopt a major reform of its pharmaceutical legislation in 2026. While Advanced Therapy Medicinal Products (ATMPs) will remain the only type of medicines specifically regulated by another legal instrument (Regulation 1394/2007 on ATMPs), the revision of general rules applicable to all medicines will impact on the legal framework for ATMPs.

Research has been conducted on the content of the pharmaceutical legislation reform along the legislative process to identify the rules that will directly impact on ATMP regulation.

RESULTS

1. SPECIFIC MEASURES IMPACTING ON ATMP IN PARTICULAR

A NEW LEGAL DEFINITION FOR GENE THERAPY MEDICINAL PRODUCTS

Current legal definition: Directive 2009/120/EC

Gene therapy medicinal product means a biological medicinal product which has the following characteristics:

(a) 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;

(b) 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.

Gene therapy medicinal products shall not include vaccines against infectious diseases

European Commission proposal 26/04/2023

'gene therapy medicinal product' means a medicinal product, except vaccines against infectious diseases, that contains or consists of:

(a) a substance or a combination of substances intended to edit the host genome in a sequence-specific manner or that contain or consists of cells subjected to such modification; OR

(b) a recombinant or synthetic nucleic acid used in or administered to human beings with a view to regulating, replacing or adding a genetic sequence that mediates its effect by transcription or translation of the transferred genetic materials or that contain or consists of cells subjected to these modifications;

European Parliament Position 1st reading 10/04/2024

'gene therapy medicinal product' means a type 1 or type 2 medicinal product

"type 1 gene therapy medicinal product" means a medicinal product that contains or consists of a substance or a combination of substances that edit the host genome in a sequence-specific manner or that contain or consists of cells subjected to such modification

"type 2 gene therapy medicinal product" means a medicinal product, except a vaccine against infectious disease that contains or consists of a recombinant or synthetic nucleic acid used in or administered to human beings with a view to regulating, replacing or adding a genetic sequence that mediates its effect by transcription or translation of the transferred genetic materials or that contain or consists of cells subjected to these modifications

Compromise 24/02/2026

'gene therapy medicinal product' means a medicinal product, except vaccines against infectious diseases, that contains or consists of:

(a) a substance or a combination of substance intended to edit the host genome in a sequence-specific manner or that contain or consists of cells subjected to such modification; or

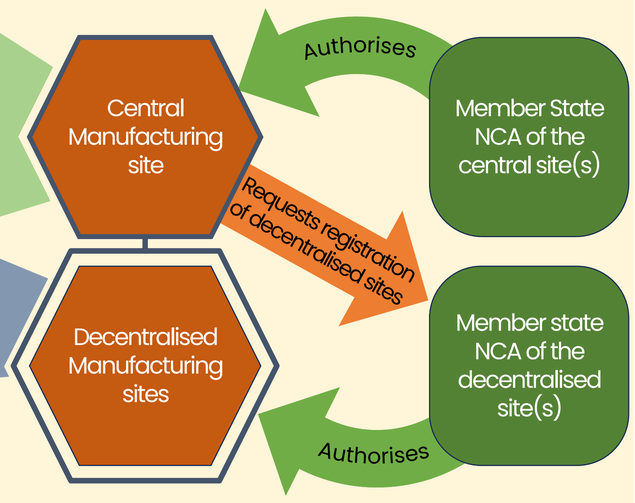
(b) a recombinant or synthetic nucleic acid used in or administered to human beings with a view to regulating, replacing or adding a genetic sequence that mediates its effect by long lasting transcription or translation of the transferred genetic materials or that contain or consists of cells subjected to these modifications;

MANUFACTURING AUTHORISATION AND DECENTRALISED MANUFACTURING SITES

Issues for ATMP: Short shelf life of medicines, highly customised and innovative manufacturing processes
→ Need to move certain manufacturing steps closer to patient (to the hospital, to the patient's bedside)

Manufacturing authorisation for:

- Manufacture of a medicine on the territory of an EU MS
- Manufactured medicines intended for export
- Imports of medicines coming from third countries
- Both total and partial manufacture
- The various processes of dividing up, packaging or presentation.



Use of decentralised manufacturing must be approved as part of MAA

Carrying out manufacturing or testing steps under the responsibility of the qualified person of a central site

Which Medicines for decentralised manufacturing

When justified by the specific properties of the manufactured medicine and consideration related to the quality, safety and efficacy of a medicine, such as short shelf life, or where proximity to the treated patient or customisation for an individual patient to their benefit

ENVIRONMENTAL RISK ASSESSMENT OF GMO-BASED MEDICINES

Issues for ATMP: Two applicable pieces of legislation (GMO and CT) with a single EC portal for CT (CTIS), but assessment and authorisation of GMO risks at national levels

Assessment of environmental risks posed by investigational medicinal products for human use containing genetically modified organisms

GMO legislation → Transfer → Pharmaceutical legislation

Competence of national GMO bodies → Transfer → **CHMP**

A single GMO application via the single portal in the context of CT authorisations, and assessment by CHMP

MAA: Marketing Authorisation Applications
MS(s): Member State(s)
NCA: National Competent Authority

HOSPITAL EXEMPTION

Hospital Exemption (HE) is maintained: same definition, approval by NCA, and GMP, traceability and pharmacovigilance requirements to be equivalent to ATMP that are not exempted.

HE developer

HE approval holder
Collection & (annual) reporting of data on the use, safety and efficacy and other relevant data (to be determined by a future EC implementation act)

National Competent authorities
Review of these HE data yearly
Approvals, revocations of exempted ATMP and subsequent changes

EMA
Publication of HE data in a repository
Dissemination of approvals, revocations, changes to other NCAs
Reports on HE implementation based on MS' assessment of possible adapted framework for certain less complex ATMPs used under HE

Possible request of scientific and regulatory advice on the further development of their ATMP, and when appropriate for the purpose of obtaining a marketing authorisation by the Union

EC Implementation acts on:

- Details of the application for approval of HE (incl. Evidence on quality, safety and efficacy of exempted ATMP for approval and subsequent changes)
- Content and format for collection and reporting of data
- Modalities for exchange of knowledge between HE approval holders within the same MS or different MSs

RECOGNITION OF PLATFORMS

Platform marketing authorisation

MA to be granted for a fixed and a variable component

The variable component shall:

- be pre-defined in the
- be justified for clinical purposes
- target different variants OR tailor the medicine to an individual patient/group of patients

Need of pre-agreement by competent authority before

Need of pre-agreement by competent authority before

Technology Platforms

"a technology or collection of technologies that has the potential to be incorporated in, or used by, more than one medicinal product and is comprehensive, well-characterised, reproducible, and standardised and used for the development, the manufacturing process or quality control of medicinal products that rely on prior knowledge and are established under the same underlying scientific principles, which have reasonable scientific certainty to remain unchanged across medicinal products"

Examples: Viral and bacterial vector systems, recombinant protein-based methods, nucleic acid sequences, viral and bacterial vectors and synthetic biology approaches (oligonucleotides and mRNA)

Rely on platform technology master file= a document, prepared by the owner of the platform technology, that contains a detailed description of the platform technology:

- Eligibility check by EMA
- Certification by EMA (→ repository)
- EMA scientific guidelines + new Annex II

Can be subject to inspection

Application as part of OR after granting of the corresponding medicinal product

REGULATORY SANDBOXES

"A regulatory framework during which it is possible to develop, validate and test in a controlled environment innovative or adapted regulatory solutions that facilitate the development and authorisation of innovative products which are likely to fall in the scope of this Regulation, pursuant to a specific plan and for a limited time under regulatory supervision"

- Set up on a case-by-case basis, for a limited time and in a limited part of a sector/area, by EC upon recommendation from EMA
- Provide specific requirements & technical adaptations to certain requirements of general medicines or ATMP legislations to test innovative medicines
- Under direct supervision of NCAs concerned, ensuring appropriate safeguards

2. GENERAL MEASURES IMPACTING ON ATMP

Most of general measures will impact on ATMP. A few of them can be highlighted here:

- Reduced timeline for assessment (from 210 to 180 days) by EMA
- EMA restructuring to reduce administrative burden: including dissolution of CAT (as almost all other current Committees), to become a working group or a pool of experts to CHMP and PRAC.

CONCLUSION

The 2026 forthcoming reform of the EU pharmaceutical legislation will establish important changes for ATMP and their regulatory incentives through a clear commitment of the EU legislator to supporting innovation,

- The definition In the compromise is identical to EC proposal, except the addition of "long lasting" transcription or translation.
- Decentralised manufacturing provisions apply to all medicines but particularly relevant for ATMP. Of note, only SoHO-derived medicines are explicitly mentioned on this topic in the explanations available in the Recitals.
- New provisions on GMO-base medicines apply to all medicines containing GMOs but particularly relevant for ATMP.
- A new structured and standardised way of reporting HE data to enable reliable and comparable results and conclusions for further possibilities of ATMP development.
- Platforms' recognition supports innovation in medicines development (personalised medicines & ATMP ++) via recognition of prior knowledge: Reduced human exposure, animal use, development time & costs, length of regulatory review, built data package → accelerate products' development & patients access to medicines
- Regulatory sandboxes as flexible and anticipatory enabler : structured context for experimentation under a controlled framework → to enable testing of innovative technologies
- Reduced timelines favour timely and equitable access to safe, effective, and affordable medicines (ATMPs)