



## **European Commission DG Health and Food Safety and European Medicines Agency Action Plan on ATMPs**

The term “advanced therapy medicinal products” (“ATMPs”) is used to designate gene therapies, somatic cell therapies and tissue engineered products.

In the EU, these products are governed by Regulation 1394/2007 on advanced therapy medicinal products (“ATMP Regulation”). The cornerstone of the Regulation is that a marketing authorisation must be obtained prior to the marketing of ATMPs. The evaluation of these products is led by a specialised committee within the European Medicines Agency (EMA) i.e. by the Committee for Advanced Therapies (“CAT”) who prepares a draft opinion before the Committee for Medicinal Products for Human Use (CHMP) adopts a final opinion and the authorisation is granted by the Commission. The ATMP Regulation also empowers Member States to permit the use of advanced therapies that have not been authorised by the Commission under certain conditions (so-called “hospital exemption”).

The 2014 report on the application of ATMPs<sup>1</sup>, concluded that the Regulation had protected patients from unsound treatments. However, it also recognised shortcomings and identified actions to help translate scientific progress into medicinal products available to patients. Such shortcomings were also discussed in a multi-stakeholder workshop organised by the EMA on 27 May 2016 and certain follow-up initiatives have already been taken, as also reflected in this action plan<sup>2,3</sup>.

The European Commission services and the European Medicines Agency, in collaboration with the authorities of the Member States, have initiated a number of initiatives to improve the regulatory environment for ATMPs so as to facilitate the development and authorisation of these products in the EU for the benefit of patients. The actions presented in this document are wide-ranging and target challenges identified by various stakeholders at all stages of development, including manufacturing, early and later phases of development, marketing authorisation process and post-marketing setting.

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<sup>1</sup> [http://ec.europa.eu/health/human-use/advanced-therapies/developments/index\\_en.htm](http://ec.europa.eu/health/human-use/advanced-therapies/developments/index_en.htm)

<sup>2</sup> [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Report/2016/06/WC500208080.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Report/2016/06/WC500208080.pdf)

<sup>3</sup> [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Other/2017/02/WC500220952.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Other/2017/02/WC500220952.pdf)

ATMP developers also benefit from existing schemes to support the development of medicinal products in the EU, such as PRIME<sup>4</sup>, or initiatives designed to support SMEs and academia.

The EU is committed to support the development of these products and will keep monitoring developments in the field to ensure that the regulatory framework supports —and not hinders — the development of ATMPs.

It is expected that the implementation of the proposed actions will increase the opportunity for patients to be treated with novel therapies (through enrolment in clinical trials and authorisation of new products). Moreover, an improved regulatory framework will also contribute to promoting innovation, investments and competitiveness of the EU biotechnology sector, whilst striving to ensure patient access.

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<sup>4</sup> [http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general\\_content\\_000660.jsp&mid=WC0b01ac05809f8439](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000660.jsp&mid=WC0b01ac05809f8439)

## ANNEX — List of proposed actions to improve the regulatory framework for ATMPs.

Work on ongoing activities identified in this document will continue. New priorities and implementing actions in the area of ATMPs have been identified in the context of EMA Regulatory Science Strategy: EMA Regulatory Science to 2025: Strategic reflection  
[https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-regulatory-science-2025-strategic-reflection\\_en.pdf](https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-regulatory-science-2025-strategic-reflection_en.pdf)

	Action	Objectives	Timings	Status update: February 2020
1	EC Guideline on GMP for ATMPs.	To reduce administrative burden and adapt the manufacturing requirements to the specific characteristics of ATMPs.  Subsequently to the adoption of the Guideline, EMA will organise specific training to inspectors with a view to achieve more harmonisation.	Complete	Final guideline adopted by EC on 22/11/17. In effect as of 22/05/18. ▶ <a href="#">Guideline</a>  A training session of GMP inspectors and assessors took place 27-28 September 2018.
2	Exchange of information on GMP inspections within the network.	IWG meetings are being used as a platform for exchange of information and experience on the application of GMP to ATMPs.	Ongoing	Ongoing
3	The European Commission services will initiate a dialogue with national competent authorities to address the interplay between the GMO and the medicines legislation.	To reduce discrepancies across the EU regarding the application of GMO rules (Directives on deliberate release or contained use) to ATMPs containing or consisting of GMOs.  Issues relevant for both clinical trials and marketing authorisation will be addressed.  The aim is to help create coherent approaches for the assessment of these novel products without changing the basic legislation.	Ongoing	A repository of national requirements has been published in the European Commission's website: ▶ <a href="#">EC webpage</a>  Other agreed actions can be consulted at the Commission's website on ATMPs: ▶ <a href="#">EC webpage</a>  Applicants are invited to check this website for further updates.
4	Revision of EMA procedures regarding the assessment of ATMPs.	To reduce administrative burden, avoid overlaps between the tasks of the various committees involved, and address the specific needs of ATMP developers (e.g. longer clock stops).	Complete	Revised guidance concerning Procedural Advice on the Evaluation of Advanced Therapy Medicinal Products published (01/02/18). ▶ <a href="#">Guideline</a> ▶ <a href="#">Additional information</a>

5	Provide enhanced scientific support for the development of ATMPs.	Increased opportunities for early dialogue with multidisciplinary or multi-stakeholder expert teams. Streamlined EMA procedures for scientific advice, incl. strengthened interaction between EMA committees.	Ongoing PRIME  Parallel EMA-HTA SA	Ongoing. ▶ <a href="#">PRIME</a> page on EMA website  ▶ <a href="#">Parallel consultation</a> page on EMA website
6	EMA Guideline on Investigational ATMPs.	To avoid discrepancies across the EU regarding the requirements for ATMPs in the clinical trial phase. The Guideline will not change the competence of Member States to approve clinical trials but it will help create common standards for the assessment of these novel products.	Ongoing	Public consultation closed on 31 July 2019. Comments from 17 stakeholders (268 pages). Finalisation of guideline ongoing (by Q4 2020)
7	EMA Scientific Guidelines on ATMPs.	The adoption of the guideline on gene therapy and the review of the guideline on genetically modified cells will support developers of these novel therapies by clarifying regulatory expectations.  The development of guidance on comparability will also address the questions commonly confronted by ATMP developers.	Complete  Ongoing  Complete	Updated guideline on 'Quality, preclinical and clinical aspects of gene therapy medicinal products (EMA/CAT/80183/2014)' was published 13/07/18. <a href="https://www.ema.europa.eu/en/quality-preclinical-clinical-aspects-gene-therapy-medicinal-products">https://www.ema.europa.eu/en/quality-preclinical-clinical-aspects-gene-therapy-medicinal-products</a>  In relation to: Guideline 'Quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells (CHMP/GTWP/671639/2008)': status: public consultation closed on 31 July 2019, comments from 19 stakeholders received (154 pages). Finalisation of guideline ongoing (by Q2 2020).  Questions and answers on comparability considerations for advanced therapy medicinal products (ATMP) published on the EMA website on 13/12/19. Link: <a href="https://www.ema.europa.eu/en/documents/other/questions-answers-comparability-considerations-advanced-therapy-medicinal-products-atmp_en.pdf">https://www.ema.europa.eu/en/documents/other/questions-answers-comparability-considerations-advanced-therapy-medicinal-products-atmp_en.pdf</a>
8	GLP for ATMPs: development of adapted guidance.	To facilitate the approval of clinical trials/granting of marketing authorisation in cases where GLP compliant preclinical studies are not feasible.	Complete	Published: ▶ <a href="#">Marketing Authorisation</a> ▶ <a href="#">Clinical Trials</a>

9	Revision of the EMA Guideline on Safety and Efficacy and Risk Management Plans for ATMPs.	To reduce administrative burden in the post-marketing phase.	Ongoing	Revision of the EMA Guideline on Safety and Efficacy and Risk Management Plans for ATMPs: on hold because of BCP
10	The European Commission services to initiate a reflection process with the Member States on the hospital exemption.	To discuss with Member States the current situation and address possible options.	Ongoing	Ongoing
11	EMA Q&A on the application of the risk-based approach for ATMPs that have not been subject to substantial manipulation.	To explain to developers the possibilities afforded by the risk-based approach (flexibility, reduction of certain requirements for the submission of a marketing authorisation application depending on specific risks).	Complete	▶ <a href="#">Document</a> published July 2017
12	GCP for ATMPs. Led by the European Commission.	To address as appropriate any specific needs to ATMP developers.	Ongoing	Ongoing
13	Scientific considerations on gene editing technologies.	To reflect on emerging techniques on gene editing.	Complete	An expert group meeting on <b>genome editing</b> technologies used in medicinal product development took place 18/10/17. Conclusions from the expert group meeting were integrated in the latest revision of the guideline 'Quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells (CHMP/GTWP/671639/2008)' – see point 7 above.
14	Awareness and training of the network.	Awareness sessions for the EU network on ATMP-related topics (e.g. AAV Vectors, genome editing); expert meetings organized by CAT	Complete	CAT expert meeting on scientific and regulatory considerations for <b>AAV-based gene therapy</b> (06/09/17). Chimeric antigen receptor ( <b>CAR</b> ) <b>T-cell therapy registries</b> workshop (09/02/18). ▶ <a href="#">EMA webpage</a> with information on the workshop
15	Increased stakeholder support - SMEs	Publication of a specific action plan for SMEs.	Complete	▶ <a href="#">Action plan</a> for SMEs

16	Increased stakeholder support - Academia	Publication of an action plan specifically designed on the framework of collaboration with academia.	Complete	▶ <a href="#">Action plan</a> for collaboration with academia
17	Increased stakeholder support - ATMP topic-specific	Update the ATMP dedicated webpage on EMA's website to act as a central resource of relevant information.	Complete	The webpage has been updated. ▶ <a href="#">EMA webpage</a> - support for advanced-therapy developers
18	Increase awareness of stakeholders on EU regulatory processes and framework.	Development of targeted communication/training material in particular for small developers, academia and stakeholders supporting ATMP development; participation at workshops and relevant fora.	Complete	<ul style="list-style-type: none"> <li>▶ EMA participation to EHC Round Table on Economics and Access, Healthcare, System and Novel Therapies, 27 February 2018.</li> <li>▶ DIA Europe 2018 – Basel, Switzerland, 17-19 April 2018: Session SP01- 'CAT spotlight: what's on the horizon for ATMPs in the near future?' and Session 0104 - 'ATMPs'.</li> <li>▶ 10th DIA China Annual Meeting – Beijing, China, 22-25 May 2018.</li> <li>▶ DIA 2018 Annual Meeting – Boston, US, 24-28 June 2018.</li> <li>▶ TOPRA Symposium – Stockholm, Sweden, 1–3 October 2018.</li> <li>▶ CAT meeting with interested parties, 13 September 2018</li> <li>▶ EMA/CAT Regulatory session at the ESGCT 2018 congress (17 October 2018)</li> </ul>
19	Interaction with EUnetHTA	Foster increased interaction between EMA and EUnetHTA on ATMPs to increase understanding of health technology assessment, regulatory processes and clinical added value of ATMPs.	Ongoing	Collaboration in the frame of the EMA-EUnetHTA 2017-2020 Work Plan