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[1], 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[2,3].

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.

[1] http://ec.europa.eu/health/human-use/advanced-therapies/developments/index_en.htm

[2] http://www.ema.europa.eu/docs/en_GB/document_library/Report/2016/06/WC500208080.pdf

[3] 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[4], 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.

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

	Action	**Objectives**	**Deadline** *(timelines are indicative and may be subject to change)*	**Status update: May 2018**
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.	Q4 2017	Final guideline adopted by EC on 22/11/17. LINK to guideline. Date for coming into effect 22/05/18. Training for inspectors scheduled for Q3 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	Q3 2018	Ongoing.

[4] http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000660.jsp&mid=WC0b01ac05809f8439

		addressed. The aim is to help create coherent approaches for the assessment of these novel products without changing the basic legislation.		
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).	Q4 2017	Revised guidance concerning Procedural Advice on the Evaluation of Advanced Therapy Medicinal Products published (01/02/18). LINK to guideline. LINK to additional information.
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 as part of PRIME. LINK to PRIME 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.	Draft guideline for consultation Q4 2018	Guideline in preparation.
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	Gene therapy guideline is expected to be adopted Q4 2017 Draft revision of the guideline on genetically modified cells for consultation Q1 2018 Guidance on comparability Q2 2019	Guideline adopted by CAT/CHMP (22 March 2018) and awaiting publication. Revision ongoing, public consultation expected for June 2018. Not yet initiated.

		questions commonly confronted by ATMP developers.		
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.	Q2 2017	Already published: LINK to Marketing Authorisation LINK to Clinical Trials
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.	Q2 2018	Revised guideline in public consultation (01/02/18-30/04/18). LINK to the revised guideline as published for consultation.
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.	Continuous process	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).	Q1 2017	LINK to published document.
12	GCP for ATMPs. Led by the European Commission.	To address as appropriate any specific needs to ATMP developers.	2019	Ongoing.
13	Scientific considerations on gene editing technologies.	To reflect on emerging techniques on gene editing.	Q2 2018	An expert group meeting on **genome editing** technologies used in medicinal product development took place on 18/10/17. A meeting report is in preparation.
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	Continuous process	CAT expert meeting on scientific and regulatory considerations for **AAV-based gene therapy** (06/09/17). A public report will be published shortly. Chimeric antigen receptor **(CAR) T-cell therapy registries** workshop

				(09/02/18). LINK to the EMA webpage with information on the workshop.
15	Increased stakeholder support SMEs	Publication of a specific action plan for SMEs.	Q2 2017	LINK to published document.
16	Increased stakeholder support Academia	Publication of an action plan specifically designed on the framework of collaboration with academia.	Q1 2017	LINK to published document.
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.	Q4 2018 See the webpage here	Ongoing.
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.	Ongoing	• CAT participation to ESGCT in preparation (October 2018). • EMA participation to EHC Round Table on Economics and Access, Healthcare, System and Novel Therapies (27th February 2018). • 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'. • 10th DIA China Annual Meeting – Beijing, China, 22-25 May 2018. • DIA 2018 Annual Meeting – Boston, US, 24-28 June 2018. • TOPRA Symposium – Stockholm, Sweden, 1–3 October 2018.
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.	Joined training / workshop planned in 2019	Collaboration in the frame of the EMA-EUnetHTA 2017-2020 Work Plan started.