



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Patient Health Protection

Committee for Advanced Therapies (CAT) Work Programme 2010 - 2015

Introduction – Problem statement

New and emerging science has been identified as an important driver for progress and change in the European Medicine Agency's (EMA) Road Map to 2015¹.

It is generally well recognised in the international scientific arena and by regulators that advanced therapies are at the forefront of scientific innovation in medicine, offering potential groundbreaking new treatments for diseases and injuries of the human body.

The continuous scientific progress, for example in the field of cellular and molecular biology, has boosted the hope for highly innovative and improved therapies and has led in the last decade to intensive research and development in the field of gene therapy and regenerative medicine (including tissue engineering and somatic cell therapy). However, whilst science has revealed the potential, only a limited number of these research projects managed to translate into products that are able to further progress to the late stage of clinical development and eventually to reach the market. Surveys performed by European operators in the sector depict a very lively sector that has not managed to unlock its potential due to a variety of hurdles, including lack of access to funding and changed regulatory environment (e.g. need for further guidance to improve predictability of registration, complex regulatory system not easily accessible by SMEs and Academia, regulatory package requiring high investment in terms of human and financial resources).

The negative effect of the hurdles, both real and perceived, is consistent with the limited number of products that are seen by the Committee for Advanced Therapies (CAT) (3 MAA, 1 certification application in 2009) and a very limited number of products heading for a MAA in 2010-2015. Some products appear to be in a more mature state but lack the resources to be brought up to regulatory standards. In addition, the CAT acknowledges messages received from interested parties and patients' organisations that such hurdles are limiting the timely access by patients to potential effective treatments².

The traditional regulatory framework for medicines is structured as an applicant-driven system, which involves regulators responding only upon receipt of applications from developers. In view of the demonstrated potential of ATMPs but lack of progress to the market, the CAT is investigating

¹ [The European Medicines Agency Road Map to 2015: The Agency's Contribution to Science, Medicines, Health](#)

² E.g. conclusions from 'World Conference on Regenerative Medicine - Leipzig, 28-31 October 2009' sessions 'Funding in Regenerative Medicine Ventures' and 'Policy and Legal Issues in Regenerative Medicine'



possibilities for adopting a more pro-active attitude. This includes an analysis of the environment in which ATMPs are developed and, by means of a work programme, listing actions to address any issues identified.

Key trends and issues

- ATMP developers are very diverse in their nature as reflected in the current list of CAT interested parties which includes organisations representing big pharma, SMEs, Trusts, Academia, hospitals. Regulatory procedures and guidelines should be easily accessible by all these stakeholders providing a clear path for the development of safe and effective ATMPs. The constant feedback with stakeholders ensures that scientific guidelines take account of the increasingly rapid progress of science and therapies.
- In 2011-2012, manufacturers and Member States will face the end of the transitional period, by which, according to the provisions of Article 29 of Regulation (EC)1394/2007, all ATMPs have to be centrally authorised. As a consequence all products now legally on the EU market should be withdrawn if they fail to receive a marketing authorisation. This is expected to have an impact on EU patients who could already be benefiting from these treatments.
- The CAT is operating in a complex Agency's architecture of six Committees and several working parties, in close cooperation with other national and international regulatory bodies: consolidation of internal and external cooperation with all the key players is crucial to maintain scientific consistency of outputs, efficiency of the system and contribution to harmonisation of requirements.
- Stakeholders are confronted with a relatively new legislative framework for ATMPs and related regulatory and procedural guidance documents. Providing appropriate training would increase the use of these procedures leading ultimately to the successful implementation of the legislation.
- It is recognised that ATMPs are new, complex products which require assessment criteria that go beyond those used in the traditional pharmaceutical field. Special tools for the assessment of these are already provided in the ATMP legislation but their optimal application needs to be fully explored.
- A number of initiatives are running at EU level in order to foster innovation and promote research in the ATMP field. Exploring cooperation with major stakeholders would bridge the gap between research and translation of ATMP to medicinal products.
- Beside the decision-making for granting a marketing authorisation, the access to ATMPs is influenced by other components in the complex model for regulation of medicines which do not fall directly under the responsibility of the Agency. These components include the conduct of clinical trials as part of the medicine development and the criteria used by Health Technology Assessment (HTA) bodies to determine the cost/effectiveness balance. Different criteria applied across Europe during the ATMP development as well as differences between the criteria used in the licensing process and the post-authorisation reimbursement process may undermine the availability of ATMPs for EU patients.

The role of CAT

The entry into force of Regulation (EC) 1394/2007 represents a milestone in providing a clear regulatory framework for the development of advanced therapies. The CAT is recognised to be a key player in the successful implementation of this legislation.

The CAT with its specific expertise is able to act as a point of reference in the Community for providing guidance on the scientific and technical requirements for marketing authorisation, to help foster innovation and research in the field and contribute to better promotion and protection of public health.

The CAT will continue to fulfil its tasks as established by Article 23 of Regulation (EC) 1394/2007 (e.g. formulation of draft opinions on quality, safety and efficacy of ATMPs for final approval by the CHMP, scientific recommendation on ATMP classification) and Regulation (EC) 668/2009 (i.e. evaluation for certification of quality and non-clinical data related to ATMPs developed by SMEs).

The issues explained in the 'Introduction' show that there is a need for the CAT to proactively contribute to establish a fertile environment for the successful implementation of the ATMP Regulation. This will be achieved by means of a structured work programme with clear objectives and transparent actions.

Objectives and actions

In order to properly address the aforementioned key trends and new issues the following objectives should be achieved.

1) To successfully respond to implementation of the provisions of Article 29 of Regulation (EC)1394/2007: assessment of products legally on the EU market.

Actions:

- Conduct an analysis on number and kind of products legally on the EU market.

- Reflect on the criteria for MAA assessment in compliance with Annex I, taking into account any flexibility built in the regulatory system.

- Adopt a proactive, open approach towards dialogue and exchange with potential applicants and National Competent Authorities.

- One year before the end of the transitional period, report to the European Commission and Member States on the experience on the implementation of the provision of Article 29 of the ATMP Regulation. The report will also include considerations on the concomitant implementation of Article 28(2) of the ATMP Regulation (hospital exemption clause) at national level (see objective 6 below).

2) To facilitate development of ATMPs and access to marketing authorisation procedure.

Actions:

- Understand the trends in research and development with a view to planning CAT workload and resources accordingly

- Strengthen dialogue with stakeholders:
 - *Draft a structured work programme facing the specific needs of different parties (industry, SMEs, Academia, research groups, patients' groups). The work programme will list specific areas identified by different parties in which there is a lack of clarity on the scientific/technical requirements which could undermine the possibility to register ATMPs. The work programme will identify action plans for improvements in the respective areas.*

 - *Continue to promote the possibility for stakeholders to participate in a direct dialogue with CAT*

 - *Engage in dialogue with charity foundations and trusts concerning products that they are developing.*

 - *Identify and establish dialogue with additional stakeholders: e.g. competent authorities for tissue establishments, clinicians, specialist advisory groups, consortia for translation of ATMPs*

 - *Reinforce dialogue and interactions with inspectors (GMP, GLP, GCP)*

- Continue to interact closely with SAWP and other working parties to provide appropriate advice on development of ATMPs.

- Strengthen cooperation with COMP and PDCO for issues related to development of ATMPs for rare diseases and paediatric indications.

- Consolidate cooperation with international regulators (e.g. FDA) for potential harmonisation of procedures and requirements.

3) To promote the use of available regulatory procedures and introduce potential improvements.

Actions:

- Provide regular tutorial training/workshop for different stakeholders.

- Set up a project with a view to improving the understanding of requirements for registration of ATMPs by developing a European training and education platform in submission of MAA for academia and SMEs.
- Provide dedicated assistance to applicants for submission of ATMP certification applications.

4) To explore possibilities offered by the current regulatory framework when applied to ATMPs with a view to improving existing procedures and reflecting on alternative procedures.

Actions:

- Reflect on optimal use of provisions concerning post-authorisation follow-up of efficacy of ATMPs.
- Reflect on possibility to optimise use of the 'Accelerated assessment procedure' for marketing authorisation of ATMPs.
- Establish an effective interaction process with EU Notified Bodies during evaluation of MAA for combined ATMPs.
- To screen, on a regular basis, the current system to identify potential changes required by the rapid progress of science and therapies.
- Address issues arising from the application of the current regulatory framework to the specific ATMP field (e.g. comparability exercise on CBMPs for new production sites).
- Reflect on possibility to extend incentives currently in place for SMEs to Academia, hospitals, trusts and small research groups.
- Reflect on how to optimally apply the regulatory framework to tailor-made products falling under the ATMP Regulation.

5) To contribute to foster innovation.

Actions:

- Establish a fruitful cooperation with major stakeholders such as EC DG Research, for the CAT to serve as a knowledgeable point of reference for scientific issues.
- Explore possibility for interaction with DG Research on inclusion of ATMP-related topics in future EU Research-Framework programmes.

- Explore possible opening of certification procedure to Academia and non-profit organisations.
- Reinforce contact with leaders of EU research project on ATMP.
- Work closely with EU National regulatory agencies to facilitate pre-marketing development of ATMPs by offering CAT advice for national procedures.

6) To promote access and availability to ATMP for EU patients.

Actions:

- Initiate interaction with the Clinical Trial Facilitation Group (CTFG) to achieve harmonisation of CTA evaluation for ATMPs, in collaboration with the EC.
- Encourage development of ATMPs for unmet medical needs without alternative treatments.
- Establish a fruitful dialogue with National Competent Authorities on possible harmonised criteria for products considered eligible for 'hospital exemption' and borderline with application of other provisions (e.g. name-patient use).

List of Abbreviations

- ATMP: Advanced Therapy Medicinal Product
- CAT: Committee for Advanced Therapies
- CBMPs: Cell Based Medicinal Products
- CHMP: Committee for Medicinal Products for Human Use
- COMP: Committee for Orphan Medicinal Products
- CTA: Clinical Trial Application
- CTFG: Clinical Trial Facilitation Group
- EC: European Commission
- EC DG Research: European Commission
- EMA: European Medicines Agency
- EU: European Union
- FDA: Food and Drug Administration
- GCP: Good Clinical Practice
- GMP: Good Manufacturing Practice
- HTA: Health Technology Assessment
- MA: Marketing Authorisation
- MAA: Marketing Authorisation Application
- MSs: Member States
- NCA: National Competent Authorities
- PDCO: Paediatric Committee
- SAWP: Scientific Advice Working Party
- SMEs: Micro, Small and Medium-sized Enterprises