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Human Medicines Research and Development Support Division

# Issues identified by stakeholders: follow-up from EMA's ATMP workshop

On 27 May 2016 EMA hosted a workshop[1] aimed to foster ATMP development and enable expanded patient access in the EU by exploring solutions to identified challenges. The workshop was attended by stakeholders from academia, industry (SMEs and large pharmaceutical companies), pharmacists, treating physicians, patient representatives, consortia, incubators, investors, health technology assessment (HTA) bodies, EU regulators and the European Commission (EC).

Ongoing EU initiatives to optimise the current regulatory framework to facilitate ATMP development have been enriched with proposals presented by stakeholders. This document presents some ongoing and planned activities of EMA and the Committee for Advanced Therapies (CAT), as well as additional areas where stakeholders identified key issues for further follow-up. Priority has been given to issues with actions that are ongoing or can be started by EMA/CAT in 2017. The document does not contain any proposals that would require changes to the legal ATMP framework and acknowledges that a proposal to revise the legislation underpinning ATMPs in Europe is currently not foreseen.

These issues and proposed outputs of the workshop will be considered for a wider EU plan to be developed by EMA, CAT, the EC and the National Competent Authorities (NCAs).

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

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| | Issues raised and on-going/planned activities | Additional details | Topic lead |
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| 1 | **ATMP scientific and regulatory guidance**<br>• Develop the following guidelines through CAT drafting groups:<br>▪ New guideline on requirements for ATMPs in clinical trials<br>▪ New guideline on comparability for cell-based MPs<br>▪ Revision of guideline 'Quality, preclinical and clinical aspects of gene therapy medicinal products (CHMP/GTWP/234523/09)'<br>▪ Revision of guideline 'Quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells (CHMP/GTWP/671639/2008)'<br>▪ Revision of guideline on 'Safety and efficacy follow-up – risk management of advanced therapy medicinal products (EMEA/149995/2008)'<br>• Develop scientific and regulatory considerations on gene editing technologies and make conclusions publically available<br>• Coordinate the sharing of relevant information from scientific advice letters and certification applications | | EMA[2] |
| 2 | **Tailored GMP for ATMP**<br>• Adoption of the EC's Guideline on Good Manufacturing Practice (GMP) specific for ATMPs<br>• Explore practicalities for decentralised manufacture including the requirements for a qualified person and manufacturing authorisation within the current legal framework in alignment with the GMP guide<br>• Facilitate the sharing of national experience of ATMP GMP inspection | The **requirements** for a qualified person and manufacturing authorisation are laid down in the Directive 2001/83/EC.<br>The **sharing of national experience** in relation to GMP inspection challenges is proposed to be coordinated through the IWG to | EMA[2] /EC (with technical support of CAT/IWG) |

[2] Where 'EMA' is mentioned the term should be understood as EMA secretariat together with its scientific committees (i.e. CAT, CHMP, PRAC etc.)

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| | challenges within the regulatory network for awareness and best practice | provide an exchange platform for the benefit of the EU network. | |
| 3 | **GLP for ATMP (practical application of GLP to ATMPs)** | A CAT position paper on the application of GLP principles to ATMPs is under development. | EC/EMA[2] |
| 4 | **Focus on benefit-risk assessment by the CAT**<br>▪ Ensure transparency and communication of the benefit-risk assessment by the CAT | Approaches for conducting and documenting **benefit-risk assessment** are well established in EMA assessment templates and guidelines and equally applicable to all product classes. There is an opportunity to explore the need for introducing adaptations specific to ATMPs, to ensure a consistent, structured approach is used, and to monitor implementation. | EMA[2] |
| 5 | **Highlight the potential of the risk-based approach for ATMP developers when preparing the dossier for submission:**<br>▪ Develop a questions-and-answers (Q&A) document on risk-based approach for minimally manipulated ATMPs<br>▪ Raise awareness amongst developers, stakeholders and the European Medicines Network | **The risk-based approach** is a tool to provide flexibility in the data requirements for the MAA dossier to take account of the specific features of the product in question and their potential impact on the benefit/risk profile. | EMA[2] |
| 6 | **Orphan similarity of ATMPs**<br>• Upon completion of the revision of the framework of the similarity concept (orphan legislation), to provide scientific and regulatory support to the EC in preparation for the future implementation of the revised | **Scientific and regulatory support** is based on experience/lessons-learnt from orphan similarity cases.<br>The EC's proposal includes the description of the principal molecular | EC to lead, EMA[2] to support |

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| | framework<br>• Support applicants with questions in relation to orphan similarity for ATMPs | structural feature of the active substance and considerations for ATMPs based on cell-based, gene therapy medicinal products and genetically modified cells[3]. | |
| 7 | **ERA consultation for GMO containing ATMPs**<br>• There is a need for a list of GMO Competent Authorities and to streamline the ERA consultation process for MAAs at EMA<br>• To contribute to EC's reflection on ERA assessment during clinical trial approval | The contribution to EC's reflection on ERA assessment during clinical trial approval is listed as an activity in the CAT work plan 2017. | EC |
| 8 | **Use of registries to collect clinical data**<br>• Explore the use of registries (including disease registries) during post-marketing data collection including specific guidance in the Guideline on safety and efficacy follow-up – risk management of advanced therapy medicinal products<br>• Reflect on the use of registries with stakeholders and network for approval and post-marketing follow-up | The **Guideline on safety and efficacy follow-up – risk management of advanced therapy medicinal products** (EMEA/149995/2008), which is currently under revision (see action 1), is proposed to include information on the use of registries.<br>The CAT intends to work closely with other relevant committees on this activity (i.e. CHMP, PRAC and PDCO). | EMA[2] |
| 9 | **Procedural guideline on the evaluation of ATMPs for MAA**<br>• Revise procedural guideline for ATMP MAA review and opinion including:<br>▪ streamlining of interaction between CAT, CHMP, PRAC and relevant | | EMA[2] |

[3] http://ec.europa.eu/health/files/orphanmp/2016_07_pc_orphan/2016_07_consultation_paper.pdf

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| | working parties<br>▪ reviewing key procedural steps (i.e. LoQ/LoOI, oral explanation and clock-stops) | | |
| 10 | **Increase awareness of support for early development**<br>• Reinforce support to academia in coordination with the NCAs and explore how to enhance support to the scientific research community, already quite active at national level<br>• Increase communication with early developers on ATMP-related topics (e.g. via EMA webpage, publications in peer review journals, stakeholder workshops) in particular to promote use of support and early development tools<br>• Create a Q&A document on early interaction tools to be published on EMA ATMP webpage | NCAs already have a high level of interaction with academia and it is suggested to explore which avenues can be further developed at EU level.<br>**Early development and access tools** include: scientific advice, orphan designation, PRIME, conditional approval, accelerated assessment.<br>**Early development support** includes ITF, EU Innovation Network, SME office User Guide, ATMP certification, pre-submission meetings, guidance and peer reviewed publications. | EMA[2] and NCAs |
| 11 | **Increase investor awareness of regulatory processes**<br>• Increase awareness of investors on EU regulatory processes and framework, in particular on indicators of regulatory conformity and other regulatory tools, by developing targeted communication/training material and increase interaction through workshops and at relevant fora | **Indicators of regulatory conformity** include use of early regulatory interaction (ITF, ATMP classification), ATMP certification, scientific advice including HTA/EMA parallel advice and adherence to scientific advice outcome. **Other regulatory tools** are PRIME, orphan designation, paediatric investigation | EMA[2] to facilitate |

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| | | plan, awareness of EMA guidelines. | |
| 12 | **Increase communication with stakeholders on ATMPs**<br>• Increase awareness of parallel SA (with HTA) for both pivotal clinical development and for post-authorisation requests<br>• Explore an EU-wide ATMP training platform with relevant stakeholders<br>• Increase awareness of public funding options (e.g. IMI)<br>• Continue the dialogue with ATMP specific stakeholders through surveys and continuously improve training according to the evolution of the ATMP field | The **training platform** should be further developed also considering existing tools such as the EU-NTC.<br>**Stakeholders** include SMEs and academia as well as large pharmaceutical companies. | EMA[2] |
| 13 | **Coordinate training and information sharing on specific scientific & regulatory matters within the network**<br>• Foster training and share information on emerging scientific and regulatory matters pertaining to ATMPs with the network (NCAs) using the EU-NTC | Within the EU regulatory network several activities are already ongoing. The intention is to make the information broadly available to all NCAs for the benefit of the network. | EMA[2] |
| 14 | **Support to more transparency in hospital exemption**<br>• Support information sharing between NCAs in relation to hospital exemption and support NCAs in the compilation of national requirements for hospital exemption<br>• Support NCAs in exploring the feasibility of clinical data collection for products in use under the hospital exemption across Member States | This action is not within the remit of EMA but considering the high demand voiced by stakeholders EMA offers support to facilitate this activity.<br>**Clinical data collection** includes use of registries as per action 8. | NCAs and EC with support of EMA[2] |

**Abbreviations:**

ATMP Advanced Therapy Medicinal Product

CAT Committee for Advanced Therapies

CHMP Committee for Human Medicinal Products

EC European Commission

EMA European Medicines Agency (EMA secretariat together with its scientific committees (i.e. CAT, CHMP, PRAC etc.))

ERA Environmental Risk Assessment

EU-NTC EU Network Training Centre

GMO Genetically Modified Organism

GMP Good Manufacturing Practice

HTA Health Technology Assessment

ITF Innovation Task Force

IWG Inspectors Working Group

LoOI List of Outstanding Issues

LoQ List of Questions

MAA Marketing Authorisation Application

MP Medicinal product

NCAs National Competent Authorities

PRAC Pharmacovigilance Risk Assessment Committee

PRIME Priority Medicines

SA Scientific Advice

SME Small and Medium Size Enterprise