

Innovative Medicines Initiative (IMI) consultation

Facilitating the translation of advanced therapies to patients in Europe

Response from the NHS ATMP Working Party – a subgroup of the National Pharmaceutical NHS QA Committee.

Introduction

The NHS ATMP Working Party (NHS ATMP WP) is a subgroup of the National Pharmaceutical NHS QA Committee. The group has been set up in order to ensure that there is appropriate expertise within the NHS to facilitate the safe introduction of ATMPs as they translate into routine practice. Due to the expertise base coming from a pharmaceutical / regulatory/ QA background, the group is able to comment from a QA perspective in relation to the manufacture of ATMPs as well as in relation to the governance required when ATMPs are manufactured elsewhere to be used within the hospital setting.

Question 1: Have the key challenges that can be addressed through collaborative, public private initiatives been properly identified?

THE NHS ATMP WP agrees that the challenges have been explored fully in the document.

We feel that it should be emphasized that the term “unregulated” relates to the manufacturing facility for sites operating under the hospital exemption. We understand that use of the hospital exemption is unregulated by the Competent Authority in most EU member states. In the UK, however, the MHRA favour the use of our Specials regulations which ensures that the facilities and quality systems in which the unlicensed medicines are made are compliant with EU GMP.

THE NHS ATMP WP agrees that the HE can disincentivise the progression of ATMPs to marketing authorisation in member states other than the UK. In the UK MHRA Guidance Note 14 prohibits the use of an unlicensed medicine where a medicine with a marketing authorisation exists. This is not the case for other member states. Hence if a manufacturer gains a centralised EU MA for an ATMP there is nothing to stop individual member states continuing to manufacture an equivalent product under the HE. Hence there is effectively no guaranteed market for the authorised product. This is especially the case for autologous products and is most certainly disincentivising companies from investing in the marketing authorisation process.

Whilst central authorisation (EMA) allows the expertise required for assessment to be collected in one place and is therefore useful, the granting of an EU wide MA carries logistical problems. Many ATMPs have short shelf lives and are very vulnerable and

therefore susceptible to quality deviations during transport. Manufacture in one member state and transport to all others is therefore not always realistic. This may prevent MA applications which would be possible to service one country or an easily accessible geographical area but cannot logistically satisfy the entire EU. This encourages the use of the Hospital Exemption and disincentives a MA application.

THE NHS ATMP WP would **recommend** HE sites should be inspected by the GMP competent authority in the member state and hospital exemption manufacture should not be permitted where an equivalent product with a MA exists but that consideration is given to granting an MA for a limited geographical area if that is what the manufacturer prefers.

Question 2: Which of the proposed potential initiatives should be prioritized?

THE NHS ATMP WP believe that the use of registries should be prioritized. If ATMP usage, safety and efficacy data is available it will help the field to advance by facilitating the targeting of ATMPs to go through to marketing authorization that have a chance of being funded due to their having big impact on patients (i.e. will be curative for rare diseases or will offer a significant benefit to quality of life for common diseases.) Currently THE NHS ATMP WP believe that there is no overarching strategy to target funding and grants to develop products which will have such an impact. The market is largely being driven by the interests of individual innovative researching clinicians who may have a niche interest only.

THE NHS ATMP WP agrees with the statement in the consultation document: *“In general there is a lack of manufacturing knowhow, regulatory sciences and Current Good Manufacturing Practice (CGMP) related to ATMP usage.”*

However, the document goes on to state: *“Besides that, there is a shortage of well-trained engineers that understand the manufacturing processes and are capable to develop automated/robotic methods and common platforms.”*

Understanding that ATMPs are medicinal products, it is incorrect to focus the manufacturing knowhow needs on the engineering profession alone. ATMP manufacturing knowledge exists in hospitals via the stem cell laboratory teams who are experts in handling cell and tissue products. When combining this practical expertise with GMP and GLP which is available in pharmacy (as pharmacists in hospitals and academia often have manufacturing sites for traditional pharmaceuticals) then stem cell laboratories offer perhaps the most suitable environment in which to manufacture ATMPs for early phase trials or under the HE. This should be better represented within this particular IMI reflection.

THE NHS ATMP WP recommends that access to early regulatory consultation should also be prioritized. There is a need to make regulatory considerations in relation to the potential marketing authorisation application as early in the process as possible, ideally at the preclinical development stage. Innovators / researchers need to understand the importance of Quality by Design thinking to develop their product in such a way that it facilitates an easier pathway through the transition to a GMP product suitable for a marketing application.

Pharmacy Quality Assurance and Regulatory colleagues may be able to help if innovation is occurring in a healthcare / academic setting.

Question 3: Are any areas missing?

There is a need to focus more on the lack of education around the field of ATMPs. Staff involved in research and development should be prioritized.

Clinicians in a variety of specialisms are interested in being an investigator using ATMPs as they are innovative and may offer tangible patient benefit. As a result healthcare settings participating in clinical trials need to have a Research and Development Team who have an understanding of ATMPs and can develop a streamlined pathway to introduce these trials whichever clinical speciality that they occur in. Clinicians, research nurses and clinical trial coordinators as well as pharmacy clinical trial staff need to be trained in relation to ATMPs.

It should also be recognised that segregated facilities for ATMPs will be required in many cases and that sites for preparation prior to administration will need to be considered and provided by pharmacy aseptic teams going forward. THE NHS ATMP WP would recommend that hospitals consider the use of facilities and staff from stem cell laboratories due to their expertise in this area, with appropriate oversight and governance from the pharmacy department.

As ATMPs become more embedded in routine use as licensed and unlicensed medicines then healthcare professionals (prescribers, nurses, pharmacists) will be critical intermediaries, and must be knowledgeable enough about ATMPs to prescribe with confidence, advise the patient on use, and ensure correct governance around use and administration to underpin safe access. This challenge should be included within the priorities.

THE NHS ATMP WP feel that the document would benefit from the addition of a recommendation to include teaching about ATMPs on a variety of university syllabuses so that medical, pharmaceutical and biomedical undergraduates become aware from an early stage in their career about this group of medicines which, whilst currently in their infancy, are likely to feature heavily during their careers.

Question 4: What are the key European or national initiatives that IMI shall synergise with?

THE NHS ATMP WP recommend that IMI synergise with regulatory bodies including

1. European Medicines Agency (EMA)

A stakeholder meeting on the subject of promoting easier access to ATMPs was recently held by the Agency with the report of that meeting published in June.

Report

here:

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

Goals of the IMI appear to be similar to the EMA goals therefore collaboration would be sensible.

2. JACIE (Joint accreditation committee of ISCT and EBMT).

JACIE's primary aim is to promote high quality patient care and laboratory performance in haematopoietic stem cell collection, processing and transplantation centres through the development of global standards and an internationally recognised system of accreditation. This is relevant to ATMP manufacturing centres and clinical sites where harvesting for autologous and allogeneic treatments occurs

THE NHS ATMP WP strongly believes that there is a need for IMI to synergise with national funding schemes. such as the Medical Research Council and British Biotechnology Science Research Council, and European funding such as Horizon 2020 initiatives. This linkage could lead to the funding of, for example, training programmes through the Marie Curie initial training Networks and collaborative networking via COST capital proposals

Question 5: Further comment

In respect to the consultation paper's reflection on pricing and reimbursement for ATMPs, consideration is required to how the early investment made by hospital sites and academic centres into ATMPs, can be returned within pricing and reimbursement systems. This does not appear well explored within the paper.

Within section 3.4 it is important to make note that when comparing traditional therapies, lifetime cost should be considered. ATMPs are often curative and therefore represent a one off cost (albeit large)but when compared with a lifetime cost it may be seen to more cost effective.

The NHS ATMP WP encourages the development of an optimal way of handling ATMPs to be devised within healthcare settings. Hospital pharmacists must conduct an appropriate role in supporting the use of ATMPs, including taking responsibility for the governance of their safe use in the hospital sectors whilst stem cell laboratory staff should be encouraged to use their existing expertise to handle and manipulate the products as required for individual studies. As such, we believe that system in which ATMPs can be safely and efficiently introduced to bring maximum benefit for our patients can be introduced.