

The Role of Pharmacy in the Successful Delivery of Advanced Therapy Medicinal Products (ATMPs)

Information for Chief Pharmacists

Edition 1

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National Pharmacy Clinical Trials Advisory Group



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An advanced therapy medicinal product is a biological medicinal product that can be classified as either one of or a combination of the following three categories¹:

Gene Therapy:- a biological medicinal product which contains an active substance which contains or consists of a recombinant nucleic acid used in, or administered to human beings, with a view to regulating, repairing, replacing, adding or deleting a genetic sequence; and its therapeutic, prophylactic or diagnostic effect relates directly to the recombinant nucleic acid sequence it contains, or to the product of genetic expression of this sequence.

Somatic cell therapy (SCT):- a biological medicinal product which contains or consists of cells or tissues that; 1) have been substantially manipulated *ex vivo*, or 2) - are not intended to be used for the same essential function(s) in the recipient and the donor.

Tissue Engineered Product (TEP):- a biological medicinal product that contains or consists of cells or tissues administered to human beings **with a view to regenerating, repairing or replacing** human tissue. A tissue engineered product may contain cells or tissues of human or animal origin, or both. The cells or tissues may be viable or non-viable. It may also contain additional substances, such as cellular products, bio-molecules, bio-materials, chemical substances, scaffolds or matrices.

ATMPs may be autologous (starting material is from the intended recipient), allogeneic (starting material originates from a donor) or xenogeneic (starting material is of animal origin).

ATMPs can also be classed as a Combined product; this is a combination of any of the above with a medical device.

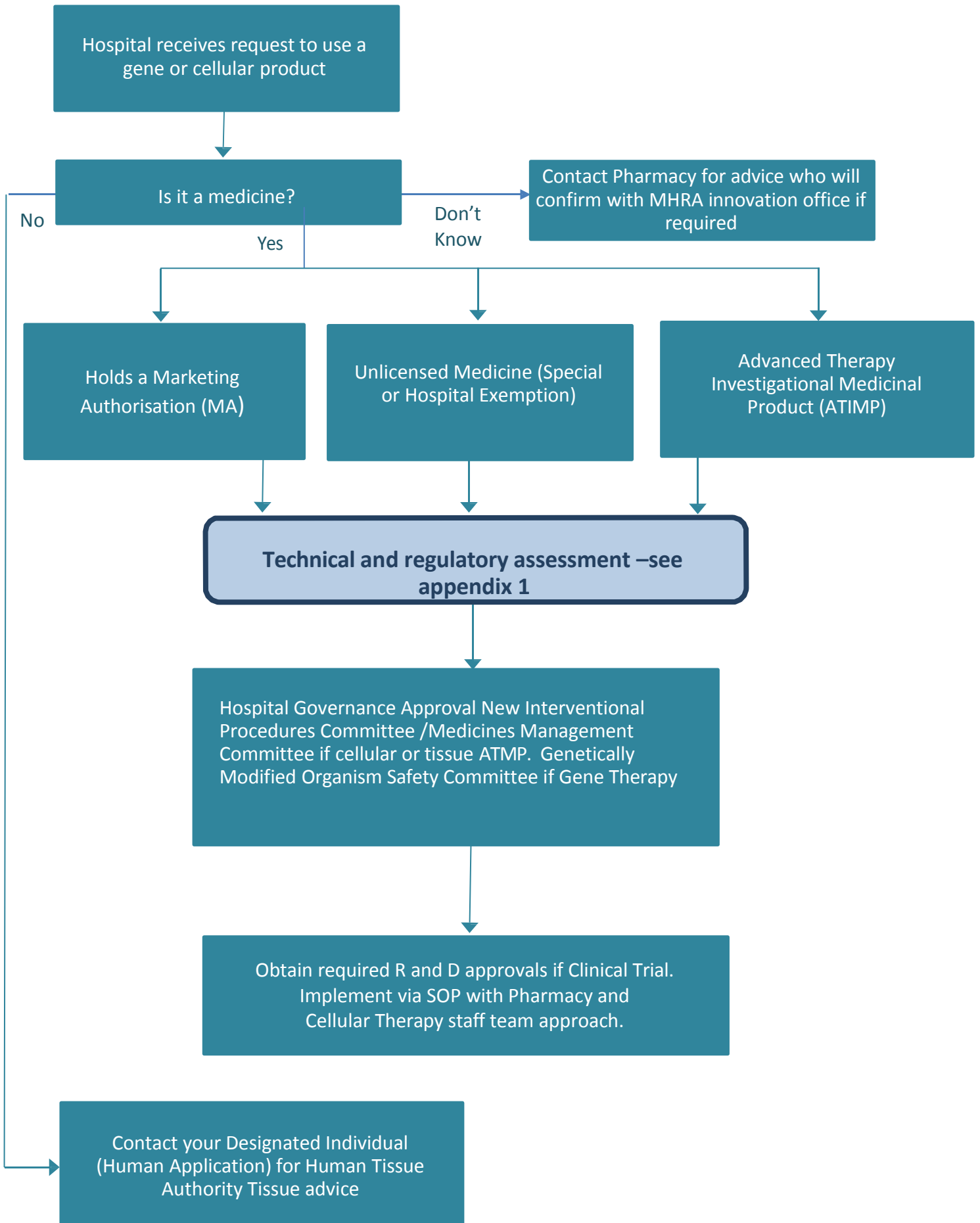
As ATMPs are medicines they are subject to the same requirements as for other medicinal products and the Chief Pharmacist is responsible for their governance and management. Most current usage is in clinical trials, but ATMPs are beginning to become available as licensed and unlicensed medicines.

The role of Pharmacy is to oversee the governance arrangements and to ensure that ATMPs used are of appropriate quality for their intended use. It is recognised that the use of some ATMPs (eg cryopreserved or those released with a very short-shelf-life) may require specialist handling and expertise which may not be immediately available in Pharmacy Departments. In hospitals holding a Human Tissue Authority licence for human application, it is recommended that the Chief Pharmacist contacts the relevant HTA Designated Individual within their organisation to develop a collaborative process to provide appropriate governance and handling procedure for ATMPs used in clinical trials, for unlicensed ATMPs and for ATMPs holding marketing authorisations.

Governance Considerations

As ATMPs are innovative products and are often associated with a novel administration procedure, it is recommended that all requests to use ATMPs are scrutinised by an appropriate organisational multidisciplinary committee such as a Medicines Management committee or New Interventional Procedures Committee. A suggested process flow for the governance process is given below:

Figure 1:



Pharmacy staff with a technical understanding of aseptics will need to advise on the technical and regulatory assessment referred to in Figure 1. A suggested process flow for the technical and regulatory assessment is given in Appendix 1.

Practical Hurdles for Pharmacy

Due to the nature of ATMPs, their handling may present some resource and training barriers to be overcome. Examples of these include the following:

Storage: ATMPs are often cryopreserved and required storage below -80 degrees Centigrade or even in nitrogen vapour. Prolonged storage will almost always require a vapour phase nitrogen storage dewar.

Handling: Cellular products are sensitive and can be rendered non-viable if not handled appropriately. They are very often patient-specific and are COSHH category 2 biohazards. Training will be required. If dedicated staff (e.g. stem cell laboratory staff or specialist haematology staff) exist outside of pharmacy then they may be the most appropriate to handle the products with pharmacy oversight and approval. In some cases ATMPs will need to be delivered directly to the end user in a clinic or within an operating theatre and may not pass through Pharmacy. Systems to allow pharmacy oversight of this practice will be required.

Preparation: Specialist components and training in handling these products will be required. Risk assessment to determine the most appropriate location for preparation will be required. If dedicated facilities exist outside of pharmacy then they may be the most appropriate place.

Logistics: ATMPs often have very short shelf lives and careful planning and liaison with clinical teams is required to ensure optimal product quality and corresponding patient safety.

Conclusion

Whilst Chief Pharmacists are finally responsible and accountable for governance of all aspects of preparation, supply and use of ATMPs within their organisation as they are for all other medicines, it is recommended that a local option appraisal is conducted to find the optimal arrangements for managing these products, using existing expertise external to pharmacy where appropriate. Pharmacy QA staff will be required to advise in relation to regulatory matters and manufacturing authorisations required, and Pharmacy Clinical Trials staff will be key in providing GCP oversight and approval for individual trial procedures. In this way it can be ensured that patient safety is prioritised by

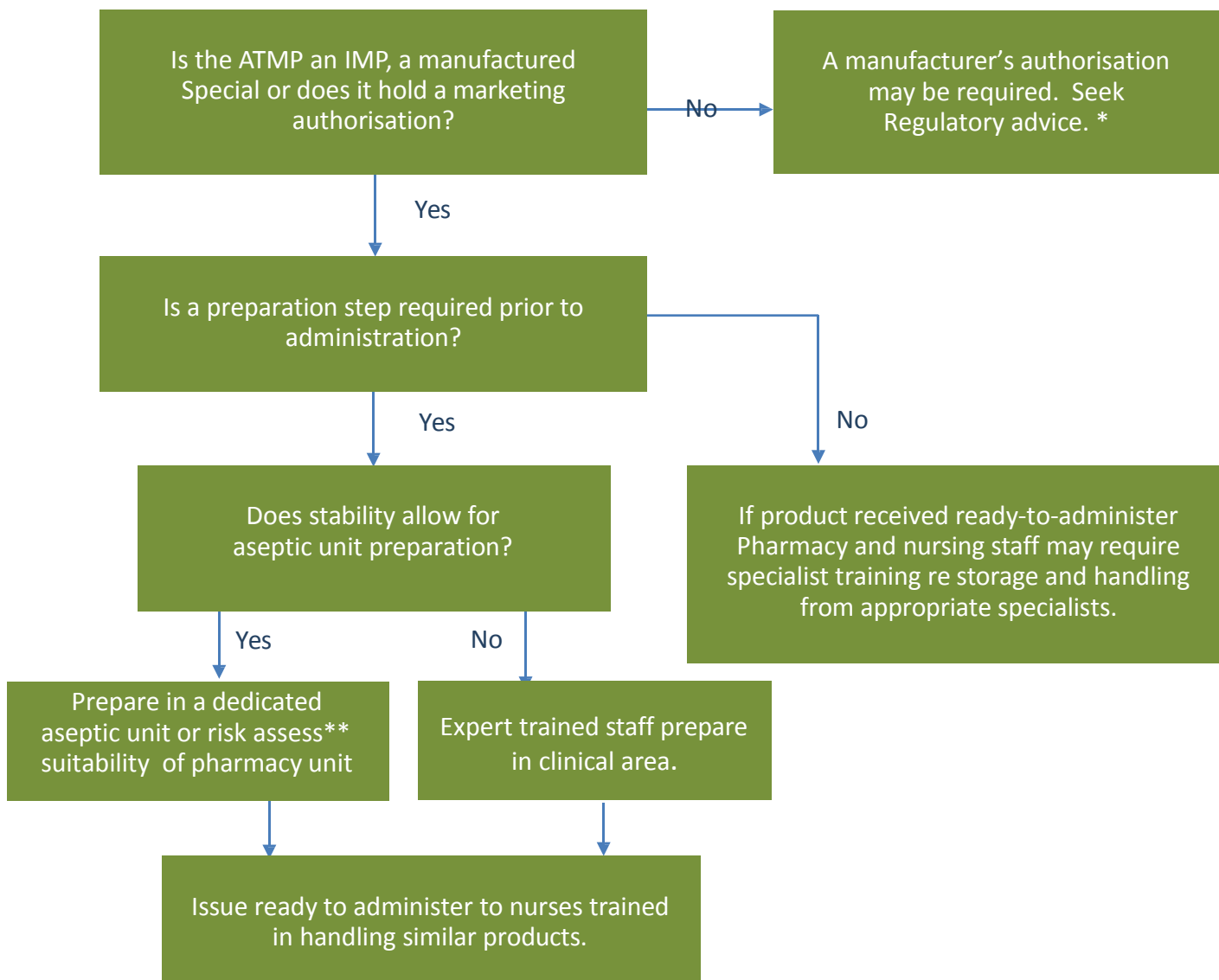
- Ensuring robust governance is in place for the introduction of ATMPs
- Ensuring that only staff with appropriate skills and expertise undertake handling and processing of ATMPs
- Ensuring appropriate technical and pharmaceutical advice is available.

Further information is available from the ATMP Working Party – a subgroup of the National Pharmaceutical QA Committee (contact: anne.black@nuth.nhs.uk)

Reference 1: Regulation (EC) No 1394/2007 of the European Parliament and the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC.

Appendix 1: Technical and Regulatory Assessment

A suggested flow chart for the initial pharmacy technical assessment of an ATMP is provided below.



This document has been produced by members of the ATMP Working Group of the National Pharmaceutical Quality Assurance Committee and members of the National Pharmacy Clinical Trials Advisory Group.

*Regulatory advice available from ATMP Working Party (contact via Chair anne.black@nuth.nhs.uk), or from the [MHRA Innovation Office](#)

**Further guidance on risk assessment considerations is given in Quality Assurance of Aseptic Preparation Services: Standards Handbook, Fifth Edition, Part B 6.

Document History	Issue date and reason for change
Version 1	Issued February 2017
Version 2	