University Hospitals of Leicester NHS
NHS Trust

Policy for the Use of Advanced Therapy Medicinal Products (including Advanced Therapy Investigational Medicinal Products)

Approved By:	Policy and Guideline Committee
Date of Original Approval:	**17 May 2024**
Trust Reference:	**B54/2024**
Version:	V1
Supersedes:	Not applicable, new policy
Trust Lead:	Helen Knight, Deputy Chief Pharmacist
Board Director Lead:	Andrew Furlong – Medical Director
Date of Latest Approval	17 May 2024 – Policy and Guideline Committee
Next Review Date:	**May 2026**

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REVIEW DATES AND DETAILS OF CHANGES MADE DURING THE REVIEW

Not applicable- Version1

KEY WORDS

Advanced Therapy Medicinal Products (ATMPs), Advanced Therapy Investigational Medicinal Products, investigational (ATIMPs), authorised ATMPs, gene therapy, biological medicinal product, tissue engineered product, somatic cell therapy medicinal product

1 INTRODUCTION AND OVERVIEW

1.1 This document sets out the University Hospitals of Leicester (UHL) NHS Trust Policy and Procedures for the Use and management of Advanced Therapy Medicinal Products including Advanced Therapy Investigational Medicinal Products.

1.2 The aim of this policy is to ensure ATMPs are used and governed appropriately within UHL and should be read in conjunction with the UHL policy for the Introduction of New Medicines Leicester Leicestershire and Rutland Policy.

1.3 An Advanced Therapy Medicinal Product (ATMP) or Advanced Therapy Investigational Medicinal Product (ATIMP) is a biological medicinal product that can be classified as either:-

- a gene therapy medicinal product (GTMPs)
- a somatic cell therapy medicinal product
- a tissue engineered product

or a combination of the 3

1.4 Throughout this policy, the term "ATMP" should be understood as referring to both Advanced Therapy Medicinal Products that have been granted a marketing authorisation, and Advanced Therapy Medicinal Products that are being tested or used as reference in a clinical trial (*i.e.* Advanced Therapy Investigational Medicinal Products).When specific provisions are only relevant for Advanced Therapy Medicinal Products that have been granted a marketing authorisation, the term "authorised ATMPs" is used. When specific provisions are only relevant for Advanced Therapy Investigational Medicinal Products, the term "investigational ATMPs" is used.

1.5 As ATMPs are medicines they must meet the definition of medicines as defined within Directive 2001/83/EC and are therefore subject to the same requirements as for other medicinal products, therefore within this Trust the Chief Pharmacist is responsible for their use.

1.6 The licensed status of ATMPs for use in the Trust may vary e.g.

- an ATMP which holds a Marketing Authorisation.
- an unlicensed ATMP such as a Special or prepared under a hospital exemption.
- or an ATMP to be used as an Investigational Medicinal Product within a clinical trial (ATIMP).

1.7 At UHL, ATMPs must only be sourced from an external supplier.

UHL Trust does not hold the appropriate licences for manufacture of a medicinal product (including ATMPs).

1.8 The Medicines and Healthcare Regulatory Authority (MHRA) is the competent authority for all medicines, including ATMPs. Their remit includes:-

- Clinical trial authorisation for all medicinal products, including ATIMPs

- Regulation of UK manufacturers or importers of all medicinal products, including ATMPs

1.9 Where a product containing human tissues or cells is classified as an ATMP the Human Tissue Authority (HTA) regulations apply for the consent, donation, procurement, storage, processing, import and testing of tissues and cells (in addition to MHRA requirements). The subsequent stages, including manufacture, storage and distribution will be regulated by the MHRA.

1.10 Investigational Medicinal Product (IMP) GTMPs are regulated by the MHRA and HSE. Licensed GTMPs are governed by the MHRA only.

The following legislation is available for consultation.

Human Medicines Regulations 2012 SI: 2012 - No. 1916
Directive 2001/83/EC
Human Tissue (Quality and Safety for Human Application) Regulations 2007
Regulation (EC) NO 1394/2007 On Advanced Therapy Medicinal Products ("The ATMP Regulation")
Health and Safety Executive (HSE) Genetically Modified Organisms (Contained Use) Regulations 2014
The Medicines for Human Use (Clinical Trials) Regulations 2004
If the gene therapy product is being used in a clinical trial reference should be made to the following :- Clinical Trials Directive 2001/20/EC Medicines for Human Use (Clinical Trials) 2004 SI: 2004- No.1031 as amended

Table 1 Legislation and guidance documentation

1.11 As ATMPs are specialist medicines Pharmacy staff have a role in ensuring they are used appropriately within the Trust. The role of Pharmacy is to:

- Oversee the governance arrangements and quality assurance (QA) for these specialist medicines.
- Provide expertise on the preparation of ATMPs, which includes safe handling. Refer to section 4 below for further roles and responsibilities of the pharmacy department.

2 POLICY SCOPE –WHO THE POLICY APPLIES TO AND ANY SPECIFIC EXCLUSIONS

2.1 This policy covers the governance, sourcing, storage, manufacturing, preparation for administration, administration and technical and regulatory assessment and disposal of any ATMP for use by a patient within UHL

2.2 This policy applies to all staff involved with any of the above processes.

Any gene or cellular products which are not deemed to be an ATMP must be managed in line with the appropriate regulations i.e. Human Tissue Authority (HTA) regulations and guidance, and will not be considered further within this document. Further information can be found at https://www.hta.gov.uk/ or by contacting the Trust's HTA Designated Individual (DI).

3 DEFINITIONS AND ABBREVIATIONS

Advanced Therapy Medicinal Product (ATMP)	A biological medicine for human use that is a gene therapy, somatic cellular therapy or tissue engineered product.
Advanced Therapy Investigational Medicinal Product (ATIMP)	An investigational medicinal product used within a clinical trial. The medicine, for human use, is a gene therapy, somatic cellular therapy or tissue engineered product.
Cellular Product	A product based on cells or tissues which have not been substantially modified and are for homologous use.
Gene Therapy Medicinal Product (GTMP)	A biological medicinal product which has the following characteristics:- a) It 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; b) 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. GTMP does **not** include vaccines against infectious diseases.
Good Clinical Practice (GCP)	This **is** an international ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials. It also serves to protect the rights, integrity and confidentiality of trial subjects
Good Manufacturing Practice (GMP)	GMPs are performance standards that WHO and many national governments

	established for pharmaceutical manufacturers. GMPs are part of the quality assurance activities that ensure that products are consistently produced and controlled to the quality standards appropriate to their intended use and required by drug regulatory authorities. The standards include criteria for personnel, facilities, packaging, quality control, and, in most cases, stability testing.
Hospital exemption (Not widely used in the UK)	Any advanced therapy medicinal product, as defined in Regulation (EC) No 1394/2007, which is prepared on a non-routine basis according to specific quality standards, and used within the same Member State in a hospital under the professional responsibility of a medical practitioner, in order to comply with an individual medical prescription for a custom-made product for an individual patient. ATMPs prepared under this exemption are deemed unlicensed medicines Is presented as having properties for, or isused in or administered to human beings, with a view to treating, preventing or diagnosing a disease through the pharmacological, immunological or metabolic action of its cells or tissues.
Medicinal product	A medicinal product is:- a) Any substance or combination of substances presented as having properties of preventing or treating disease in human beings; b) Any substance or combination of substances that may be used by or administered to human beings with a view to restoring, correcting or modifying a physiological function by exertinga pharmacological, immunological or metabolic action, or making a medical diagnosis.
Medicines and Healthcare products Regulatory Agency (MHRA)	The MHRA regulates medicines, medical devices and blood components for transfusion in the UK.
Pharmaceutical Quality Control (QC)	As defined by WHO, quality control is the part of the firm's process concerned with medicine sampling, specifications, testing, and the organization's release procedures that ensure that the necessary tests are carried out and that the materials are not released for use,

	nor products released for sale or supply, until their quality has been judged satisfactory.
Quality Assurance (QA)	Pharmaceutical quality assurance may be defined as the sum of all activities and responsibilities required to ensure that the medicine that reaches the patient is safe, effective, and acceptable to the patient.
Somatic cell therapy medicinal product (SCTMP)	A biological medicinal product which has the following characteristics:- a) It contains or consists of cells or tissues that have been subject to substantial manipulation so that biological characteristics, physiological functions or structural properties relevant for the intended clinical use have been altered, or of cells or tissues that are not intended to be used for the same essential function(s) in the recipient and the donor; b) Is presented as having properties for, or is used in or administered to human beings, with a view to treating, preventing or diagnosing a disease through the pharmacological, immunological or metablic action of its cells or tissues.
Special	An unlicensed medicine manufactured or imported under a manufacturing specials (MS) licence.
Tissue engineered product (TEP)	A medicinal product that:- Contains or consists of engineered cells or tissues and is 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.

Other Definitions

The use of the terms ‘oversight’ and ‘supervision’ in this policy are to be considered in the context of this document relating to pharmacists responsibilities and refer to ATMPs only, not to other medicinal products.

The following are definitions relevant to this policy.

Oversight: Where the term pharmacist oversight is used; oversight of an activity or process is required., but the pharmacist’s presence for the activity or process to be carried out each time by qualified members of staff is not necessarily required, providing the appropriate training has been provided and a Pharmacy approved SOP is in place e.g. if a stem cell staff member has been trained and is competent to carry out the activity, it is good practice for the pharmacist to be present the first time the activity is performed and to monitor the activity at future intervals to ensure continued compliance, but it is not necessary for the pharmacist to be present each time the staff member performs the activity.

As oppose to

Supervision: where the term pharmacist supervision is used, the presence of a pharmacist is required for an activity or process to be carried out e.g. where a product is reconstituted outside of the requirements stated in the summary of product characteristics (SmPC), this must be performed under the supervision of a pharmacist using the Section 10 exemption, of the Medicines Act 1968

4 ROLES – WHO DOES WHAT

4.1 The executive director responsible for this policy is the Medical Director

4.2 Chief Pharmacist

The Chief Pharmacist has overall responsibility for:

4.2.1 The safe management, governance, use and prescribing of all ATMPs within the Trust and the UHL pillar of the Alliance.

4.3 Pharmacy ATMP Lead

4.3.1 Delegated responsibility from the Chief Pharmacist for the operational management and oversight of the use of all ATMPs within the Trust.

4.4 Principal Pharmacist Aseptic Services

4.4.1 With respect to Immune Effector Cells, classified as ATMPs, is responsible for auditing the Stem Cell Laboratory as necessary to ensure GCP & GMP compliance following advice from the Regional QA Pharmacist.

4.5 Pharmacy Department

4.5.1 The relevant CMG Lead / Principal Pharmacist for the applicable area will support the Senior Medic with Oversight for the following roles: Providing

advice and oversight of MHRA Manufacturing licences, and be the link for providing and interpreting associated advice from the relevant Qualified Person (QP) where appropriate

4.5.2 Sourcing licensed (authorised), unlicensed and investigational ATMPs from appropriate external suppliers or Sponsors, including approval of any Supply Agreement.

4.5.3 Processing of orders and invoices through the pharmacy stock management system

4.5.4 Providing advice on and approve the procedures for handling and storage of ATMPs

4.5.5 Providing advice, technical expertise and oversight of preparation activities required for ATMPs

4.5.6 Principal Pharmacist Aseptic Services should be involved in any strategic decisions/policy making about the most appropriate place to prepare ATMPs

4.5.7 Pharmacy will complete the Technical Assessment.

4.5.8 Pharmacy will provide training as required and support development of procedures relating to preparation, handling and storage of all ATMPs.

4.5.9 Pharmacy will provide Quality Control Advice and approval for an unlicensed ATMP such as a Special or prepared under a hospital exemption in accordance with the Trust's Unlicensed Medicines Policy.

4.6 Pharmacy Quality and Safety Committee

4.6.1 To provide final pharmacy governance approval for all ATMPs used within the Trust on behalf of the Chief Pharmacist.

4.7 Therapeutic Advisory Service (TAS)

4.7.1 All requests for ATMPs, other than formal investigational studies with R&I approval, must be submitted to TAS usng the usual application form for formulary review

4.7.2 TAS is responsible for assessing the request for formulary addition and either approving the ATMP on to the formulary or not.

4.8 Genetic Materials Safety Committee (GMSC)

4.8.1 Provide assessment and review of all ATMPs that are to be used at UHL both in clinical trials and in standard practice.

4.8.2 For GTMPs and combinations products (e.g. somatic cell and gene therapy products, provide:

4.8.2.1 Approval of the risk assessment and action plan, SOPs and training, ensuring compliance with necessary legislation and regulations for GTMPs (assessment of risk to human health and safety to environment, containment and control measures, classification of organism)

4.8.2.2 Review and approve of the facilities for preparation, handling, storage and administration and disposal

4.8.2.3 Approval of studies (e.g. GTMP clinical trials) with appropriate controls in place

4.8.2.4 Provide recommendations for approval to the Medicine Optimisation Committee before final governance approval is received for authorised ATMPs.

4.8.2.5 Co-ordinate communication with HSE for Genetic Modified Organisms (GMO) activities

4.8.2.6 Assign the classification and containment levels for GTMPs

4.9 Medicines Optimisation Committee

4.9.1 Responsible for providing final Trust governance approval for the use of all authorised ATMPs.

4.10 Cancer Research Strategy Group (CRSG)

4.10.1 The Cancer Research Strategy Group are responsible for reviewing the evidence around the use of all ATIMPs in this specific CMG and reviewing and providing approval for the management and use of the ATMP within their CMG.

4.11 Clinical Management Group (CMG)

4.11.1 The Clinical Director and Head of Nursing for that CMG are responsible for ensuring all staff involved with any of the processes in the use of ATMPs within their CMG are aware of this policy.

4.11.2. The Clinical Director and Head of Nursing for that CMG are responsible for ensuring all staff involved with the management of the ATMP have received appropriate applicable training relevant to their role.

4.11.3 The CMG are responsible for providing CMG approval for the use of the authorised ATMP within their CMG and responsible for ensuring the appropriate funding is available for its use.

4.11.4 The CMG are responsible for ensuring all staff involved with the use of an investigational ATMP follow and are trained on the appropriate clinical trial procedures.

4.12 Senior Medic wth Oversight / Prescribers

4.12.1 The Senior Medic with Oversight/ Prescriber is responsible for ensuring all appropriate approvals have been received by the relevant committees for the use of the ATMPs before initiation of any treatment.

4.12.2 The Prescriber is responsible for ensuring the appropriate approved procedures and practices are in place before initiation of treatment commences.

Completion of the usual TAS application for formulary submission

Completion of the risk assessment and action plan. For GTMPs, a specific risk assessment is available.

4.12.3 Where the Senior Medic with Oversight/Prescriber is a Principal Investigator (PI) within a trial, they may delegate responsibilities to other members of the trial team but still remain overall responsible for the above

4.12.4 To develop, oversee and ensure all governance, SOPs and training are in place prior to the introduction of the ATMP.

4.13 **Nursing Staff**

4.13.1 Nursing staff involved with the storage, handling, preparation, administration and disposal of all ATMPs are responsible for ensuring they are aware of this policy and its guidance.

4.13.2 The nursing staff involved with the storage, handing, preparation, administration and disposal of all ATMPs are responsible for ensuring they follow the appropriate procedures for use of that ATMP.

4.14 **Research and Innovation (R&I)**

4.14.1 All requests for ATIMPs and ATMPs for formal investigational studies must have appropriate R&I approval

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4.15 **HTA Designated Indiviual**

- 4.15.1 Provide advice and approval for procedures related to the Human Tissue Authority Human Application licence e.g. consent, testing, procurement (e.g. of cells, cartilage biopsy), storage, processing* and distribution.

  * if ‘processing’ of tissues or cells is involved under the UHL HTA licence ie on UHL premises, then the DI must complete a PPD (Preparation Process Dossier) on the HTA website and submit to the HTA for approval prior to commencing processing.

5. POLICY IMPLEMENTATION AND ASSOCIATED DOCUMENTS –WHAT TO DO AND HOW TO DO IT

An overview of the policy is provided in Appendix 1. Contact details for key personnel is provided in Appendix 5.

5.1 Receipt of a Request for the use of an ATMP.

5.1.1 The definition of an ATMP, stated within the Directive 2001/83/EC, should be referred to prior to submitting the request for a new ATMP to ensure the desired product

is in fact classified as an ATMP and a medicinal product. Where there is any ambiguity, the Principal Pharmacist Aseptic Services should be contacted who can discuss with the MHRA.

5.1.2 As for all new medicines, the Introduction of New Medicines Leicester, Leicstershire and Rutland Policy (http://insitetogether.xuhl-tr.nhs.uk/pag/pagdocuments/Introduction%20of%20New%20Medicines%20Leicester%20Leicestershire%20and%20Rutland%20Policy.pdf). must be followed for a request for an authorised ATMPs. Approvals of ATMP products will be performed by the relevant committees as described in section 5.3 below

5.1.3 Where the ATMP is classified as an unlicensed medicine, the Unlicensed Medicine Policy must be followed in addition.

5.1.4 Where the ATMP is classified as an investigational ATMP, normal clinical trial approval and review processes must be adhered to and followed.

5.2 Technical and Regulatory Assessment

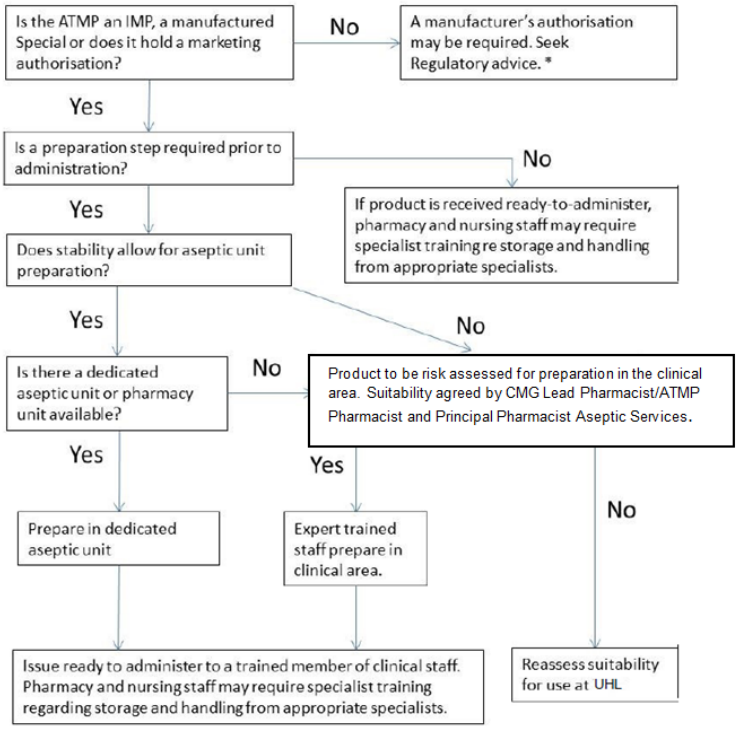
A flow diagram of the process is defined in Appendix 1

5.2.1 An assessment will be made by the Pharmacy Department to determine

- If the ATMP requires to be manufactured (e.g. does it require substantial manipulation or is it for a different physiological function).
- If manufacturing authorisations / licences are needed (as appropriate) for either the manufacture or sourcing of an ATMP. See 5.4. below.
- If the ATMP requires storage and/or preparation manipulation prior to administration.
- The location in which any additional preparation steps (if necessary) are to take place, for example, another facility within UHL (e.g. the Stem Cell Laboratory) or within the clinical area can be identified .
- Whether any additional training needs regarding storage and handling of the ATMP are required.
- The preferred location for preparation taking into account the shelf lfe and product characteristics of the ATMP.

5.2.2 Pharmacy will provide advice and oversight of Trust Manufacturing licences and Qualified Person services.

The Technical Assessment flow diagram of this process is shown below (also appendix 6):



* Regulatory advice available from the ATMP Working party (contact via chair anne.black@nuth.nhs.uk), or from the MHRA Innovation Office.

5.2.3 A Trust risk assessment, including but not limited to clinical (including administration, tracking and traceability of the product), financial and information governance rsks, should be completed for the introduction and use of SCTMP/TEPs whch will inform the need for dedicated SOPs. For GTMPs and mixed products, see Appendix 2 for specific risk assessment template.

5.2.4 SOPs developed should cover as a minimum:

- Ordering, receipt (including product integrity, temperature compliance during transit across UHL sites, product labelling, review of certificate of analysis if applicable – see appendices 3 and 4 for an example checklist), storage, preparation,handling and record keeping
- Management of Storage/Temperature deviations
- Cleaning, spillage, waste disposal and destruction
- Cancellation of patient and/order
- Record keeping
- Training

5.2.5 Pharmacy will support completion of the relevant medicine management checklist to ensure all aspects of entire process have been completed (See example checklist appendices 3 and 4)

5.3 Approvals

5.3.1 All requests for new ATMPs will be subject to governance procedures within the Trust including approval by the appropriate committee(s), Trust policies and formulary control.

5.3.2The applicable approval Committees are shown below:

For authorised ATMPs

- Genetic Safety Materials Committee
- Therapeutic Advisory Service Systemic Anti-Cancer Therapy (SACT group

For investigational ATMPs used within a clinical trial

- Genetic Materials Safety Committee
- Other local approvals depending upon the individual clinical trial, e.g. Cancer Research Strategy Board or equivalent

5.3.3The Unlicensed Medicines Policy must also be followed for any ATMPs which are deemed unlicensed e.g. a 'Special'.

5.3.3 SOPs will be approved by the Pharmacy Quality and Safety Committees and also the Genetic Materials Safety Committee (GMSC) for GTMPs.

5.4 Sourcing

5.4.1. ATMPs will be sourced from an external provider supplier.

5.4.2 ATMPs purchased from an external supplier:- Pharmacy Procurement are responsible for sourcing licensed or unlicensed ATMPs for use within the Trust. This will be in line with current policies and procedures for the general purchase of medicinal products. Refer to Pharmacy Purchasing for Safety Policy and Procurement and Acquisition of Medicines LMC Chapter 3 (http://insitetogether.xuhl-tr.nhs.uk/pag/pagdocuments/Unlicensed%20Medicines%20UHL%20Policy.pdf) / add in links for safety policy)

5.4.3 The Unlicensed Medicines Policy and associated pharmacy procedures must be followed to source an unlicensed ATMP. (http://insitetogether.xuhl-tr.nhs.uk/pag/pagdocuments/Unlicensed%20Medicines%20UHL%20Policy.pdf)

5.4.4 All ATMPs must be sourced from an appropriate pharmaceutical supplier who holds the necessary MHRA licence / authorisation to sell / supply medicinal products, e.g. a wholesale dealer licence.

5.4.5 The sponsor of an investigational ATMP and UHL internal requestor must liase with the Clinical Trials Pharmacy Team when sourcing an investigational ATMP that is required.

5.4.6 Batch QP certification checks will need to be performed by the Pharmacy Department to ensure ATMPs sourced have been manufactured in line with appropriate GMP principles where appropriate.

5.5 Manufacturing

5.5.1 Manufacture as defined by the MHRA cannot occur at UHL as the Trust does not hold the appropriate licences. Therefore all ATMPs used at UHL must be sourced from an external supplier as described in section 5.4 above.

5.6 Preparation and Administration

5.6.1 The Trust Injectable Medicines Policy, principles from Chapter 6 Administration of Medicines, LMC and Supporting Information must be adhered to by any staff member preparing and/or administering an ATMP in the clinical area. See links: (http://insitetogether.xuhl-tr.nhs.uk/pag/pagdocuments/Administration%20of%20medicines%20for%20inpatients%20LMC%20chapter%206.pdf)

5.6.2 The technical assessment performed by Pharmacy will determine the location that an ATMP will be prepared, i.e. a specific facility such as the stem cell laboratory or the clinical area. The assessment will need to be reviewed and approved at both the Pharmacy Quality and Safety committee and the Genetic Materials Safety Committee. (Due to the potentially complex nature of ATMPs, traditional pharmacy aseptic facilities at UHL are not able to provide operarational facilities for products including tissues and cells).

5.6.3 The technical assessment will include a risk assessment and consideration of the ATMP shelf life and operator plus other staff safety. Example templates can be found in Appendix 2.

5.6.4 ATMPs requiring preparation in a specific Trust facility will be prepared by staff from the facility according to internal procedures (e.g. Stem cell laboratory) and then transferred to the clinical area for administration by a trained member of clinical staff. The specific facility is responsible for providing a labelled, ready to administer dose. The procedures and labelling will be overseen and approved by Pharmacy.

5.6.5 As authorised ATMPs must only be prepared exactly as specified in the summary of product characteristics (SmPC), preparation under the supervision of a pharmacist is not routinely required. However it is important that any preparation activity is undertaken by trained and competent staff. For example, stem cell laboratory staff may prepare the product as per their standard processes.

5.6.6 Where the preparation is performed according to the SmPC instruction outwith pharmacy (e.g. by stem cell laboratory staff) then pharmacist oversight is required, as is the case for any medicine.

5.6.7 Where any aspects of preparation (receipt and or storage) are outsourced pharmacy oversight will be required. In addition, it is recommended that in this

circumstance a technical agreement is put in place to ensure that roles and responsibilities are clear and product quality is optimised.

5.6.8 ATMPs requiring preparation in a clinical area will be prepared by a trained member of the clinical team (e.g. registered nurse). The same or another trained member of the clinical team will administer the ATMP to the patient. (Reconstitution of a medicinal product ATMP under the regulations is defined as requiring a step prior to preparation). Refer to IV administration

5.6.9 The preparation instructions (SOP) will be overseen and approved by the Pharmacy Quality and Safety Committee and the Genetic Materials Safety Committee, and any training required will be provided.

5.6.10 Part IV EudraxLex Volume 4 (Good Manufacturing Practice specific to ATMPs) specifies that activities required after batch release prior to administration of an ATMP, which are not considered to be a manufacturing step can be perfomed outside of an MHRA licensed GMP environment at the administration site (e.g. in clinical areas). This is in line with the requirements for all medicines.

5.6.11 ATMP reconstitution steps defined in Part IV EudraLex Volume 4 include thawing of cryopreserved products in a ready to administer presentation. Pharmacists should therefore be involved in the process of producing / approving the SOP and ensure that it is performed in line with the SmPC. Where thawing only is required, physical supervision from pharmacy staff is not a requirement.

5.6.12 Where administration of an investigational ATMP is being considered, all of the above requirements apply, however these will be taken in consideration with the approved guidance supplied by the Trial Sponsors. Processes and procedures will be developed in conjunction with the approved Sponsors for the study and will be reviewed by the Pharmacy Quality and Safety Committee and the Genetic Materials Safety Committee.

5.6.13 Administration of an investigational ATMP will only be approved once the appropriate Research and Innovation (R&I) capability approvals have been received.

5.7 Receipt, Storage and Handling

5.7.1 Pharmacy or another specific facility within UHL (e.g. the Stem Cell Laboratory) must receive all ATMPs following a pharmacy approved SOP.

5.7.2 ATMPs often require specialist handling and storage, e.g. in vapour phase liquid nitrogen dewers, freezing at -80 degrees Centigrade. The Stem Cell Laboratory has appropriate storage facilities and expertise to undertake this.

5.7.3 Where an ATMP is received in Pharmacy packed within dry ice (solid carbon dioxide) then an approved SOP for unpacking & handling the ATMP, and disposing of the dry ice in a well ventilated area must be followed. A risk assessment & COSHH documentation will be required for staff safety.

5.7.4 Where storage or handling of an ATMP is required in the clinical area by clinical staff, appropriate training and advice regarding storage / handling must be undertaken in accordance with the dedicated approved SOP.Pharmacy is responsible for providing training and advice for this process. The clinical staff are responsible for monitoring any specialist storage devices within their specialist area. Actions in the event of an alarm should be specified.

5.7.5 Storage of an ATMP for use in a clinical trial must be in a pharmacy approved area. Delivery to and storage within the clnical area is subject to the outcome of a pharmacy led risk assessment to ensure controls can be implemented.

5.7.6 Storage within the clinical area (e.g. as emergency access is required) is subject to the outcome of a pharmacy led risk assessment to ensure appropriate controls can be implemented. Pharmacy Clinical Trial **procedures** are to be followed to perform this assessment. **(SOP 406 - CLINICAL TRIALS INVOLVING MEDICINES STORED ON WARDS OR IN CLINICS -http://insitetogether.xuhl-tr.nhs.uk/SP2007/Pharmacy/SOP%20406%20Clinical%20Trials%20Involving%20Medicines%20Stored%20on%20Wards%20or%20Clinics.pdf / SOP 405 - STORAGE OF CLINICAL TRIALS SUPPLIES AND TEMPERATURE MONITORING - http://insitetogether.xuhl-tr.nhs.uk/SP2007/Pharmacy/SOP%20405%20Storage%20and%20Temperature%20Monitoring%20of%20Clinical%20Trials.pdf)**

5.7.7 The Pharmacy Quality and Safety Committee (on behalf of the Chief Pharmacist) are responsible for overseeing and approving all procedures relating to the handling and storage of ATMPs.

5.8 Clinical Trials Specifically

5.8.1 Management and use of an investigational ATMP within UHL must follow the principles and guidance stipulated in Chapter 11 - Clinical Trials LMC and have received the appropriate R&I Capacity and Capability approval before use within the Trust.

5.8.2 The Principal Pharmacist Clinical Trials (on behalf of the Chief Pharmacist) is responsible for GCP oversight of any clinical trial where the ATIMP is administered to a patient at UHL. The UK Policy Framework for Health and Social Care Research and Good Clinical Practice must be followed for any ATIMP used as an investigational medicinal product as part of a clinical trial.

5.8.3 The Principal Pharmacist Clinical Trials (on behalf of the Chief Pharmacist) is responsible for technical oversight and governance of any clinical trial in which the investigational ATMP is prepared on site for administration to a patient at UHL.

5.8.4 Within the remit of a clinical trial, the Principal Investigator (PI) still retains overall responsibility for the oversight of investigational ATMPs within the remit of the trial; however, these duties will be delegated to the Principal Pharmacist Clinical Trials.

5.8.5 All requests / orders for investigational ATMPs are to be provided to pharmacy as defined on the Clinical Trial Prescription in line with the trial protocol.

5.8.6 The Principal Pharmacist Aseptic Services (on behalf of the Chief Pharmacist) will audit the Stem Cell Laboratory for compliance with GCP and GMP as necessary.

5.9 Waste Disposal

5.9.1 In the case of the use of an investigational ATMP, disposal may be arranged with the approved Sponsor and the remaining waste or surplus supplies of the ATMP will be removed from the Trust by the Sponsor.

5.9.2 In the case of all other ATMPs, waste associated with the procedure will be disposed of in accordance to the COSHH Risk assessment requirements and will follow the relevant guidance in the Waste Management and Guidance Policy (http://insitetogether.xuhl-tr.nhs.uk/pag/pagdocuments/Waste%20Management%20UHL%20Policy.pdf).

6 EDUCATION AND TRAINING REQUIREMENTS

6.1 The prescribing & administration of medication is covered in core competencies. Staff should familiarise themselves with relevant policies relating to this.

6.2 The relevant CMG Lead / Principal Pharmacist is responsible for ensuring all the appropriate training has been delivered in accordance with the approved procedures before the ATMPs are released for administration.

6.3 The ATMP introduction risk assessment should inform the training and competency requirements needed for the safe and effective handling, storage, preparation and administration and how this will be provided.

6.4 Training requirements should be stipulated within the dedicated SOP.

6.5. Clinical staff are not permitted to prepare ATMPs (where applicable) without this additional training being completed.

7 PROCESS FOR MONITORING COMPLIANCE

POLICY MONITORING TABLE

Element to be monitored	Lead	Tool	Frequency	Reporting arrangements Who or what committee will the completed report go to.
Reported incidents relating to ATMPs / ATIMPs	ATMP Pharmacist	Review of Trust datixes	Quarterly review / Annual report to MedOC	Medicines Optimisation Committee (MedOC)

8 EQUALITY IMPACT ASSESSMENT

8.1 The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.

8.2 As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

9 SUPPORTING REFERENCES, EVIDENCE BASE AND RELATED POLICIES

9.1 European Commission. Directive 2001/83/EC, Volume 1 - Pharmaceutical Legislation for Medicinal Products for Human Use. http://ec.europa.eu/health/documents/eudralex/vol-1/ Accessed 29.05.19

9.2 European Commission. Regulation (EC) No 1394/2007 of the European Parliament and of the Council. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:324:0121:0137:en:PDF Accessed 29.05.19

9.3 The Role of Pharmacy in the Successful Delivery of Advanced Therapy Medicinal Products (ATMPs) - Information for Chief Pharmacists (Edition 1 February 2017)

9.4 Quality Assurance of Aseptic Preparation Services: Standards Handbook (Fifth Edition 2016, Part B 6: Advanced therapy medicinal products (ATMPs))

9.5 Good Clinical Practice Guide (MHRA 2012) - Annex 3 Advanced therapy investigational medicinal product trials

9.6 Practical guidance on Pharmacy Oversight and Pharmacy Supervision of licensed ATMPs requiring a preparation / reconstitution step. Pan Uk Pharmacy Working Group for ATMPs. www.sps.nhs.uk9.7 Human Tissue (Quality and Safety for Human Application) Regulations 2007

9.8 The Medicines for Human Use (Clinical Trials) Regulations 2004 SI 2004-No 1031 as amended

9.9 POLICY FOR THE INTRODUCTION OF NEW CLINICAL PROCEDURES INCLUDING NICE MEDICAL TECHNOLOGIES CL/CGP/009

9.10 The SACGM Compendium of guidance: Guidance from the Scientific Advisory Committee on Genetic Modification available at http://www.hse.gov.uk

9.11 Human Medicines Regulations 2012 51:2012- no1916

9.12 Health and Safety Executive (HSE) Genetically Modified Organisms (continued Use) Regulations 2012

9.13 Clinical Trials Directive 2001/201EC

9.14 Waste Management Policy and Guidance. UHL Policy. Trust Reference B39/2024

9.15 Leicestershire Medicine Code. Chapter 6. Administration of Medicines

9.16 Unlicesned Medicines Policy. UHL Policy. Trust Reference B29/2004

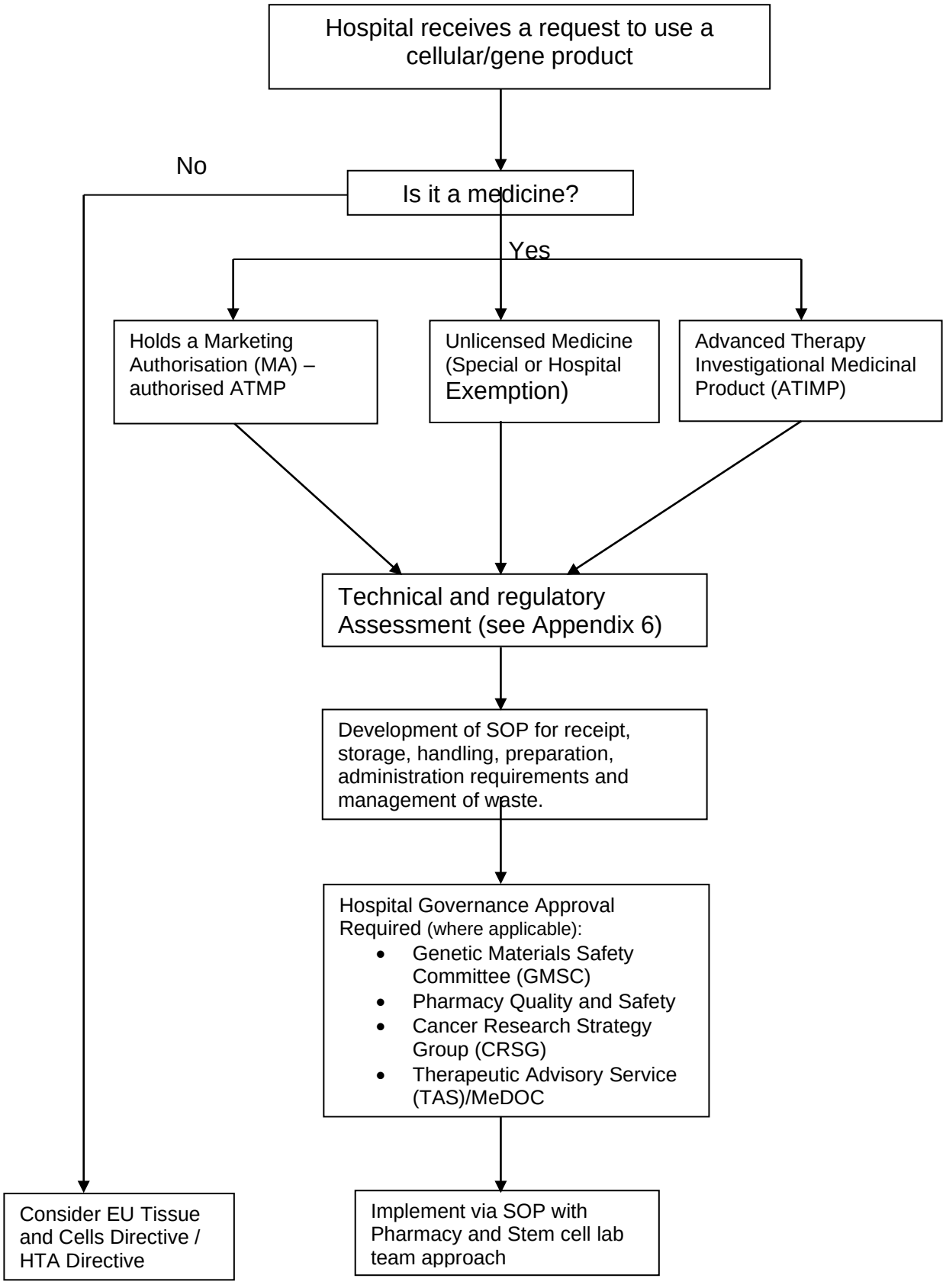
9.17 Policy for the introduction of New Medicines into Leicester, Leicestershire and Rutland. Trust Policy. Trust Reference B28/2011

10 PROCESS FOR VERSION CONTROL, DOCUMENT ARCHIVING AND REVIEW

10.1 This policy will be uploaded onto the UHL Policies and Guidelines Library accessible by staff via InSite. It will be stored and archived using this system.

10.2 This policy will be reviewed every 3 years or sooner in response to any clinical or risk issues

Appendix 1: Overview of the Process



Appendix 2

Risk Assessment for Gene Therapy Medicinal Product (GTMP) or Combination ATMPs that Include Gene Therapy

SECTION 1

Name of medicinal product (ATMP)	
Is the ATMP: **a) Gene Therapy Medicinal Product (GTMP) or** **b) Combination of a GTMP with a Somatic cell therapy medicinal product or Tissue engineered medicinal product (please state)**	
Indication	
Lead Clinician (Name)	
Lead Clinician (Telephone)	
Lead Clinician (e-mail)	
Specialty and Division	

This risk assessment should be submitted for approval by:
Pharmacy Quality and Safety Committee
Genetic Materials Safety Committee
CMG Director (after all other approvals, see “Flow Chart for Process of Introducing an ATMP into the Trust”)

SECTION 2

Information on the proposed Gene Therapy Medicinal Product (GTMP) product

This information should be available in the risk assessment from the GTMP manufacturer.

Full description of the vector. Include information on the extent to which it is attenuated/disabled.	
Full description of the insert including function.	
How will the product be administered?	
Where will the product be administered? (i.e. clinical area)	

State any provisional containment level that has been assigned by the GMSC for the GM product /activities. (see Scientific Advisory Committee on Genetic Modification (SACGM) for guidance)	

SECTION 3

Assessment of risk to humans

This information should be available in the risk assessment from the GTMP manufacturer.

Vector: Factors to consider include whether the recipient microorganism is listed in ACDP hazard groups 2, 3 or 4.

Other relevant factors may be the micro-organism's mode of transmission, disease symptoms, host range, and tissue tropism as well as an indication as to whether vaccines or chemotherapeutic agents are available.

Information should also be provided on any disabling mutations and whether there is any possibility of any

disabling mutations being complemented or reverting.

Insert: Consideration should be given to whether the inserted DNA encodes a toxin, an oncogenic protein, an allergen, a modulator of growth or differentiation (hormone or cytokine) or any other protein, which may result in potentially harmful biological activity. Please note that even a normal human gene may be harmful if over

expressed, especially if the over expression is in tissues that do not normally express the protein.

Risks associated with the vector	
Risks associated with the insert	
Is there the potential for genetic material to be transferred to a related micro-organism (e.g. gene transfer/recombination)	

SECTION 4
Assessment of risk to the environment
This information should be available in the risk assessment from the GTMP manufacturer.
Vector: Factors to consider include whether the recipient microorganism is capable of infecting any plants, animals or insects in the environment and whether there is any possibility of any disabling mutations being complemented or reverting. In particular it should be ascertained whether the recipient microorganism is a pathogen that is controlled by DEFRA.
Insert: Factors to consider include whether the sequence encodes an insect or animal toxin or a product which can cause silencing of a gene encoding a crucial metabolic enzyme in susceptible hosts.

Environmental risks associated with the vector	
Environmental risks associated with the insert	

SECTION 5

Nature of the work and control measures

This information should be contained in information/SOPs/risk assessment provided by the GTMP manufacturer. HOWEVER, it is important to take into account and detail local arrangements.

a) Handling of the GTMP product prior to administration.

It is strongly recommended that the pharmacy department is consulted when completing this section.

Specify arrangements for safe receipt of the GTMP	
Specify arrangements for safe storage of the GTMP	
Specify arrangements for the safe preparation of the GTMP	
Specify arrangements for the safe transport of the GTMP including to the site of administration.	

b) Administration of the GTMP.

Investigators may wish to discuss this section with the GMSC chair or Infection Control and
Pharmacy

Identify any procedures which will involve sharps, and specify arrangements for their safe use	
Identify any work procedures likely to generate aerosols, and the control measures to be applied.	
Specify the protective clothing and any other personal protective equipment to be used at each stage.	
Specify the disinfectants to be used at each stage.	
Specify specific actions in the event of an accidental spill.	
Does the nature of this work preclude it being undertaken by any workers who have a serious skin condition (e.g. eczema) or other health problems that might make them more susceptible to infection?	
Specify any health surveillance	

requirements for staff involved in the work.	
Will potentially contaminated clinical samples (e.g. fluids, tissues) be collected from the patient for routine analysis by hospital laboratories? Specify arrangements for their safe handling.	

Is there potential for shedding of the GTMP after administration? If yes answer the following questions:	
Will the patient be isolated following the procedure? Provide details.	
Specify precautions for HCWs in contact with the patient or patient's body fluids.	
Identify any specific precautions or restrictions required for visitors to the patient.	
Other than standard arrangements, are any additional safety measures or procedures required for cleaning the patient's bed linen or laundry?	
Other than standard hospital cleaning procedures, specify any additional arrangements required when cleaning the patient's room during and at the end of the treatment period.	
Will the patient need to be transported within the hospital following administration of the GM product? Identify any specific safety procedures required for such transportation of the patient.	

c) Management of Waste.

It is strongly recommended that the Trust Waste Officer is consulted when completing this section.

Detail how residual/unused GTMP will be safely disposed of.	

Detail what contaminated waste is expected during administration and how this will be safely disposed of.	
Is there potential for shedding of the GTMP after administration? If so, how will subsequent contaminated waste be disposed of.	

d) Identify any stages of the work or manipulations of the GTMP not already covered, which may pose increased risk, and the measures which will be applied to control those risks.

SECTION 6: Risk Mitigation Action Plan (to be completed before new product is introduced into clinical areas and incorporated into the overall action plan)

No	Main Risks Identified	Score (Likelihood 1-5 x Severity 1-5)_	Action proposed to reduce the risk	Person responsible	Timescale
1					
2					
3					

The above determines what is required for an SOP

SECTION 7
Final assignment of containment measures and risk class (to be completed by the GMSC)

The following aspects of this project are assigned to class 1:

The following aspects of this project are assigned to class 2:

Each Trust will have capability approved by HSE. Where the classification is out with the approval the HSE must be notified.

Appendix 3

In-vivo, Ex-vivo GTMP Class Medicines Management and Containment Checklist

Product Name			
Type of ATMP (In-vivo GTMP or Ex-vivo GTMP)			
Supplier			
Manufacturer (if different to above)			
Regulatory status	Licensed / Unlicensed / Clinical Trial (Record EudraCT number if applicable)		
Class and containment level **circle as appropriate*	Class 1* / 2* / 3* / 4*		
Check hospital / organisation is registered with HSE to handle gene therapy medicines for appropriate class (coordinated by GMSC)	Yes	No	
Risk assessment	Yes	No	
NPSA 20 risk assessment considered/completed (including inclusion in Medusa guide)	Yes	No	
Treatment centre selected by NHSE to deliver this treatment	Yes	No	
Treatment centre qualified by manufacturer to deliver product	Yes	No	NA
Genetic Modification Committee (GMC) and/or Advanced Therapy Medicinal Products (ATMP) Committee Approval and/or New Interventional Procedures Committee approval			
Governance approvals in place for use of product including risk assessment and action: - GMSC - Specialty Governance committee - DTC including formulary review - Clinical trial approval - HTA licence appropriate for starting material	Yes	No	

and export, if applicable - Divisional Director			
SmPC/PIL/Protocol available	Yes		No
Prescription added to electronic prescribing system (ePMA, Chemocare)	Yes	No	NA
Product added to Pharmacy stock management system	Yes		No
Product specific training identified and undertaken	Yes		No
If prepared by nurses: worksheet, SOPs, staff training is in place	Yes	No	NA
Ensure product being tracked by Medicines Finance team and Contracts for Trust reimbursement in place	Yes Yes		No No
SOPs for Ordering, receipt (including product integrity, temperature compliance during transit, product labelling, review of certificate of analysis if applicable), storage, preparation, handling, PPE and record keeping	Yes		No
SOP Management of Storage/Temperature deviations	Yes		No
SOP Cleaning, spillage, waste disposal and destruction	Yes		No
SOP Cancellation of patient and/order	Yes		No
Pharmacy SOP in place for cancellation of order	Yes		No
Pharmacy SOP in place for credit claims	Yes		No
Staff Training and competence agreed	Yes		No
Preparation Facilities: • Within Pharmacy • External to Pharmacy • Freezer storage • Transport • Aseptic facilities risk assessment • Personal Protective Clothing	 Yes Yes Yes Yes Yes Yes		 No No No No No No
Product Administration: • Approved prescription • Administration Guideline including adverse reaction guide, patient monitoring, supportive drugs/concomitant medication, if required	Yes Yes		No No

Shedding management/ containment: • Patient information • PPE • Interactions with other patients/staff/visitors • Advise to family/carers	Yes Yes Yes Yes	No No No No	
Discharge Procedure: • Patient information • Discharge letter	Yes Yes	No No	
GMSC approval received and class communicated to governance groups as appropriate?	Yes	No	
Pharmacist Final Check	***Print Name***	***Signature***	***Date***
Lead Clinician Final Check	***Print Name***	***Signature***	***Date***

Appendix 4

Somatic Cell Therapy Medicinal Products (SCTMP) and Tissue Engineered Product (TEP) Medicines Management Checklist

Product Name			
Type of ATMP (SCTMP or TEP)			
Supplier			
Manufacturer (if different to above)			
Regulatory status	Licensed / Unlicensed / Clinical Trial (Record EudraCT number if applicable)		
Checking step			
Treatment centre selected by NHSE to deliver this treatment	Yes	No	
Treatment centre audited and approved by JACIE* (or other as appropriate) to deliver SCTMP	Yes	No	NA
Treatment centre qualified by manufacturer to deliver product	Yes	No	NA
Governance approvals in place for use of product including risk assessment and action: -Specialty Governance committee - DTC including formulary review - Clinical trial approval - HTA licence appropriate for starting material and export, if applicable - Divisional Director	Yes Yes Yes Yes Yes	No No No No No	NA NA NA NA NA
SmPC/PIL/Protocol available	Yes	No	NA
Prescription added to electronic prescribing system (ePMA, Chemocare)	Yes	No	NA
Product added to Pharmacy stock management system	Yes	No	
Product specific training identified and undertaken	Yes	No	
NPSA risk assessment considered/completed (including inclusion in Medusa guide)	Yes	No	NA
If product requires aseptic	Yes	No	NA

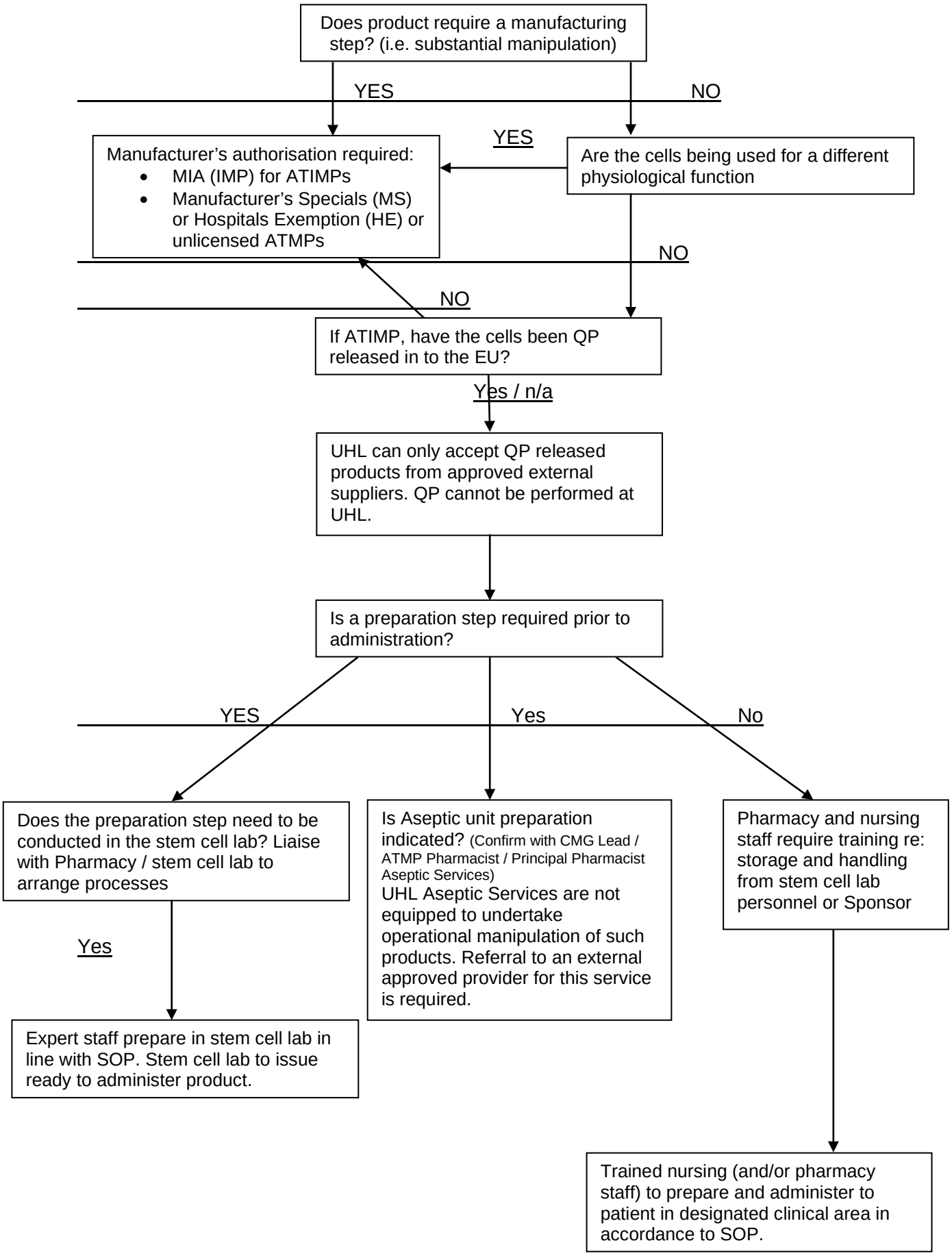
manipulation by stem cell laboratory or is outsourced out with the organisation, then a technical agreement is in place.			
If prepared by nurses: worksheet, SOPs, staff training is in place	Yes	No	NA
Ensure product being tracked by Medicines Finance team and Contracts for Trust reimbursement in place	Yes Yes	No No	
SOPs for Ordering, receipt (including product integrity, temperature compliance during transit, product labelling, review of certificate of analysis if applicable), storage, preparation, handling, PPE and record keeping	Yes	No	
SOP Management of Storage/Temperature deviations	Yes	No	
SOP Cleaning, spillage, waste disposal and destruction	Yes	No	
SOP Cancellation of patient and/order	Yes	No	
Pharmacy SOP in place for cancellation of order	Yes	No	
Pharmacy SOP in place for credit claims	Yes	No	
Staff Training and competence agreed	Yes	No	
Pharmacist Final Check	***Print Name***	***Signature***	***Date***
Lead Clinician Final Check	***Print Name***	***Signature***	***Date***
Comments			

***** JACIE Accreditation Committee of the International Society for Cellular Therapy and European Society for Blood and Marrow Transplantation (https://www.ebmt.org/)

Appendix 5: Contact Details for Key Personnel

Name	Designation	Tel:	Email:
Marie Watson	Principal Pharmacist Aseptic Services	0116 258 5462	Marie.watson@uhl-tr.nhs.uk
Rakhee Rawal	Principal Pharmacist Clinical Trials	07970940092	Rakhee.rawal@uhl-tr.nhs.uk
Nigel Brunskill	Director of Research and Innovation (chair of GMSC for ATIMPs)	0116 258 8043	Nigel.brunskill@uhl-tr.nhs.uk
Antonella Ghezzi	Lead Nurse for Research	07966730340	Antonella.ghezzi@uhl-tr.nhs.uk
Neil R Smith	Health, Safety and Local Security Specialist	07961294329 / 0116 2583392	Neil.R.Smith@uhl-tr.nhs.uk

Appendix 6: Technical and Regulatory Assessment



Appendix 7 : Example Standard Operating Procedure Template for Administration, auditing and COSHH assessment paperwork.

4

……. Administration Instructions (for the…….. study)

Caution –……..*has been classed as a biohazard level 2 for use in the Trust. This means that the product could cause human disease and may be a risk to staff (but is unlikely to spread to the community). Effective prophylaxis is available and the steps of this process should be followed to minimise risk as much as feasible.*

Location

The product needs to be administered in a side room with access restricted to the patient and the nurses who will administer the dose (during the administration process). The plan will be for all doses to be administered in one of the HOPE unit side rooms. Whilst drug is being administered a caution sign should be placed on the external side of the door to prevent interruptions (located in main study file)

Staff

As ……*is a cellular product, the drug should be administered by nurses who have been trained and signed off to administered stem cell products (usually given as part of a bone marrow transplant). In addition the administrating nurses should not be pregnant or immunocompromised in view of the biohazard risk. Any nurse involved in the study who becomes immunocompromised or pregnant should inform the lead nurse for the HOPE unit prior to being involved in any further dosing of …….*

All staff administering……should have completed trial specific training on how ……is administered PRIOR to administering first dose

Equipment

All staff in the room when ……..is administered should wear personnel protective equipment (PPE). This includes a disposable apron, gloves and disposable mask.

Method

Administer dose as per sponsor supplied / Pharmacy procedure SOP …….and /or as per sponsor supplied trial specific training.

Prior to starting dosing ensure that all axillaries are available in the room

- ……..

Stability Data:

Each dose has a ……. hour expiry once reconstituted is complete by the stem cell lab. Dose specific expiry will be listed on the trial label.

……..will be transported on wet ice and should be stored on wet ice until immediately prior to administration.

Compatibility Data

No specific requirements

Waste

All items that have been in contact with……need to be disposed of as bio-contaminated waste as per the UHL waste management policy. Mainly that waste should be disposed of in orange bags that are tied in a swan neck to seal and sent off for incineration.

Decontamination in case of spillage

In the unlikely event of a spillage staff should obtain the cytotoxic spillage kit and put on the personal protective equipment inside (gloves, googles, mask and apron).

Contain the spill by mopping up with dry towel. Once the spillage is contained rinse well with soap and water

Once area is cleared staff involved should clean their hands (and any affected areas) thoroughly with soap and water.

Any spillages should be notified to the PI……and if unreachable the lead study pharmacist……..or Clinical Pharmacist responsible……. It will be their responsibility to inform the study sponsor where applicable and seek further advice.

Reference:
UHL Pharmacy SOP 635 – Health and Hygiene in the aseptic unit version 5. Written Feb 2019
UHL Waste Management Policy, version 4, April 2016

Appendix 8 Example Standard Operating Procedure Template for Auditing

ATMP Pharmacy Monitoring Plan

Study Title (where applicable):

EudraCT No: Sponsor:

EDGE No:

Principal Investigator:
Research Nurse:

Introduction

The……study involves the ATIMP……. which as a medicine is the responsibility of pharmacy to ensure correct handling whilst on site.

For this study a risk assessment has been carried out which clarified that the Stem Cell Lab is the most appropriate location for ……to be stored, processed and dispensed from due to their extensive experience with other stem cell products.

To ensure pharmacy oversight of the product outside of pharmacy the clinical trial (CT) pharmacy staff will visit on pre-planned dates to ensure that the stem cell lab processed meet usual pharmacy standards. The plan is for a pharmacist will check each dose prior to release and conduct quarterly monitoring visits. See appendix 1 for the Pharmacy Monitoring form for each visit and appendix 2 for the quarterly Pharmacy monitoring checklist

The plan is at each monitoring visit to ensure any previous actions have been followed up and to review all results from either the date of last monitoring visit or the time of first drug delivery (whichever is sooner)

– Pharmacy Monitoring form – Section 1

Date _____

Parameter to be checked	Specifics on what to check	Comments by pharmacy staff	Checked and satisfied parameters are in range
Are there any actions from previous visit left outstanding	Check most recent visit log to ensure all actions have been completed		
Check Stem cell lab monitoring records (both microbial and physical)	Ask Stem cell staff for their monitoring folder. All acceptable limits are stated in the folder next to results. Need to check air handling Pressure results AND microbial plate results		
Check temperature monitoring system	Ensure that temperature has remained within acceptable limits		
Check drug delivery documentation	Is the appropriate QP documentation filed within the trial folder. Have all deliveries been added to the accountability logs		
Check accountability logs	Do they tally with deliveries received and doses administered. For each dose administered is there a prescription filed and the correct label for retention in the folder		
Check Worksheets for any doses thawed	For all thawed doses has the appropriate preparation worksheet been completed and been signed off by relevant staff		
Check training log	Have all staff who have been involved in the study signed the up to date training folder		

– Pharmacy Quarterly Visit Monitoring form – Section 2

Documents

Item checked	Yes	No	N/a	Comment
Current protocol in Lab site file	☐	☐	☐	
Document Version History checked	☐	☐	☐	
Comments:				

Training Log

Item checked	Yes	No	N/a	Comment
All current lab staff on training log	☐	☐	☐	
Have signed off training paperwork from sponsor	☐	☐	☐	
Comments:				

Issuing

Item checked	Yes	No	N/a	Comment
Current Dispensing procedure present in folder	☐	☐	☐	
Proforma Worksheet present in lab folder	☐	☐	☐	
Comments:				

Accountability

Item checked	Yes	No	N/a	Comment
Accountability log complete and corresponds to QP certificates	☐	☐	☐	
Check receipt documentation matches Accountability logs	☐	☐	☐	
Comments:				

Prescriptions

Item checked	Yes	No	N/a	Comment
Check prescriptions appropriately checked	☐	☐	☐	
Check worksheets / prescriptions and accountability logs reconciled	☐	☐	☐	
Check any completed worksheets signed off appropriately	☐	☐	☐	
Comments:				

Monitoring

Item checked	Yes	No	N/a	Comment
Review Tempertaure logs for stem cell lab	☐	☐	☐	
Check microbial monitoring reports	☐	☐	☐	

Check current protocol and drug preparation SOP is present in folder	☐	☐	☐	
Comments:				

Action log

Issue	Action required	Action taken	Complete