Standard Operating Procedure

UHBW REVIEW OF CLINICAL TRIALS INVOLVING ATIMPS

SETTING Trustwide

AUDIENCE All staff who undertake or support research involving Advanced Therapy Investigational Medicinal Products (ATIMPs) at UHBW

ISSUE Research involving the use of ATIMPs must be reviewed by the UHBW ATIMP committee in addition to standard Capacity and Capability review prior to commencing at site.

QUERIES Contact Commercial Research Manager or Research Operations Manager on 0117 34 20233

Document History

SOP number	SOP 021	**SOP Version**	3.2
Effective Date	10/JAN/2024	**Review Date**	10/JAN/2026

Review date	Version number	Version date	Effective date	Author/ Reviewer	Authorised by
N/A - original	V1.0	11/APR/2018	27/JUL/2018	Jess Bisset	Diana Benton
SEP/2020	V2.0	21/SEP/2020	23/NOV/2020	Jake Harley	Diana Benton
JAN/2021	v3.0	12/JAN/2022	02/MAR/2022	Katharine Wale/Jake Harley	Diana Benton (on behalf of TRG)
FEB/2023	V3.1	21/FEB/2023	01/APR/2023	Lucy Riddolls	Nicola Manning
JAN 2024	V3.2	10/JAN/2024	10/JAN/2024	Jake Harley/Amelia Lowe	Jess Bisset

Version Number	Reason for change
Original V1.0	N/A original
V2.0	Insertion of exceptions to the process of reviewing ATIMPs at UHBW e.g., in a global pandemic. Other minor updates and clarifications as part of biennial review.
V3.0	Major update to proportionate review process and other minor updates and clarifications including to the references section.
V3.1	Departmental name change from Research & Innovation to Research & Development. Updated throughout SOP as a minor amendment.
V3.2	Minor updates as part of biennial review and clarification of process for changes to a previously approved ATIMP risk assessment.

1. Introduction

An ATMP as defined by Directive 2001/83/EC, amended by 2003/63/EC annex 1, Part I is a biological medicinal product that can be classified as one or a combination of the following:

- Gene Therapy Medicinal Product (GTMP)
- Somatic Cell Therapy Medicinal Product (CTMP)
- Tissue Engineered Product (TEP)

Research involving use of the above products require review and approval from the UHBW ATIMP committee prior to the study commencing at UHBW. This is to ensure patient safety and compliance with applicable legislation, that is, SI 2004/1031 and any amendments.

2. Purpose

The purpose of this SOP is to describe the application and review process of the UHBW ATIMP committee.

3. Scope

In Scope: All research involving the use of ATIMPs at UHBW
Out of scope: All other research which does not involve the use of ATIMPs at UHBW

4. Responsibilities

Researchers wishing to undertake research at UHBW involving ATIMPs are responsible for ensuring that approval is sought from the UHBW ATIMP committee prior to commencement of the research by completing the risk assessment form (TMPL_087) and submitting it to Research and Development (R&D) as instructed (as well as all other applicable approvals e.g., Capacity and Capability review see SOP_017 Confirmation of Capacity and Capability to Deliver Research at UHBW)

UHBW ATIMP committee are responsible for providing a detailed review of the ATIMP application in compliance with the committee's terms of reference.

R&D staff are responsible for providing advice to researchers on the process. On receipt of a completed risk assessment form R&D staff will submit this and all relevant supporting documents to the committee, facilitating any discussions with committee members as required and on receipt of the approval from the committee sharing that with the applicable researchers and updating the research management database.

5. Abbreviations and Definitions

Abbreviations	
ATIMP	Advanced Therapy Investigational Medicinal Product
C&C	Capacity & Capability
GTAC	Gene Therapy Advisory Committee
GM	Genetically Modified
HRA	Health Research Authority
HTA	Human Tissue Act
IMP	Investigational Medicinal Product
PI	Principal Investigator
R & D	Research and Development
RMF	Research Management Facilitator
UHBW	University Hospitals Bristol and Weston NHS Foundation Trust

Definitions	
ATIMP	An ATMP as defined in Article 2(1) of Regulation 1394/2007 which is tested or used in a clinical trial (in accordance with Article 2(d) of Directive 2001/20/EC). If any researchers are unclear whether their trial involves an ATIMP they must contact the R&D department as soon as possible on 0117 342 9873
Gene Therapy Medicinal Product	Biological medicinal product with 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.
Somatic Cell Therapy Medicinal Product	Somatic cell therapy medicinal products involve: a) substantial manipulation of cells or tissues not intended to be used for the same essential function(s); b) administration to human beings with a view to treating, preventing or diagnosing a disease through the pharmacological, immunological or metabolic action.
Tissue Engineered Product	Tissue engineered products involve: a) engineered cells or tissues. b) administration to human beings with a view to regenerating, repairing or replacing a human tissue.

6. Procedure

On receipt of a protocol confirming that the intended research will involve the use of ATIMP(s) the Principal Investigator identified at UHBW in conjunction with members of the local research team should complete the applicable sections of TMPL_087 ATIMP Risk Assessment Form (henceforth referred to as the 'application'). Once completed they should submit the application with the Protocol and any other supporting documents (R&D can advise on what is required, but as a minimum; the Protocol, Investigator Brochure and IRAS form) to ResearchApprovals@uhbw.nhs.uk

If it is a commercial trial the application should be sent to the Commercial Research Projects Manager and relevant Research Management Facilitator (RMF).

If it is a non-commercial trial the application should be sent to the Research Operations Manager and one of the relevant RMFs who will be allocated the trial.

Depending on the type of ATIMP and potential risk, the trial should then be submitted for either proportionate or full review by UHBW ATIMP committee.

a. Proportionate review

Proportionate review will be applied to research which meet the following criteria:

(i) Involves an ATIMP which does not fall under the GM regulations (e.g., somatic cell therapy)

(ii) The level of perceived risk is low (e.g., ATIMP is stored and administered at another site)

(iii) The ATIMP committee have previously reviewed and approved a trial using the same ATIMP where all processes and handling of the product are the same

On receipt of the application and supporting documents the RMF allocated to the study should submit the application to the Director of Research who is Chair of the ATIMP committee, for consideration.

Where a new trial meets criterion (iii) above, and all processes and handling of an ATIMP have been previously reviewed by the committee, a new ATIMP Risk Assessment Form may not be required to be completed, upon agreement from the Director of Research. In this instance a copy of the approved ATIMP Risk Assessment Form for the previous trial will be provided for information.

The Director of Research should review the paperwork and in consultation with Senior Managers within R&D and members of the ATIMP Committee (as required) should agree whether it can go through proportionate review. If it is accepted for proportionate review the Director should primarily conduct the review with consultation with members of the ATIMP committee as required. If approved the authorisation section on the application should be completed electronically and the authorised form sent back to the allocated RMF who in turn should send this to the PI and applicable research team. If a new ATIMP Risk Assessment Form has not been completed, written agreement will be obtained via email from the Director of Research.

The RMF should then continue to liaise with the PI and research team in line with SOP_017 Capacity and Capability review at UHBW to ensure C&C is provided.

b. Full review by the UHBW ATIMP committee

For research not meeting any of the criteria set out in section 6a above, a full review by the UHBW ATIMP committee is required.

On receipt of the application and supporting documents the RMF allocated to the study should submit the application to the members of the UHBW ATIMP committee for consideration via email. A list of the applicable members can be found in GD_019 which is held in the electronic shared drive of the R&D department (commonly referred to as J drive).

Each committee member should review the application and add comments to the relevant section of the submitted form. Any queries raised by the committee should be returned to the RMF assigned to the study to discuss and obtain a response from the PI and applicable research staff. Once each committee member's comments have been addressed, they should complete the relevant authorisation section on the application and return to the RMF. Authorisations will be collected electronically. Whilst there is no deadline for reviews, it is expected that each committee member should undertake the review in a timely manner with the individual trial timelines in mind.

In some instances, a meeting may be required of the core members of the ATIMP committee to discuss the application. This meeting should be convened in line with the committee's Terms of Reference. Following this meeting any actions should be followed up by the RMF and the PI.

Once all sections have been authorised the application and associated study documents should be submitted by the RMF to the UHBW ATIMP committee Chair for review and final sign-off before being returned to the RMF, who in turn should send this to the PI and applicable research team.

The RMF should then continue to liaise with the PI and research team in line with SOP_017 Capacity and Capability review at UHBW to ensure C&C is provided.

c. Changes to a previously approved ATIMP Risk Assessment

Any changes to the ATIMP processes outlined in the initial approved application should be notified in writing to the R&D team by contacting the relevant RMF. The RMF will send the summary of the change(s) to the ATIMP committee Chair, who will confirm whether an updated application is required.

Exceptions

In some instances, it may not be feasible to follow the processes described above e.g. if an expedited review is required due to an urgent public health need, such as during the COVID19 pandemic. The Chair of the Committee will discuss and agree the most appropriate proportionate approach with senior management at R&D and that process will be clearly documented.

7. Dissemination and training in the SOP

This SOP will be disseminated to applicable research staff (including R&D) and will be available on the R&D website.

Plan Elements	Plan Details

The Dissemination Lead is:	Research Operations Manager
Is this document: A – replacing the same titled, expired SOP, B – replacing an alternative SOP, C – a new SOP:	A- Replacing the same titled, expired SOP
If answer above is B: Alternative documentation this SOP will replace (if applicable):	N/A
This document is to be disseminated to:	All applicable research staff (including R&D)
Method of dissemination:	For major updates to the SOP dissemination will be: 1. To Chief Investigators of UHBW Sponsored CTIMPs 2. Research Unit leads across UHBW 3. Head of Research Governance at UoB (where SOP is applicable) All updates (major and minor to the SOP) will be: 1. Updated on the trust Document Management System 2. Updated on the R&D website 3. Cascaded in the R&D e-bulletin
Is Training required:	All staff whose activities are subject to this SOP should ensure that they read and understand the content of the SOP. The personal training log of the individual (and the Investigator Site File/Trial Master File if required) should be completed to document that the content of this SOP has been read and understood as described in *SOP_007 Research Training UHBW*

REFERENCES	Directive 2001/83/EC, amended by 2003/63/EC annex 1, Part I https://eur-lex.europa.eu/legal-content/en/ALL/?uri=CELEX%3A32003L0063 Directive 2001/20/EC https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2001_20/dir_2001_20_en.pdf Regulation 1394/2007 https://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:324:0121:0137:en:PDF Statutory Instrument 1031: The Medicines for Human Use (Clinical Trials) Regulations 2004 http://www.legislation.gov.uk/uksi/2004/1031/pdfs/uksi_20041031_en.pdf The Medicines for Human Use (Clinical Trials) (Amendment) (EU Exit) Regulations 2019

	https://www.legislation.gov.uk/uksi/2019/744/contents/made?view=plain
RELATED DOCUMENTS AND PAGES	• SOP_017 Capacity and Capability review at UHBW • GD_018 ATIMP Committee members • TMPL_087 ATIMP Risk Assessment Form • UHBW ATIMP Committee Terms of Reference Latest versions of SOPs, guidance documents and templates can be found on the Research & Development Department section of UHBW's website: http://www.uhbristol.nhs.uk/research-innovation/for-researchers/templates-and-sops/
AUTHORISING BODY	Trust Research Group
SAFETY	N/A
QUERIES AND CONTACT	Research & Development (R&D) department 0117 34 20233 or research@uhbw.nhs.uk
AUDIT REQUIREMENTS	R&D departmental Quality Management System audits are undertaken annually.