Standard Operating Procedure			**17.013**
Study site coordination and delivery of an ATIMP study			
Version	**1.0**		
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1. SOP Category

NHS GG&C Clinical Research Facility – Clinical

2. Staff Category

GCRF Clinical
Principal Investigators

3. Scope

This procedure applies to all GCRF clinical staff and Principal Investigators.

4. Purpose

The purpose of this Standard Operating Procedure (SOP) is to describe the role and procedures the GCRF clinical team have in the coordination and delivery of Advanced Therapy Investigational Medicinal Product (ATIMP) clinical trials in NHS Greater Glasgow & Clyde (NHS GGC).

An advanced therapy medicinal product is either (or combination of):

- A gene therapy medicinal product
- A somatic cell therapy medicinal product
- A tissue engineered product

5. Procedures

5.1 GMO Safety Committee Approval

In NHS GGC, all Clinical Trial ATIMPs involving administration of substances based upon genetically modified organisms are required to be reviewed by the NHSGGC Genetically Modified Organism (GMO) Safety Committee, even if the IMP is delivered in a site outside NHS GGC. The GMO Safety Committee will review risks associated with movement of the GMO (inter-hospital, inter-department), patient pathway, waste product handling, and describe any specific environmental conditions the study team need to meet over and above CTIMP/experimental medicine trial delivery. Cellular therapies do not all fall under this classification, but some may – Clinical Trials Pharmacist will advise if required. The nominated GCRF health and safety representative for the ATIMP should be included on the trial delegation log.

5.2 Trial Sponsor Training and Trial–specific Documentation

The Trial Sponsor will provide trial-specific documentation (SOPs, Lab Manuals) training and guidance on ATIMP delivery from any tissue acquisitions required through to manufacture and receipt of products onsite prior to and during administration; associated clinical tests and safety procedures; sample handling and waste management. GCRF clinical team are required to ensure they can comply with all Trial Sponsor requirements in advance of the trial being opened in GCRF.

The GMO Safety Committee Risk Assessment will detail any restrictions to personnel involved such as immunosuppressive conditions, pregnancy etc. All staff involved in the delivery of the ATIMP and their role will be listed on the Risk Assessment Form.

5.3 ATIMP receipt and administration

The NHS GGC Site Clinical Trial Pharmacy team & NHS GGC Haematopoietic Stem Cell Lab (HSCL) team will be responsible for the receipt, storage and specialist handling of ATIMPs, depending on type. Some GMO products will be stored in pharmacy; all cellular therapies will be stored in HSCL. Only staff with training specific to the product will handle the ATIMP.

All ATIMPs are likely to require to be transported to GCRF or Bone Marrow Transplant Unit at QEUH – either from Pharmacy at Beatson West of Scotland Cancer Centre (where Gene Therapy Isolator is located for assembly of the product) or NHS GGC HSCL at Gartnavel General Hospital. The time of this transfer prior to administration must be considered when planning patient visits.

Cellular-based therapies will be administered to patients in the Cellular Therapy Unit within the Bone Marrow Transplant Unit at the QEUH. Communication pathways with the Cellular Therapy Unit and, where applicable other units responsible for acquisition of tissues to manufacture ATIMPS are essential to establish at study set-up, e.g. Apheresis unit, surgical units. Cellular-based therapies such as CAR T Cells can trigger severe pathological responses such as Cytokine Release Syndrome (CRS), Haemophagocytic Lymphohistiocytosis (HLH) or Macrophage Activation Syndrome (MAS). The Cellular Therapy Unit within the Bone Marrow Transplant Unit is JACIE accredited and the patient pathway will follow the related BMT Unit Quality System SOPs, including ensuring stock of tocilizumab is available, ICU transfer and communication pathways.

Some gene therapy medicinal products may be administered within GCRF, as long as the requirements of the GMO Regulations and GMO Safety Committee review of the Risk Assessment are met. Communication paths and coordination with relevant service teams are the responsibility of the GCRF staff. For early phase ATIMPs follow SOP 57.014.

The GMO Safety Committee Risk Assessment will specify requirements for administration such as appropriate Personal Protective Equipment (PPE), exposure reduction measures such as single room and a sign on the door (Do Not Enter Biohazard) to restrict access.

When a patient has received a gene therapy medicinal product, GCRF staff are responsible for ensuring a 'clinical alert' is put on Clinical Portal which includes study reference, title, type pf product, date of administration and PI contact details (FORM 17.013A).

All biological samples to be sent from the site to an external site (e.g. central laboratory) must be packed in accordance with IATA group B transport requirements. Packing instructions will be available in the Trial Sponsor lab manual.

For samples transported to internal labs, the GMO Safety Committee Risk Assessment will describe any specific precautions (such as any additional packaging or labeling).

5.4 Spillage, cleaning and decontamination

Accidental exposure to GMOs can occur via inoculation, inhalation, ingestion and splashes. GMO Regulations require that any accidents, including accidental spillages, involving a GMO product be reported to the Health and Safety Executive (HSE). A DATIX report must be completed and the Principal Investigator informed, who will inform the GMO Safety Committee. Possible adverse events and any pre or post exposure prophylaxis required will be detailed in the GMO Safety Committee Risk Assessment.

Any spillage of the GMO or body fluids must be dealt with following the GMO Safety Committee Risk Assessment instructions. All staff at risk of exposure must be trained to manage biohazard spillage prior to the study visit for drug administration. A spill kit should be prepared prior to gene therapy medicinal product administration

Patients can use hospital crockery and cutlery (unless prohibited by the specific study protocol or GMO Safety Committee Risk Assessment) and can be washed in the dishwasher using a standard cycle along with other crockery and cutlery.

Linen and equipment will be treated as per normal practice, unless the GMO Safety Committee Risk Assessment stipulates decontamination is required (autoclaving or other deactivation). Special waste uplift may be required.

5.5 Safety reporting and follow-up

Patient safety reporting to the Trial Sponsor is the responsibility of the Principal Investigator (PI) and delegated site study team. The PI should ensure that site team are up to date with guidance from the Sponsor in relation to new events related to the conduct of the trial or the development of the ATIMP and likely to affect the safety of the subjects should be reported according to the existing timelines for expedited reporting. The protocol will provide guidance for the duration and nature of follow up which should be determined by a risk assessment of the current knowledge of the ATIMP, its mode of action and the risk to close contacts. After administration of some GMO products patients may require isolation within GCRF for a specified period, for example.

5.6 Documentation

ATIMP clinical trial documentation is required to be retained for a minimum of 30 years from the expiry of the product, specifically all records related to the traceability of the product. Traceability procedures (from sourcing, manufacturing, packaging, storing, transport, delivery to the hospital, administration, reconciliation and destruction) should be described in the protocol and where relevant in trial-specific SOPs.

Where patients receive the ATIMP in a hospital outside NHS GGC (dosing site), consideration should be given to best practice for documentation: full and complete referral letters including description of ATIMP delivery. Form 17.013B should be used to identify method and timescale for inter-site communication required from the primary site to the dosing site, and post-dosing from the dosing site to the primary site. The clinical alert should be placed on clinical portal (Form 17.013A) when the patient has been dosed.

6. Referenced documents

SOP 57.014 GCRF Support of Early Phase Clinical Trials
FORM 17.013A Clinical Alert for TrakCare GM ATIMP
FORM 17.013B Intersite communication form for ATIMP
GMO Safety Committee Risk Assessment Form
The Genetically Modified Organisms (Contained Use) Regulations 2014
The SACGM Compendium of guidance, Part 6 Guidance on the use of genetically modified microorganisms in a clinical setting.
http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/part6.pdf

7. Related documents

Bone Marrow Transplant Unit Quality System

8. Document History

Version	Date	Description
1.0	20/12/19	SOP creation