STANDARD OPERATING PROCEDURE

Handling of Material Containing Genetically Modified Organisms (Class 1 and 2)

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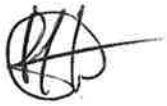
SIGNATURE 	SIGNATURE 	**REVIEW DATE** 30-OCT-2025	

RESEARCH AND DEVELOPMENT

LCRF

BACKGROUND

A genetically modified organism (GMO) is any organism in which the genetic material has been altered in a way that does not occur naturally. This includes, for example, viruses or bacteria that have been genetically modified to be used in a medicinal product such as a vaccine or gene therapy.

The handling and disposal of GMOs, including GMO-containing medicinal products, is covered by specific legislation in the UK, depending on whether the GMO will be contained in laboratories and/or clinical areas or deliberately released into the environment.

- Contained Use: this is where human and environmental exposure to the GMO is kept under control by the use of appropriate containment measures, and will include most clinical research studies. Such activities are covered by the Genetically Modified Organisms (Contained Use) Regulations, and are regulated by the Health and Safety Executive (HSE).

- Deliberate Release: if the GMO will be deliberately released into the environment, the Genetically Modified Organisms (Deliberate Release) (Scotland) Regulations may apply.

Under the Contained Use Regulations, the control measures that must be in place are determined by the risks to human health and the environment. On this basis, GMOs are classified into one of four activity classes: class 1 (no or negligible risk), class 2 (low risk), class 3 (moderate risk) and class 4 (high risk).

This standard operating procedure specifically refers to GMOs in the lowest risk categories (class 1 and 2) which will cover the vast majority of GMO products used in clinical research studies.

Before any GMO study commences, a risk assessment must be completed which takes into consideration risks to the participants, the research team, any other members of staff or the public who may be exposed, and the environment. The risk assessment must be reviewed and approved by the GMO committee. A suitable notification to the Health and Safety Executive (contained use or deliberated released) must be in place before commencing a GMO clinical trial.

PURPOSE/OBJECTIVE

This SOP provides guidance on the safe handling, transport and disposal of material containing GMOs (class 1 and 2) used in research studies conducted in the NIHR Lancashire Clinical Research Facility (LCRF).

SCOPE

This applies to all research studies conducted in the LCRF in which a class 1 or 2 GMO is used, and where no guidance has been provided by the sponsor or such guidance is deemed inappropriate, insufficient or not suitable at site level. This SOP does not cover activities related to receipt, storage, preparation or administration of GM products, as these aspects are routinely described in study-specific documentation.

This SOP is applicable to any LCRF or research staff, including the Principal Investigator (PI), pharmacy clinical trials team or external staff, involved in the handling of a GMO as part of a research study.

PROCEDURE

1. WHO?

1.1 It is the responsibility of all staff handling GMO materials to familiarise themselves with this SOP and study specific procedures relating to the safe handling of the material, and to ensure that they have completed and documented any relevant study specific training prior to undertaking the activity.

1.2 It is the responsibility of the PI to ensure that risks associated with the GMO and related control measures have been identified in the study/site specific GM risk assessment, and that this has been reviewed and approved by the GMO Committee prior to the commencement of the study activities in the LCRF.

1.3 It is the responsibility of the PI to ensure staff members have received appropriate training prior to delegating those staff members' tasks that involve handling GMO materials.

1.4 It is the responsibility of the LCRF Manager and the Lead Research Nurse to identify any processes, facilities, materials and documentation required to support the GMO control measures described in this SOP, the GM risk assessment and any relevant study specific procedures, and to ensure that these are in place prior to the start of the study in the LCRF.

2. WHEN?

2.1 This SOP must be followed when handling, transporting and disposing of GM materials in the LCRF and other departments within Lancashire Teaching Hospitals involved in the GMO clinical trial.

3. HOW?

3.1 Staff and Facilities

3.1.1 Before beginning work with a GMO, suitable facilities, materials and controls must be in place on site to provide protection to both staff and the environment. Any specific controls required in addition to this SOP will be indicated in the GM risk assessment.

3.1.2 All staff involved in handling the GMO must have received appropriate training and been made aware of the risks, prior to undertaking the activity.

3.1.3 All staff involved in working with a GMO should be made aware of the nature of the work being carried out and associate dangers.

3.2 Personal Protective Equipment (PPE)

3.2.1 When handling class 1 or 2 GMOs, appropriate personal protective equipment (PPE) must be worn to minimize the risk of exposure.

3.2.2 The minimum PPE requirement for handling a class 1 and 2 GMO is nitrile gloves, an apron, mask and suitable eye protection. Additional PPE requirements may be indicated in the GM risk assessment.

3.2.3 All PPE must be:

- Compliant with the relevant CE mark in accordance with the Personal Protective Equipment (Enforcement) Regulations 2018.
- Stored to prevent contamination in a clean area and close to the point of use.
- Within the expiry date

- Single-use only and changed immediately after each patient and/or procedure.
- Disposed of after use in the correct waste stream (please see section 3.9)

3.3 Handling and Preparation of the GMO – Pharmacy

3.3.1 Pharmacy staff involved in the handling and preparation of GMO products must have received appropriate training prior to undertaking any activities.

3.3.2 Appropriate PPE must be worn when handling or preparing GMO products. This must be proportionate to the risk associated with the class of GMO being handled/prepared.

3.3.3 Equipment and facilities used must be appropriate for the class of GMO being handled. Assessment of operator risk, GMO classification, and safety data from the study sponsor, will inform the assessment, and the equipment needed. This may include but is not limited to; dedicated class I or class II isolators/biological safety cabinets, negative pressure isolators, positive pressure containment/cascade suites. Further details on equipment are referenced within the "Genetic Modification Code of Practice (Code of Practice for Gene Therapy Clinical Trials Categorised at Levels 1 and 2)" Policy.

3.3.4 All waste created during the preparation must be disposed of as per the Disposal of Waste Management section 3.9 below.

3.3.5 All surfaces used to prepare the GMO IMP must be cleaned as detailed in section 3.8.3 below.

3.4 Storage and Transportation of GMO Materials

3.4.1 **GMOs which are also medicinal products to be used in clinical trials are referred to as Gene Therapy Medicinal Products (GTMPs)**. GTMPs must be stored with the clinical trials section of the in-patient pharmacy department within Lancashire Teaching Hospitals NHS Foundation Trust (LTHTr). Trained pharmacy staff are responsible for the receipt of the product and have appropriate oversight of the storage.

3.4.2 The GTMP must be stored according to the specific requirements in the pharmacy manual or other study-specific documentation and local risk assessment. The storage must be temperature monitored, alarmed and access restricted.

3.4.3 Staff involved in transporting the GTMP from pharmacy to the LCRF must have received appropriate training and be aware of what they are transporting and what to do if there is a spillage.

3.4.4 GTMPs must be packaged safely and transported using a suitable robust, sealed container, clearly labelled as containing a biohazard material. Appropriate temperature monitoring controls and monitoring must be in place if required. For specific packing and temperature control requirement please refer to the study documentation supplied by the trial Sponsor and the GMO risk assessment.

3.4.5 Timelines for handling the GTMP i.e. time removed from storage/thawing until administration, must be documented.

3.4.6 The route of transfer should be carefully considered to minimise the risk of potential exposure of staff, patients, visitors and the environment to the GMO and should avoid outside areas and patient areas where possible. The most appropriate route from pharmacy to the LCRF would be along the main corridors. These can be very crowded at times therefore careful consideration must be given as to the timing when the IMP is to be transported (i.e. it would be good practice to avoid break times (lunch and dinner)).

3.4.7 An appropriate spill kit must accompany the GTMP during transport which must include PPE. Details to manage a spillage are referred to below.

3.4.8 After use, the GTMP transport container must be cleaned using a suitable disinfectant before being returned to pharmacy. Details on cleaning are in the relevant section below.

3.5 Preparation of the Investigational Medicinal Product (IMP) in the LCRF

3.5.1 All LTHTr/OCS waste containers and sharps bins must be removed from the preparation and administration room prior to handling and administering the GMO IMP.

3.5.2 All GMO products must be prepared as per the Sponsor requirements usually specified in the Pharmacy Manual.

3.5.3 Only trained individuals must be delegated to prepare the GMO prior to administration.

3.5.4 All GMO Investigational Medicinal Products must be prepared in a location specified within the trial GMO risk assessment.

3.5.5 Personal Protective Equipment (PPE) must be worn when preparing the IMP and Aseptic Non-Touch Technique (ANTT®) must be used when appropriate following the LTHTr ANTT procedure.

3.5.6 In the event of a spillage of several vials of GMO the same procedure for managing a spillage below must be followed unless specified by the Sponsor.

3.5.7 All waste created during the preparation must be disposed of as per the Disposal of Waste Management section 3.9 below.

3.5.8 Unless specified by the Sponsor, GMO IMP must be prepared in the clinical room whether the participant will be dosed. Any specific precautions required by the Sponsor must be documented in a study specific procedure or guidance document.

3.5.9 All surfaces used to prepare the GMO IMP must be cleaned as detailed in section 3.8.3 below.

3.6 Spillage of a GMO Material – pharmacy, clinic or in transport

3.6.1 In the event of a spillage of several vials of GMO the same procedure for managing a spillage below must be followed unless specified by the Sponsor.

3.6.2 All waste used to manage a spillage must be double bagged in yellow clinical waste bags and tied. This must be transferred to the LCRF by a trained individual and placed in the GMO secure waste container located in the dirty utility. Under no circumstances must any GMO waste be mixed with LTHTr waste.

3.6.3 Any spillage involving any GMO material must be cleaned in a manner which minimises exposure to the staff member, other people and the environment, and is compliant with Trust policies on infection control and waste management.

3.6.4 Staff members involved in the receipt, handling, storage, transport, preparation, administration and disposal of a GMO material must be appropriately trained and aware of the procedures to follow in the event of a spillage in order to protect themselves, others and the environment.

3.6.5 A suitable spillage kit must be available at all times where GMO materials are being handled. Spill kits must be located in all areas where there is a risk of spillage, including at the site of receipt, storage, preparation and administration, and must be available during transport of the GMO.

3.6.6 Spill kits must contain as a minimum:

- Spray dispenser containing Virkon 1%. Virkon will be prepared in pathology and dispensed in a 500ml spray container. This must be collected from pathology on the day pathology prepare the Virkon and stored safely for 7 days. After 7 days the Virkon must be disposed of down the sluice (pharmacy and LCRF).
- Disposable nitrile gloves x 2
- FFP3 disposable mask
- Disposable apron / gown
- Eye protection / face visor
- Paper towels or an alternative absorbent material
- Clinical waste bag and tie
- Instructions for use of the kit

3.6.7 Spillages must be cleaned by following the process below:

Pregnant staff or those with a compromised immune system must leave the room or area of spillage and not be involved in cleaning any GMO spill.

- Put on PPE (face mask, apron, nitrile gloves, eye protection).
- Clear up the spillage with paper towels and dispose of in an appropriate clinical waste bag.
- Thoroughly clean the area with in date Virkon 1% followed by washing with water.

Dispose of all PPE used and cleaning materials in the same clinical waste bag, and ensure double bag before disposal into the correct waste stream, and secure using a cable tie. Please refer to the relevant section below for waste disposal.

3.7 Cleaning

3.7.1 Surfaces and non-disposable equipment used during the GMO handling activities must be cleaned after each patient use.

3.7.2 Staff must wear PPE to clean any surfaces or equipment that has been used in GMO handling activities.

3.7.3 The research team must ensure all windows are open to ventilate the room prior to cleaning. Firstly, clean the surfaces using hot water and neutral detergent, then wiped with a solution of Virkon 1%.

3.7.4 The room must be kept ventilated for a maximum of two hours after cleaning with Virkon.

3.7.5 Once the equipment and surfaces are cleaned the room must be deep cleaned. Cleaning services to the LCRF are provided by OCS therefore a request for a deep clean must be ordered via the OCS helpdesk. The room must not be used until the room has been sufficiently cleaned. To ensure the room is not accessed until appropriate cleaning has taken place, a suitable poster/signage will be displayed outside the room.

3.7.6 Cleaning materials must be disposed of into appropriate clinical waste bags, for disposal into the correct waste stream. Please refer to the relevant section of waste disposal below.

3.8 Disposal of GMO Waste

3.8.1 GMO contaminated waste includes the product container (vials), equipment used to prepare and administer the product (e.g. syringes, needles, giving sets), PPE worn during the GMO handling activities, materials used for cleaning up spills or general cleaning and disposable food/drink containers handled by the participant.

For some studies, used product containers e.g. vials, may need to be kept and returned to the Sponsor for drug accountability purposes. In this case a study specific procedure must be agreed with pharmacy.

3.8.2 All GMO waste must be placed immediately in a suitable container:

- Sharps, such as needles, used vials and syringes must be placed in an appropriate sharps bin (supplied by Stericycle). These must be sealed and labelled correctly.

- Other waste such a swabs, PPE, food/drink containers and cleaning materials must be disposed of immediately in an appropriate clinical waste bag (supplied by Stericycle), labelled as per the requirements of the vendor and secure tied using a cable tie. The number of the cable tie must be documented before disposal.

3.8.3 All GMO material waste (sharps bin or clinical waste bags) must be stored the locked, secure unit located in the LCRF dirty utility room until it is collected by the vendor, Stericyle. This unit should be clearly labelled and access must be restricted to trained individuals from the LCRF and pharmacy teams.

4. Health Surveillance

In line with LTHTr procedure, all staff handling Virkon must undertake a health surveillance questionnaire. This questionnaire will be sent to the Health and Safety Manager and a copy kept on the LCRF T drive.

5. Related Documents & References

Management of Biological Spillages including Disinfection of Equipment.
LTHTr Procedure for the Control of Substances Hazardous to Health
LTHTr Aseptic Non-Touch Technique (ANTT®) Procedure,
Genetic Modification Code of Practice (code of Practice for Gene Therapy Clinical Trials Categorised at Levels 1 & 2)

4. OTHER RELATED PROCEDURES;

LTHTr Health Surveillance Questionnaire

CONSULTATION WITH STAFF AND PATIENTS

Name	Role
Jean Kilroy	Pharmacy Clinical Trials Lead
Dr Robert Shorten	BSO Consultant Immunologist
Professor Anthony Rowbottom	GMO Committee Chair, Deputy Director R&I, Consultant Clinical Scientist
Maureen Cowburn	Health and Safety Manager
GMO Committee	Ratification
Vaccitech BSO	Advisory
Jacqueline Bramley	Clinical Operations Manager / LCRF Lead
Rebecca Wilby	Quality Assurance Lead / Research Access Project Manager

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