SOP number	**52.013**	Version	**2.0**
Title	**Process for approving studies and trials involving a Genetically Modified Organism (GMO)**		

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SOP category	NHS GG&C Hosted R&I
Staff category	

Staff Category	**R**	**A**	**C**	**I**
Research Governance Manager		X		
R&I Sponsor Co-Ordinators	X			
R&I Commercial Co-Ordinators	X			
Research Facilitator	X			
Genetic Modification Safety Committee (GMS committee) Members	X			
Principal Investigator (PI) – Involved in GMO trial	X			
Lead Pharmacist Clinical Trials			X	
Portfolio Team - Pharmacists			X	
GCRF Clinical Research Manager			X	
Beatson CRF Head of Trial Coordination			X	
Clinical Trials Monitor				X
R&I Quality Assurance Manager				X
Quality Co-Ordinator				X
QA Leads				X

1. Scope

This procedure applies to:

- R&I Co-ordinators/Research Facilitators when receiving notification of new trials.
- Local principal investigator submitting a risk assessment form.
- The GMS committee reviewing and approving research involving a Genetically Modified Organism (GMO).
- Research audit checking that safety requirements have been implemented by the local site research team.

2. Purpose

This procedure covers legislation, the local process and the remit of the GMS committee for research that is identified as involving a GMO. This SOP covers hosted research within NHS Greater Glasgow and Clyde Board. If the trial is also identified as First in Human at an NHSGGC site the GMO paperwork will be required and the committee will provide the Phase I committee with the review for information.

3. Procedures

The Scientific Advisory Committee on Genetic Modification (Contained Use) SACGM(CU) has prepared a compendium of guidance on how to classify GMOs and how to comply with the Regulations. Part 6, 'Guidance on the use of genetically modified organisms in a clinical setting.' is of particular relevance.

3.1. Identifying which Regulations Apply

Research that involves a GMO comes under two types of legislation, as detailed below. It is the responsibility of the Principal Investigator to identify which regulation is applicable and inform the Co-ordinator/Research Facilitator, as detailed in Section 3.3.

3.1.1. The Genetically Modified Organisms (Contained Use) Regulations, 2014

These Regulations cover research activity involving GMOs where barriers are used to limit contact with the GMO to protect humans and the environment. The barriers used must provide a high level of safety and can be physical, chemical or biological. NHSGGC sites carrying out trials involving GMOs require notification to the HSE prior to any contained use activity taking place for the first time. GMO activity can only take place on sites that have been notified to the HSE. Further notification to the HSE is required for any activities where the GMO is defined as Class 2 or above.

3.1.2. The Genetically Modified Organisms (Deliberate Release) Regulations, 2002

These regulations define an activity involving GMOs, as a deliberate release when "An organism under a person's control is released if he deliberately causes or permits it to cease to be under his/her control or the control of any other person and to enter the environment". For example, if subjects in a clinical trial were expected to shed viable GMOs into the wider environment, the research will have to be considered as a deliberate release activity. If the trial is defined as coming under these Regulations the Sponsor and local PI require written permission from the Scottish Executive Environment and Rural Affairs Department (SEERAD) prior to submitting to the GMS committee and an advert placed by an appropriate medium (e.g. notices, local papers) indicating this work will be taking place to allow any objections to be made.

3.2. Process for R&I Co-ordinators/Research Facilitator

3.2.1. The R&I Co-ordinator/Research Facilitator will provide the PI with the appropriate risk assessment Form, based on the notification of which Regulation is applicable by the PI.

- Form 52.013A will be completed for research that comes under the Contained Use Regulations and where the GMO is prepared and /or administered within an NHSGGC hospital.
- Form 52.013B will be completed for research that comes under the Deliberate Release Regulations and where the GMO is prepared and /or administered within an NHSGGC hospital.
- When the GMO is not being prepared or administered within a hospital of NHSGGC, but the patients are being followed up within an NHSGGC hospital Form 52.013C will be completed. Examples include patients receiving the GMO in another hospital due to logistical reasons, but are being followed up within NHSGGC. This includes handling of the collection of samples of bodily fluids from these patients or samples being stored, processed and or analysed within an NHSGGC hospital after GMO administration.

3.2.2. The R&I Co-ordinator/Research Facilitator will provide the PI with a copy of this SOP 52.013 or a link to the www.glasgowctu.org website for information purposes. A read and comprehend record (Form 01.008B) will be required for the PI to confirm they have read this SOP and filed in the ISF.

3.2.3. The R&I Co-ordinator/Research Facilitator will notify the Research Governance Manager of the research and inform the local PI of the managers contact details.

Note: The Research Governance manager will notify the R&I Co-ordinator/Research Facilitator when approval by the GMS committee has been given.

3.2.4. If the PI has not already been in touch with the site Pharmacy team, the R&I Co-ordinator/Research Facilitator will notify the NHSGGC Site Clinical Trials Pharmacist to ensure Pharmacy has input to the risk assessment process and has capacity and resource to undertake the trial.

Note: NHSGGC Site Pharmacy teams must provide support to the PI in completing Forms 52.013A and 52.013B.

3.2.5. If the PI has not already been in touch with the site Glasgow CRF or Beatson CRF the R&I Co-ordinator/Research Facilitator will notify the manager of the appropriate unit to ensure the unit has capacity and resource for the GMO trial. The study will follow local CRF processes.

3.2.6. **GMS committee are required to give approval for all GMO trials hosted within NHSGGC**. If the study is sponsored or co-sponsored NHSGGC the GMS committee are required to give approval at the point the trial is being approved for hosting. GMO trials will also come under the Medicines for Human Use (Clinical Trial) Regulations, 2004 as amended. The standard processes for the R&I approval of sponsored and hosted clinical trials should also be followed.

3.2.7. The R&I Co-ordinator/Research Facilitator will only provide Board management approval following approval by the GMS committee.

3.3. Process for Principal Investigators (or Chief Investigators when appropriate)

3.3.1. The PI will provide the R&I Co-ordinator/Research Facilitator with a summary, based on information from the Sponsor, on which Regulations apply to the GMO for the trial. The PI can consult with the GMS committee or R&I Governance committee, if guidance is required.

3.3.2. Provide the local R&I Co-ordinator/Research Facilitator with R&I Details of the trial and confirm full document set has been submitted through the relevant coordinating centre. Please refer to Forms for information PI is required to submit as this is different depending on type of study (e.g. Contained use, Deliberate release)

3.3.3. Contact the NHSGGC site Pharmacy to ensure there is capacity and resource for the trial. The NHSGGC Site Pharmacy Team and R&I Lead Pharmacist Clinical Trials will help to complete the relevant GMO Form. Informing the R&I Co-ordinator/Research Facilitator if this has been completed.

3.3.4. Contact the Glasgow Clinical Research Facility (CRF) Manager or Beatson CRF Manager (cancer trials taking place in the Beatson) to ensure there is capacity and resource to support the trial. Informing the R&I Co-ordinator/Research Facilitator if this has been completed.

3.3.5. Request information from the Sponsor in regard to availability of risk assessment from the manufacturer, any other GMO product-specific safety precautions and training required for NHSGGC site staff to help complete Form 52.013A, B or C.

3.3.6. Provide reference that a favourable opinion has been provided from a Gene Therapy Advisory Committee (GTAC) NHS Research Ethics Committee and the MHRA. If this is not in place the committee may defer review. Any recommendations or conditions of approval from these organisations must be provided to the Research Governance Manager with the appropriate risk assessment form.

Note: the Sponsor will have been required to submit an environmental risk assessment to GTAC. If the Sponsor allows this should be provided to the GMS committee but if not the Sponsor should be requested to assist the local PI in completing the local risk assessment Forms.

3.3.7. Request the Sponsor provides the pharmacy manual or and specific pharmacy staff safety instructions if local Pharmacy cannot locate a copy

3.3.8. Complete the appropriate risk assessment Form 52.013A, B or C and submit to the GMS Committee via the Research Governance Manager, with any additional information as detailed. The version of the protocol used to complete Form 52.013A, B or C should also be sent to the Research Governance Manger.

3.3.9. Update Form 52.013A, B or C with actions requested by the GMS committee after review.

3.3.10. Sign the appropriate risk assessment Form and submit the final copy to the Research Governance Manager.

3.3.11. Send updates to the local GMS committee of any significant changes which may alter the risk assessment such as

- Change of premises
- SUSARS
- Urgent safety measures
- Changes or amendments which may change or add to the risks identified in Form 52.013A, B or C.

3.3.12. File all appropriate documentation relating to the Risk Assessment, correspondence with the GMS Committee as well as approvals within the appropriate section of the ISF.

3.4. Process for the Research Governance Manager and GMS Committee approving research involving a GMO Product.

3.4.1. The GMS Committee will review complete applications within a 21 working day timeframe and make comment and provide conditions, if required. Delays due to resource or leave will be communicated to the PI and R&I Co-ordinators/Research Facilitator.

3.4.2. The Committee will make a decision on whether the study can commence following local R&I approval (including REC and MHRA approvals).

3.4.3. For research that is identified as Contained Use involving GMOs the following should be checked:

- A suitable risk assessment has been provided taking into account all aspects of the planned work including handling, transport, decontamination, inactivation, disposal and waste management including contractors. The key areas to cover in the risk assessment include identification of harmful effects, characteristics of the activity, severity and likelihood of harmful effects and disposal of waste.
- Identification of GMO Hazard group which then determines the containment level and classification of activities. This should be provided by the Sponsor.
- Appendix 1 details the containment levels in two tables. This information is taken from Schedule 8 of The Genetically Modified Organisms (Contained Use) Regulations 2014 and can be referred to for additional guidance, if required. Table 1 refers to containment levels applicable to the use of micro-organisms in laboratories. Table 2 refers to containment measures applicable to contained use in premises other than laboratories. Schedule 8 of The Genetically Modified Organisms (Contained Use) Regulations 2014 details measures applicable to animal units and plant growth facilities. These should be referred to, if applicable.
- Following selection of containment and control measures appropriate to the activities proposed, the risk classification will be checked against the classification submitted by the PI.
- The Sponsor will determine the Hazard Group, containment levels and classification of activities and the GMS Committee will document whether they are considered appropriate.
- Evidence of notification to the competent authority in respect of the first use of premises if required. The notification is made to the Health and Safety Executive (HSE) and guidance can be found within Schedule 5 of the Contained Use Regulations.
    - A person responsible for contained use can submit a single notification for premises in different geographical locations (within Wales, England and Scotland). The sponsor may have notified the premises and this should be checked with the local investigator and noted on Form 52.013A.
- If premises have previously been notified to the HSE for GMO activities, the centre number must be confirmed on the public register by the GMSC. The register may require to be updated with specific wards/clinical areas added as premises under the centre number, if not already listed.
- If the research is identified as Class 2, 3 or 4 Contained Use the HSE requires to be notified of all projects. The information required to be followed for the notification can be found within Schedule 6 of the Contained Use Regulations. The local PI is required to make this notification with support from Research and Innovation.
- For research that is identified as Contained Use involving larger organisms e.g. plants notification to the HSE is only required if the GMO poses a greater risk than the unmodified parent organism. The information required for the notification can be found within Schedule 6 of the Contained Use Regulations.
- A suitable risk assessment is required but classification is not required.

3.4.4. For research that comes under the Deliberate release regulations the GMS committee should review the paperwork submitted in Form 52.013B to ensure

- The Environmental Directorate of the Scottish Government (commonly and previously referred to as SEERAD) has been notified and when appropriate the equivalent for the rest of the UK (DEFRA- department for Environment and Rural Affairs).
- There is evidence of notifying the public of the GMO
- Risks to staff and members of the public have been addressed.

3.4.5. For patients who have been administered with a GMO at a non- NHSGGC site but who are in follow up or having samples collected or analysed within NHSGGC the GMS committee should ensure that Form 52.013C has been completed and the risks to staff and the public have been addressed.

3.5. Audit of GMO trials

If the GMO trial is Sponsored or Co-Sponsored by NHSGGC it is likely to also come under the Medicines for Human Use (Clinical Trial) Regulations 2004 as amended. The trial will be monitored by NHSGGC monitors following SOP 53.004. Adherence to the local site GMO risk assessments and recommendations by the local GMS committees may be checked for compliance at the hosted sites. This may form part of the monitoring plan, if identified as a risk.

GMO trials hosted within NHSGGC may be recommended for audit following SOP 53.005 for adherence to the local GMO risk assessment and compliance with recommendations made by the GMS committee.

4. Referenced documents

- The Genetically Modified Organisms (Contained Use) Regulations 2014
- The Genetically Modified Organisms (Deliberate Release) Regulations 2002
- The Scientific Advisory Committee on Genetic Modification (Contained Use)
- The Scientific Advisory Committee on Genetic Modification (Deliberate Release)
- The Medicines for Human Use (Clinical Trial) Regulations, 2004 as amended
- Form 52.013A – GMO Contained Use Regulations
- Form 52.013B – GMP Deliberate Release
- Form 52.013C – GMP Trials
- SOP 53.004 – Monitoring Clinical Research – Site Monitoring Visit
- SOP 53.005 – GCP Audit of Research Studies and Systems Supporting Research
- Form 01.008B – Read and Comprehend Training Record Form

5. Related documents

- N/A

6. Document history

Version	Date	Description
1.0	23/12/19	First release of SOP. Released previously under process development SOP March 2018 version
2.0	28/09/2023	Change from R&D to R&I, minor updates to process. Change of timescales.

Appendix 1

The Genetically Modified Organisms (Contained Use) Regulations 2014 Schedule 8

Containment measures

Table 1 Containment measures applicable to contained use involving micro-organisms in laboratories

Containment Measures		***Containment Levels***			
		1	***2***	***3***	***4***
Facilities					
1	*Laboratory suite: isolation*[1]	*not required*	*not required*	*required*	*required*
2	*Laboratory: sealable forfumigation*	*not required*	*not required*	*required*	*required*
Equipment					
3	*Surfaces impervious to water, resistant to acids, alkalis, solvents, disinfectants and decontamination agents and easy to clean*	*required for any bench*	*required for any bench*	*required for any bench and floor*	*required for any bench, floor ceiling and walls*
4	*Entry to laboratory via airlock*[2]	*not required*	*not required*	*Required where and to extent the risk assessment shows it is required*	*required*
5	*Negative pressure relative to the pressure of the immediate surroundings*	*not required*	*not required*	*Required except for activities where transmission does not occur by the airborne route*	*required*
6	*Extract and input air from the laboratory must be HEPA filtered*	*not required*	*not required*	*HEPA filters required for extract air except for activities where transmission does not occur by the airborne route*	*HEPA filters required for input and extract air*[3]
7	*Microbiological safety cabinet/enclosure*	*not required*	*Required where and to extent the risk assessment shows it is required*	*required, and all procedures with infective materials required to be contained within a cabinet/enclosure*	*required, and all procedures with infective materials required to be contained within a cabinet/enclosure*
8	*Autoclave*	*required on site*	*required in the building*	*required in the laboratory suite*[4]	*double ended autoclave required in laboratory*

Containment Measures		***Containment Levels***			
		1	***1***	***1***	***1***
System of work					
9	*Access restricted to authorised personnel only*	*not required*	*required*	*required*	*required (via airlock key procedure)*
10	*Biohazard sign on door*	*not required*	*required*	*required*	*required*
11	*Specific measures to control aerosol dissemination*	*not required*	*required so as to minimise*	*required so as to prevent*	*required so as to prevent*
12	*Shower*	*not required*	*not required*	*Required where and to extent the risk assessment shows it is required*	*required*
13	*Protective clothing*	*Suitable protective clothing required*	*Suitable protective clothing required*	*Suitable protective clothing required; footwear required where and to extent the risk assessment shows it is required*	*Complete change of clothing and footwear required before entry and exit*
14	*Gloves*	*not required*	*Required where and to extent the risk assessment shows they are required*	*required*	*required*
15	*Efficient control of disease vectors (eg rodents and insects) which could disseminate GMMs*	*Required where and to extent the risk assessment shows it is required*	*required*	*required*	*required*
Waste					
16	*Inactivation of GMMs in effluent from hand-washing sinks and showers and similar effluents*	*not required*	*not required*	*Required where and to extent the risk assessment shows it is required*	*required*
17	*Inactivation of GMMs in contaminated material and waste*	*required by validated means where and to extent the risk assessment shows it is required*	*required by validated means*	*required by validated means, with waste inactivated within the laboratory suite*	*required by validated means, with waste inactivated within the laboratory*

Containment Measures		***Containment Levels***			
		1	***2***	*3*	*4*
Other measures					
18	*Laboratory to contain its own equipment*	*not required*	*not required*	*required, so far as is reasonably practicable*	*required*
19	*An observation window or alternative is to be present so that occupants can be seen*	*Required where and to extent the risk assessment shows it is required*	*Required where and to extent the risk assessment shows it is required*	*Required where and to extent the risk assessment shows it is required*	*required*
20	*Safe storage of GMMs*	*required where and to extent the risk assessment shows it is required*	*required*	*required*	*secure storage required*
21	*Written records of staff training*	*not required*	*Required where and to extent the risk assessment shows it is required*	*required*	*required*

1 "isolation" means, in relation to a laboratory, separation of the laboratory from other areas in the same building, or being in a separate building.

2 Entry must be through an airlock which is a chamber isolated from the laboratory. The clean side of the airlock must be separated from the restricted side by changing or showering facilities and preferably by interlocking doors.

3 Where viruses are not retained by the HEPA filters, extra requirements will be necessary for extract air.

4 Where the autoclave is outside the laboratory in which the contained use is being undertaken, but within the laboratory suite, there must be validated procedures for the safe transfer of material into that autoclave, which provide a level of protection equivalent to that which would be achieved by having an autoclave in that laboratory.

Table 2 Containment measures applicable to contained use involving micro-organisms in premises other than those referred to in Tables 1

Containment Measures		***Containment Levels***			
		1	***2***	***3***	***4***
General					
1	*Viable micro-organisms must be contained in a system which separates the process from the workplace and wider environment (closed system)*	*required where and to extent the risk assessment shows it is required*	*required*	*required*	*required*
2	*Closed systems located within a controlled area*	*not required*	*required where and to extent the risk assessment shows it is required*	*required*	*required*
3	*Control of exhaust gases from the closed system*	*not required*	*required so as to minimise release*	*required so as to prevent release*	*required so as to prevent release*
4	*Control of aerosols during sample collection, addition of material to a closed system or transfer of material to another closed system*	*required where and to extent the risk assessment shows it is required*	*required so as to minimise release*	*required so as to prevent release*	*required so as to prevent release*
5	*Inactivation of bulk culture fluids before removal from the closed system*	*required where and to extent the risk assessment shows it is required*	*required by validated means*	*required by validated means*	*required by validated means*
6	*Seals must be designed so as to minimise or prevent release*	*not required*	*required so as to minimise release*	*required so as to prevent release*	*required so as to prevent release*
7	*The controlled area designed to contain spillage of the entire contents of the closed system*	*required where and to extent the risk assessment shows it is required*	*and to extent the risk assessment shows it is required*	*required*	*required*
8	*The controlled area sealable to permit fumigation*	*not required*	*required where and to extent the risk assessment shows it is required*	*Required where and to extent the risk assessment shows it is required*	*required*
9	*Biohazard signs posted*	*not required*	*required*	*required*	*required*

Containment Measures		***Containment Levels***			
		1	***2***	***3***	***4***
Equipment					
10	*Entry via airlock*	*not required*	*not required*	*Required where and to extent the risk assessment shows it is required*	*required*
11	*Surfaces resistant to water, acids, alkalis, solvents, disinfectants and decontamination agents and easy to clean*	*required for any bench*	*required for any bench*	*required for any bench and floor*	*required for any bench, floor, ceilings and walls*
12	*Specific measures to ventilate adequately the controlled areas in order to minimise air contamination*	*required where and to extent the risk assessment shows they are required*	*required where and to extent the risk assessment shows they are required*	*Required where and to extent the risk assessment shows they are required*	*required*
13	*The controlled area maintained at an air pressure negative to the immediate surroundings*	*not required*	*not required*	*Required where and to extent the risk assessment shows it is required*	*required*
14	*Extract and input air from the controlled area must be HEPA filtered*	*not required*	*not required*	*required for extract air, required where and to extent the risk assessment shows it is required for input air*	*required for input and extract air*

Containment Measures		***Containment Levels***			
		1	***2***	***3***	***4***
System of Work					
15	*Access restricted to authorised personnel only*	*not required*	*required*	*required*	*required*
16	*Personnel must shower before leaving the controlled area*	*not required*	*not required*	*Required where and to extent the risk assessment shows it is required*	*required*
17	*Personnel must wear protective clothing*	*work clothing required*	*work clothing required*	*required*	*complete change required before exit and entry*
18	*Written procedures and records of staff training*	*not required*	*required where and to extent the risk assessment shows they are required*	*required*	*required*
Waste					
19	*Inactivation of GMMs in effluent from hand-washing sinks and showers or similar effluents*	*not required*	*not required*	*Required where and to extent the risk assessment shows it is required*	*required*
20	*Inactivation of GMMs in contaminated material and waste including those in process effluent before final discharge*	*required by validated means where and to extent the risk assessment shows it to be required*	*required by validated means*	*required by validated means*	*required by validated means*