

**FORM 52.013A**

GMO Contained Use Regulations

**RISK ASSESSMENTS OF PROPOSED ACTIVITIES INVOLVING**

**GENETICALLY MODIFIED ORGANISMS**

**Background Information**

Studies involving Genetically Modified Organisms (GMO) come under one of two types of legislation. The NHS GG&C Genetically Modified organism Safety Committee (NHS GG&C GMS Committee) will review studies, taking place within NHS Greater Glasgow and Clyde Board, that come under these regulations to ensure safeguards are in place to ensure patient, staff, public and environmental safety.

This form should be completed for studies that come under The Genetically Modified Organisms (Contained Use) Regulations, 2014.The key aspects to consider when completing this form include:

(a) identification of any potentially harmful effects;

(b) characteristics of the proposed activity;

(c) the severity of any potentially harmful effects; and

(d) the likelihood of them occurring.

**Studies/Trials that come under the Contained Use Regulations**

In accordance with requirements of Part 2 of the Genetically Modified Organisms (Contained Use) Regulations 2014, GMO(CU), requires that a suitable and sufficient assessment of the risks to human health, and the environment to be carried out before any activity involving genetic modification of micro-organisms commences. Approval by the NHS GG&C’s Genetic Modification Safety Committee (GG&C GMSC) is required, in advance of the work commencing. Local R&D approval is also required.

Guidance on risk assessment and appropriate containment measures for larger GMOs can be found in **The SACGM** compendium of guidance. <http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/>

Those completing this form should be familiar with the requirements of the above regulations and guidance document.

In addition to this form please include

* MHRA /REC approved protocol
* Environmental Risk assessment completed by Sponsor (if available)
* Any additional requirements identified by MHRA or REC
* Investigator Brochure or preclinical work if not capture in this form

**Form 52.013A**

GMO Contained Use

**Research under the Genetically Modified (Contained Use) Regulations, 2014**



**risk assessment for Clinical Research Involving Genetically modified organisms**

**THE INFORMATION IN THIS BOX MUST BE READ BEFORE COMPLETING THE RISK ASSESSMENT FORM**

**Work must not commence** until all relevant parts of this form have been reviewed and approved by the Board Genetically Modified Safety (GMS) committee.

It is the responsibility of the person directing the research (i.e. the Principal Investigator) to ensure that all these requirements are complied with and any changes to the risk assessment or accidents involving the Genetically Modified Organism are reported to the GMS committee.

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| *Person responsible for this clinical trial (the Principal Investigator)* |
| Name:  | Position:  | Sites where GMO will be stored and /or prepared: |
| Department:  | Contact details : |  |
| Site(s) study will take place  :  | NHS GG&C R&D Ref. no. :  |  |
| *Person conducting this study (if different from above)* |
| Name:  | Position:  |  |
| Department:  |  |  |
| *The project- Title, EudraCT, GTAC ref. CTA No. and Sponsor details* |
| Title: EUDRACT No.:GTAC Ref: CTA No: Status of MHRA approval:Sponsor: Sponsor contact details: |
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| *Notification of premises to be used for contained use (refer to Regulation 9 of 2014 Regulations* |
| Details of notification to HSE: |  |

#  Summary of proposed investigation including goals and objectives.

The goals of the trial should be explained and justified. The trial aims, endpoints, inclusion and exclusion criteria and potential benefits should be detailed.

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#  An Overview of the Different Genetically Modified Organisms (GMOs) that will be used.

**2.1** Describe the different types of GMO that will be used describing their characteristics, donor(s), recipient vector (s) and construction. Outline the scope of the project. All individual GMOs must be listed. Indicate whether the GMOs are micro organisms or larger organisms.

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* 1. **Names and functional properties of all inserted gene(s)**

Describe the listed genes in such a way that an outside reviewer will have a general idea of their function i.e. providing an abbreviation may not be sufficient. Provide details of any known homologues if the function of a gene is unknown.

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##  Indicate the most hazardous GMO

Identify the most hazardous GMO to be used in this work giving consideration to both human health and the environment. This will be the most hazardous combination of recipient strain, vector or virus and inserted material from the lists made above. With some projects it will not be clear that one GMO will be more hazardous than any of the others (e.g. if all the work is Class 1). If this is the case, this should be stated.

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# Identification of the hazard to human health

### In which hazard group is each host organism placed by the Advisory Committee on Dangerous Pathogens?

**Hazad Group:**

###  Hazards associated with each host organism (e.g. viral vector)

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### What are the hazards associated directly from the inserted gene product?

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### If the function of the inserted gene is unknown, describe the function of any known homologues

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### 3.1.4 Hazards arising from the alteration of existing traits of the host

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### Hazards arising from the sequences within the GMO being transferred to related microorganisms

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#  Identification of the hazard to the environment.

### Hazards associated with the recipient microorganism (e.g. viral vector). Indicate bio-safety level, if relevant and whether shedding occurs

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### Hazards arising directly from the inserted gene product

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### Hazards arising directly from the alteration of existing traits (e.g. alteration of pathogenicity, host range or tissue tropism)

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### The potential hazards of sequences within the GMM being transferred to related microorganisms

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# Risks, likelihood & Control Measures

### Managing risks within the clinical trial environment

Describe the procedure(s) involving the handling and administration of the gene therapy product. Consider both the patient pathway and the GMO pathway. Identify the risks associated with each of the procedures and the likely effect if it did go wrong. Describe control measures in place to reduce/minimise risk. Please refer to section 5.2 for guidance.

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##  Identifying procedures involved in the handling and administration of the GMO

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| This section acts as guidance for identifying the procedures involved in the patient and GMO pathways. If the following sections have already been covered in section 5.1 please state this in the relevant section. If not, please complete**.** |

### Preparation of gene therapy product

a) Is the use of a microbiological safety cabinet required for the preparation of the gene therapy product material? Will aerosols or splashes be generated during any stage of the activity and do these aerosols pose a risk of infection to personnel? If yes, specify the type(s) and when it/ they will be used.

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b) Is any other form of Local Exhaust Ventilation required?

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c) Are there any particular requirements for the room ventilation e.g. negative pressure, temperature control?

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d) With reference to the room where the gene therapy product will be administered to the patient, are there any particular requirements for the room ventilation e.g. negative pressure, temperature control?

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### 5.2.2 Centrifugation

Will the gene therapy product need to be centrifuged? If yes, describe amounts (conc. & volume) to be centrifuged?

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Will sealed rotors and buckets be used for this? If yes, where will these rotors/buckets be opened?

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Describe the procedures in place to deal with leaks or spillages in the centrifuge or rotor.

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### 5.2.3 Use of incubators

a) Will the gene therapy product be cultured in an incubator? If yes, what type of incubator (e.g. shaking or static shelf) is this and describe the measures to be used to prevent and contain any spillages therein.

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### 5.2.4 Administration of gene therapy product

Where will the gene therapy product be administered to the patient?

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Is this room adequately separated from other areas? Provide details.

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Is/are the room(s) to be used for this trial to be shared with other patients not involved directly in this trial? If yes, provide details and explain why separate room(s) are not being used.

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Is access to this room restricted? Provide details.

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How long after the administration of the gene therapy product will the patient have to remain inhospital for? Where will they be transferred to?

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Is this room adequately separated from other areas? Provide details. Is this required?

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Is/are the room(s) to be used for this trial to be shared with other patients not involved directly in this trial? If yes, provide details and explain why separate room(s) are not being used.

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Is access to this room restricted? Provide details of the procedure to ensure restricted access

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How long will the GM organism persist following administration? Is shedding expected? What

evidence do you have to support this? (Please attach any relevant references)

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What is the route of shedding, if applicable?

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k) What level of shedding could occur?

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How will shedding be monitored?

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How will the shedding of the gene therapy product be contained?

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What are the consequences for other body systems (i.e. non-target tissues) from the systemic administration of the gene therapy product? e.g. autoimmune response

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What is the normal mode of transmission of the GMM?

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What other routes of transmission are possible? E.g. needle stick injuries, how will these be minimized?

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What are the possible consequences of an accidental exposure? (to the person compounding or administering the gene therapy product)

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What samples are required to be taken from the patients following administration of the gene therapy product? Will standard NHS procedures for handling samples suffice?

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How will these samples be removed from the patient? Will sharps be used? How and where will these sharps be disposed of?

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Who will take these samples?

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What Personal Protective Equipment will they be required to use?

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Where will these samples be taken to for analysis? How will the samples be transported?

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Who will analyse these samples? How and where will this waste be disposed of?

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## 5.2.5 Storage

Which department and personnel will receive the gene therapy product? Provide contact details.

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How will the product be transported to the storage location?

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Where will the gene therapy products be stored? Are there any particular requirements for the room ventilation e.g. negative pressure, temperature control? Who will receive the gene therapy product on site?

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If to be stored in Liquid Nitrogen, describe the precautions to be taken to prevent a release of infectious material whilst either loading or removing a sample from storage.

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In the event of breakdown of the storage equipment is backup storage available? If yes, where is this located?

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In the event of breakdown, is this equipment alarmed? Who will be alerted by this alarm?

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g) What security measures are in place? Would you be able to easily and rapidly identify that a sample was missing?

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### 5.2.6 Administration of GMMs to patients

a) How long will the GM organism persist following administration? Is shedding expected? What evidence do you have to support this? (Please attach any relevant references)

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b) What is the route of shedding, if applicable?

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c) What level of shedding could occur?

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d) How will shedding be monitored?

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e) How will the shedding of the gene therapy product be contained?

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f) What are the consequences for other body systems (i.e. non-target tissues) from the systemic administration of the gene therapy product? e.g. autoimmune response

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g) What is the normal mode of transmission of the GMM?

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h) What other routes of transmission are possible? E.g. needle stick injuries, how will these be minimized?

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i) What are the possible consequences of an accidental exposure? (to the person compounding or administering the gene therapy product)

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j) What samples are required to be taken from the patients following administration of the gene therapy product? Will standard NHS procedures for handling samples suffice?

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k) How will these samples be removed from the patient? Will sharps be used? How and where will these sharps be disposed of?

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l) Who will take these samples?

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m) What Personal Protective Equipment will they be required to use?

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n) Where will these samples be taken to for analysis? How will the samples be transported?

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o) Who will analyse these samples? How and where will this waste be disposed of?

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### 5.2.7 Sharps

Are sharps to be used at any stage during this activity? If yes, what sharps, justify their use and describe their use and disposal. Also describe any additional precautions required to ensure their safe use

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### 5.2.8 Other hazardous procedures

 Describe any other hazardous procedures to be undertaken and the control measures to be implemented

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### 5.2.9 Personal Protective Equipment (used for handling the gene therapy product)

Describe protective clothing to be worn, where will they be stored and the procedures for decontamination and laundering.

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Will gloves be worn? If yes, what type are these and where will they be stored?

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Is any other type of personal protective equipment to be used?

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### 5.2.10 Personal Protective Equipment (used for administration of the GT/GM material to patients)

Describe protective clothing to be worn, where will they be stored and the procedures for decontamination and laundering.

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Will gloves be worn? If yes, what type are these and where will they be stored?

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Is any other type of personal protective equipment to be used?

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### 5.2.11 Risks to personnel other than patients

Consider personnel potentially exposed to the gene therapy product at all stages of the trial i.e. preparation, transport, administration, follow-up care, removal of samples, through to inactivation.

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Will visitors to the patients be allowed? How will their risk of exposure to the gene therapy product be minimised? What information will they be provided with?

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## 5.2.12 Controls

### Delegation log (Please include a Health and safety section within the delegation log)

Provide the delegation log for the trial containing the names of individuals who are delegated Health and Safety responsibilities e.g. training of staff in handling, administering, disposing and cleaning, dealing with concerns and issues from staff exposed to activities involving the GMO

### 5.2.13 Information, Instruction and Training

a) Describe the training of all staff identified as being at risk of exposure. Include details on record keeping.

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b) Has a Local Code of Practice been prepared? If yes, is this available to all those at risk of exposure?

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## 5.2.14 Medical issues (for staff involved in this GT/GM Clinical Trial)

**Who is the contact if any trial staff or personnel who may be exposed to the GMO have concerns or issues.**

### Name and Contact Details

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### How will staff be informed of this individual

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## Specify any health surveillance requirements for staff involved in the work

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## 5.2.15 Specify any health issues or conditions that will exclude staff from working with the GMO? What is the process to inform staff of this and for staff to indicate they may be excluded from working on the trial?

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### 5.3 Routine Decontamination

### 5.3.1 Waste handling

All waste potentially contaminated with GMO culture material must be rendered non-viable (inactivated by a validated means) prior to leaving the site for final disposal. This includes GMO material disposed of at the preparation of the gene therapy product stage, administration to patient stage, waste generated when removing and analysing samples.

List waste types and methods of inactivation and disposal

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| **Waste type** **e.g. liquid, blood, syringes, swabs** | **Detail (spillage, disposal of blood)** | **Storage location of waste prior to inactivation** | **Chemical Inactivation specify type of disinfectant, concentration, contact time and conditions of use** | **Validation of treatment (evidence inactivation works)** |  **Route of Disposal** |
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### If autoclaving is used to inactivate the GMO waste, please provide the following details:

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|  | **Detail the type of waste** | **Storage location of waste prior to inactivation** | **Autoclave Cycle*****Specify temp, and cycle time*** | **Monitoring of treatment*****e.g. Chart recorder attached to autoclave***  | **Validation of treatment** **e.g. Annual 12 point thermocouple testing of autoclave** | **Route of Disposal** |
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| **Location of autoclave** |  |  |  |

# 5.4 Transport

a) How will the gene therapy product be transported within the hospital e.g. between incubator and safety cabinet? Detail the containment measures which will be used to prevent or contain accidental splashes or spillages.

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b) Will viable GT/GM material be transported to or from these labs? If yes, describe the route of transportation and describe in detail the containers to be used. Note that this includes the movement of waste containing viable GT/GM material e.g. to an autoclave elsewhere in the building.

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c) How will the gene therapy product be transported to the administration location? Detail who will transport the material and the containment measures to be used.

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d) How will specimens be transported around the hospital? Describe the containment measures to be used.

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e) Will any GT/GM material or specimens be transported to other NHS GG&C Board sites or external locations? If yes, please describe the transportation and containment measures to be used.

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#  Emergency Procedures

Describe the procedures in place for dealing with the spillages

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Describe the procedures in place for an accidental exposure (if necessary describe different procedures for different types of exposure e.g. eye splash or percutaneous inoculation) Please attach any supporting documentation from the sponsor e.g. drug company exposure guidance.

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c) Describe the specific arrangements required to evacuate a patient in the event of a fire or other emergency e.g. air handling failure

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d) Describe the actions to be taken in the event of death of the patient before the end of the treatment period.

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e) Describe whether any specific procedures are required to be followed in the event of any unexpected clinical events e.g. the patient requiring resuscitation following cardiac arrest or other acute medical emergency. Will other departments be involved e.g. ICU, CCU? Have these departments been fully informed?

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f) Describe the procedures to be followed if the patient suffers from post-operative infection. Would the patient require transfer to another location? Detail the potential for exposure to other personnel and the control measures in place to minimize this.

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## Assignment of Containment Level and Classification

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| Containment Level | Classification | Refer to Part 2 and Schedule 8, Part 2 of the Contained Use Regulations |
| 1 [ ]  | 1 [ ]  |       |
| 2 [ ]  | 2 [ ] *HSE notification is required prior to commencement of work* |       |
| 3 [ ]  | 3 [ ] *HSE approval is required prior to commencement of work* |       |

## 8 Personnel

8.1 Names of all other personnel involved in the handling of the GMO

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| --- | --- | --- | --- | --- |
| Surname | Initials | location | Job title  | Employer |
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## 8.1.1 List other people who may be at risk from the activity

For example, other researchers, cleaners or maintenance workers

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| Details ( including their names if known) | Employer | Involvement with this trial and exposure opportunity |
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8.1.2 Who will be responsible for managing Health and Safety risks for non-NHS GG&C Board personnel involved in this clinical trial?

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8.1.3 Who will be responsible for providing Occupational Health support, where necessary for non-NHS GG&C Board personnel involved in this clinical trial?

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# 9 Declarations

[ ]  ***To be completed by the PI responsible for this project****.* By ticking this box I confirm that all information contained in this assessment is correct and up to date. Any changes to the project will be forwarded to the GMO Safety committee.

I also undertake to ensure that no work will be carried out until this assessment has been completed and approved and that all necessary control measures are in place. Also, I accept that a statutory notification period may be required before work can commence.

[ ]  I confirm that this information has been discussed with the Departmental/Divisional Safety Officer.

[ ]  I confirm that the information detailed on this risk assessment form has been provided to the relevant person with responsibility for the clinical care of patients and also to the person with managerial responsibility for all staff involved in this clinical trial

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| Investigator signature  |
| Name:  |  |
| Signature:  | Date:  |

# GMS Committee Approval

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| GMS COMMITTEE approval  |
| Name:  | Position: |
| Signature:  | Date:  |

**Data protection**

The information provided on this form will be processed in accordance with the Boards Data Protection Policy.