**Note:** Form A applies only to clinical research studies involving Genetically Modified Organisms (GMO). It is recommended that the Principal Investigator discuss their clinical research study with the Biological Safety Officer or Secretary of the NHS Tayside Advanced Therapy and Gene Modification Safety Committee (ATGMSC) and refer to the TASC ATGMSC Standard Operating Procedure (SOP) before completing and submitting this form.

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List of Abbreviations

Appendix 1

**Section 1: Details of Proposed Research Study**

**1.1 – Study Details**

|  |  |
| --- | --- |
| NHS R&D number: |  |
| Study full title: |  |
| Study short title: |  |
| Planned start date for Recruitment: |  |
| Planned end date for Recruitment: |  |
| Planned end date of patient follow up: |  |
| Location(s): | *Please identify all rooms/facilities where GMOs will be handled and stored including the name of the trust buildings and campus/site locations.* |

**1.2 – Principal Investigator (PI) Details**

|  |  |  |  |
| --- | --- | --- | --- |
| Principal Investigator: | *Person who will have local responsibility for the work* | Position: |  |
| Department: |  |
| Full postal address: |  |
| E-mail address: |  | Phone no: |  |

**1.3 – Alternative Contact Details**

|  |  |  |  |
| --- | --- | --- | --- |
| Alternative contact person: | *Person who will have responsibility in the absence of the PI* | Position: |  |
| Full postal address: |  |
| E-mail address: |  | Phone no: |  |

|  |
| --- |
| **FOR COMMITTEE USE ONLY** |
| Date Received by ATGMSC: |  |
| ATGMSC Reference: |  |

**Section 2: Approvals, Consents, Notifications and Licences**

Give details of approvals/notifications for this research study.

|  |  |  |
| --- | --- | --- |
|  | **Reference Number** | **Date approved or notification date if not yet approved** |
| Gene Therapy Advisory Committee (GTAC) |  |  |
| Health Research Authority (HRA)  |  |  |
| Research Ethics Committee (REC) (if not a Gene Therapy research study) |  |  |
| Medicines & Healthcare products Regulatory Agency (MHRA) |  |  |
| Status of any notification to Health & Safety Executive (HSE) if applicable (Reference Number) |  |  |
| GMO release consent for research and development (Scotland)<https://www.gov.uk/gmo-release-consent-research-development-scotland> |  |  |

**Section 3: Lay Summary of the Research Study**

A summary of the research study, its background, goals and the justification of the research should be detailed in a manner that may be understood by all reviewers. This should include the patient pathway and not exceed 400 words.

|  |
| --- |
| *Can refer to Lay Summary from Integrated Research Application System* (*IRAS) Form (Section A6-1)* |

**Section 4: Scientific Detail of the Research**

Full detail of the proposed research including the scope of the research.

|  |
| --- |
| *Write in free text, no more than 3 paragraphs. Do not simply direct reviewers to sections in the protocol or Investigator Brochure (IB).* |

**Section 5: Details of the GM(O) Products**

**5.1 – Full Description of the Host Microorganisms**

List all species and strains that will be recipients for any genetic material. For each species, list the name of any strains and the name of the wild-type organism(s) from which it is derived and the extent to which it is disabled.

|  |
| --- |
| *Source, supplier, origin* |

**5.2 – Full Description of the Vector(s)**

List and describe the vectors used to modify the genetic sequences of the host microorganisms.

|  |
| --- |
| *Source, supplier, origin* |

**5.3 – Full List and Description of the Insert(s)**

Describe the listed inserts/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.

|  |
| --- |
| *Source, supplier, origin* |

**5.4 – *In vitro* use of the GMO**

Describe any *in vitro* handling, manipulation and preparation of the GMO that will be required as part of this research study.

|  |
| --- |
|  |

**5.5 – *In vivo* use of the GMO**

Describe the intended *in vivo* activities, and methods of delivery, for the GMOs.

|  |
| --- |
|  |

**Section 6: Risks to Human Health**

*This section looks at the possible harmful effects /hazards to human health from the pathogenicity, biological effects and toxicity of the host organism, foreign gene insert/product and the attenuation/virulence properties of the vector and the mobility of the plasmids. Therefore, consider host, vector, final GMO/GMM and survivability. Also severity of effects if an accident or exposure were to occur.*

**6.1 – Unaltered Host Organisms/Vectors**

Detail which hazard group are the unaltered host organisms assigned to by the Advisory Committee on Dangerous Pathogens and any known, or expected, hazards associated with the host organisms. Reference should be made to the [Approved List of Biological Agents](http://www.hse.gov.uk/pubns/misc208.pdf) prepared by the Advisory Committee on Dangerous Pathogens (ACDP).

| **Organism** | **ACDP Hazard Group *(****for parental or wild type organisms if relevant).* *For cell lines give strain/line**information as well as species If GMOs/GMMs have been**imported into the site, information on the construct must be**obtained from the supplier.* | **Human Health Hazards** |
| --- | --- | --- |
|  |  |  |
|  |  |  |
|  |  |  |

**6.2 – Inserts**

Detail the hazards associated with each of the inserts. Reference may also be made to known homologues where this aids clarity.

| **Insert** | **Hazards** |
| --- | --- |
|  |  |
|  |  |
|  |  |

**6.3 – Modified Host Organisms / Vectors**

Describe the hazards arising from altering the genetic traits of the host organism(s).

|  |
| --- |
|  |

**6.4 – Recombination**

Describe the risks associated with the GMO transferring the inserted sequences to related microorganisms.

|  |
| --- |
|  |

**6.5 – Hazards to Human Health**

Describe both the intended, and possible unintended, effects of the GMO to human health. Consider the possibility of the effects on both the target and non-target tissues. In addition, consider the risks from shedding of the GMO, route of infection, and the possible infection of healthcare workers and patient contacts. Detail any groups that may be at increased risk from the GMO including the young, elderly, pregnant or immunocompromised.

|  |
| --- |
|  |

**6.6 - Assessment of Risk to Human Health**

Using the table in Appendix 1, please state whether you consider the risk to human health to be High, Medium, Medium/Low, Low or Effectively Zero.

|  |  |
| --- | --- |
| The risk to Human Health from the Genetically Modified Organisms used in this research study is: |  |

**6.7 – Interim Assignment of GM Class (Human Health)**

Consider the containment level required to control the risk of the host to human health, making a judgement as to whether the GMO will be more, or less, hazardous than the host microorganism.

Please note that where measures to control the risk from, and spread of, aerosols are required to protect human health, the genetically modified organism activity will be Class 2 or higher.

|  |  |
| --- | --- |
| **Organism** | **GM Class (1, 2 or 3)** |
|  |  |
|  |  |
|  |  |

**Section 7: Risk to the Environment**

*This section considers the possible harmful effects /hazards to the environment (in particular to environmental species that could be affected. What is the likelihood of release/escape of the organism from containment? Consider host, vector, final GMO/GMM, scale and survivability. Also severity/consequences if an accident or release were to occur.*

**7.1 – Unaltered Host Organisms/Vectors**

Detail any known, or expected, hazards to the environment associated with the host organisms and vectors.

| **Organism** | **Environmental Hazards** |
| --- | --- |
|  |  |
|  |  |
|  |  |

**7.2 – Inserts**

Detail the hazards to the environment associated with each of the inserts. Reference may also be made to known homologues where this aids clarity.

| **Insert** | **Hazards** |
| --- | --- |
|  |  |
|  |  |
|  |  |

**7.3 – Modified Host Organisms/Vectors**

Describe the hazards to the environment arising from altering the genetic traits of the host organism(s)

|  |
| --- |
|  |

**7.4 – Recombination**

Describe the risks associated with the GMO transferring the inserted sequences to related microorganisms in the environment if released.

|  |
| --- |
|  |

**7.5 – Environmental Hazards**

Describe the possible effects of the GMO to the environment and the consequences were it to be released.

|  |
| --- |
|  |

**7.6 – Likelihood of Release**

How likely is release of the organism and how could this occur? Release of the organism could be through shedding from the patient while in the hospital or the community or through accidental release from an unplanned event.

|  |
| --- |
|  |

**7.7 – Contained Use or Deliberate Release?**

Consider whether this research study should be considered as a ‘Contained Use’ or ‘Deliberate Release’.

Contained Use: The organism will remain within the control of the organisation through the implementation physical, chemical or biological controls. This can be through the ‘Standard infection, protection and control precautions’ or additional measures including facilities, disinfection or biological controls including disablements of the organism such that it is not viable outside of the facility or its progeny are harmless.

Deliberate Release: The organism will not remain in control of the organisation, will intentionally be released to the environment and its progeny will be viable and may pose a risk to the environment. This may include shedding from the patient at any stage of the study.

|  |
| --- |
| **This research study is assessed as being a Contained Use/Deliberate Release** (delete as appropriate) |

If the research study is classed as a ‘Deliberate Release’ then a [GMO release consent for research and development (Scotland)](https://www.gov.uk/gmo-release-consent-research-development-scotland) must be obtained. Provide details in Section 2 and provide copies with this application.

**7.8 - Assessment of Risk to Environment**

Using the table in Appendix 1, please state whether you consider the risk to the environment to be High, Medium, Medium/Low, Low or Effectively Zero.

|  |  |
| --- | --- |
| The risk to the environment from the Genetically Modified Organisms used in this research study is: |  |

**7.9 – Interim Assignment of GM Class (Environmental Risk)**

For ‘Contained Use’ research studies only:

Consider the containment level required to control the risk of the host to the environment, making a judgement as to whether the GMO will be more, or less, hazardous than the host microorganism.

Please note that where measures to control the risk from, and spread of, aerosols are required to protect the environment, the genetically modified organism activity will be Class 2 or higher.

|  |  |
| --- | --- |
| **Organism** | **GM Class (1, 2 or 3)** |
|  |  |
|  |  |

**Section 8: Final Assignment of GM Class and Containment Level**

Assign the GM Class of each GMO activity. For each organism, this will be the highest assigned for either human health (Section 6.7) or environmental risk (Section 7.9)

|  |  |
| --- | --- |
| **Organism** | **GM Class (1, 2 or 3)** |
|  |  |
|  |  |

**Section 9: Occupational Health**

If the GMO is GM Class 1, please enter N/A for sections 9.1-9.7 but ensure that all precautions are being taken.

Where the GMO is GM Class 2, or higher, this section must be completed by the Occupational Health Physician following approval by the Committee.

**9.1 – Health Effects**

|  |
| --- |
|  |

**9.2 – Medical Risk Assessment**

|  |
| --- |
|  |

**9.3 – Pre-Exposure Arrangements**

|  |
| --- |
|  |

**9.4 – Post-Exposure Action**

|  |
| --- |
|  |

**9.5 – Antibiotic Treatment or Chemoprophylaxis**

|  |
| --- |
|  |

**9.6 – Health Surveillance Required**

|  |
| --- |
|  |

**9.7 – Additional Notes & Comments**

|  |
| --- |
|  |

**Section 10: Arrangements to Control Risk**

Consider the list of issues in the table below and detail how the risks posed by the GMOs will be controlled for each item. Reference should be made to Standard Operating Procedures (SOPs). These may be existing TASC, local or Study Specific SOPs.

|  **10.1 - Administration to Patient** | **COMMENT/ACTION (specify SOP if appropriate)** |
| --- | --- |
| Will safeguards against aerosols be required during patient administration? How will this be achieved? |  |
| How long will the patient have to remain in hospital following administration of the Advanced Therapy Investigational Medicinal Product (ATIMP)? Where will they be transferred to (if applicable)? |  |
| Will shedding of the GMO occur and will this pose a risk to humans or the environment? If so, by what routes will shedding occur and how will this be monitored, controlled and contained? |  |
| Are there risks to personnel other than patients?Will visitors be permitted? |  |

| **10.2 - Patient Care** | **COMMENT/ACTION (specify SOP if appropriate)** |
| --- | --- |
| Will clinical samples (e.g. fluids, tissues) be collected from the patient for routine analysis by hospital laboratories? Specify arrangements for their safe handling. |  |
| Specify clinical samples to be collected for specialised analysis by research laboratories? Specify arrangements for their safe handling. |  |
| Identify any specific precautions or restrictions required for visitors to the patient. |  |
| Will the patient need to be transported within the hospital following administration of the GMO? Identify any specific safety procedures required for such transportation of the patient. |  |
| Identify any actions to be taken should the patient suffers from an iatrogenic infection.Will the patient require transport to another location? |  |
| Identify any specific safety arrangements required if it is necessary to evacuate the patient in the event of fire. |  |
| Identify any specific arrangements required in the event of the patient requiring resuscitation following a cardiac arrest or other acute medical emergency  |  |
| Identify any actions to be taken in the event of the death of the patient before the end of the treatment period. |  |

| **10.3 - Patient Follow up** | **COMMENT/ACTION (specify SOP if appropriate)** |
| --- | --- |
| Identify any specific safety arrangements required in the event of death of the patient before the end of the treatment period. |  |
| Are there specific precautions in the event of the death of the patient at home? |  |

| **10.4 - Staff Safety and Surveillance** | **COMMENT/ACTION (specify SOP if appropriate)** |
| --- | --- |
| Specify any health surveillance requirements for staff involved in the work. Has a standard protocol been arranged with Occupational Health to this effect? |  |
| Specify the protective clothing and any other personal protective equipment (PPE) to be used at each stage.If this is different to the normal PPE provided, please specify where the PPE will be stored and the named individual responsible for its issue. |  |
| Are there any hazards associated with the accidental inoculation of a Health Care Worker with the GMO? Specify precautions to be followed. |  |

| **10.5 - Waste Management** | **COMMENT/ACTION (specify SOP if appropriate)** |
| --- | --- |
| In addition to standard infection, protection and control precautions, are there any additional safety requirements for handling the patient’s body fluids? |  |
| In addition to standard hospital procedures are any additional safety arrangements required for the disposal of clinical waste from the patient’s room? |  |
| Other than standard arrangements, are any additional safety measures or procedures required for cleaning the patient’s bed linen or laundry? |  |
| Other than standard hospital cleaning procedures, specify any additional arrangements required when cleaning the patient’s room during and at the end of the treatment period. |  |
| Specify the disinfectants to be used at each stage, and the concentrations at which they will be used. |  |
| Specify the arrangements for safe disposal of contaminated materials appropriate for each stage of the work. Specify the arrangements for safe disposal of contaminated materials appropriate for each stage of the work. |  |
| Identify any procedures which will involve sharps, and specify arrangements for their safe use and disposal |  |
| If any waste is to be autoclaved, specify:* Types of waste
* Storage location prior to inactivation, Autoclave cycle parameters
* Monitoring & recording of inactivation
* Validation of inactivation (e.g. validation of autoclave)
* Final disposal route of the wastes.
 |  |

**10.6 - Emergency procedures**

|  |
| --- |
|  |

**10.7 - Information, Instruction, Supervision and Training**

List any relevant local SOPs and Codes of Practice specific to this study.

|  |
| --- |
| *e.g. disposal of GMO, administration of vaccines* |

Describe the training of all staff at risk of exposure. Include details of record keeping

|  |
| --- |
|  |

**Section 11: Accommodation**

Where will the GMO be stored, handled and administered?

|  |  |  |  |
| --- | --- | --- | --- |
| **Room** | **Building** | **Campus** | **Responsible Person** |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

**Section 12: Personnel**

**12.1 – Names of key persons directly involved in the research study at site**

|  |  |  |
| --- | --- | --- |
| **Name** | **Position** | **Employer** |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |

**12.2 – Other personnel at risk from this research study at site**

List other groups of research staff, cleaners, maintenance workers and ancillary staff that may be at risk, but not directly involved in this research study.

|  |  |  |
| --- | --- | --- |
| **Details (including names, if known)** | **Employer** | **Involvement with this research study and exposure opportunity** |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |

**12.3 – Responsible Persons**

Who will be responsible for managing risks to non-NHS/University of Dundee personnel involved in this research study?

|  |
| --- |
|  |

Who will be providing Occupational Health support for each category of personnel involved in this research study?

| **Category** | **Occupational Health Contact** |
| --- | --- |
| NHS Personnel |  |
| Other Personnel |  |

**Section 13: Pharmacy**

*This section should be completed with the guidance of a research pharmacist and authorised by a pharmacy member of the ATGMSC.*

**13.1 – Manufacture**

|  |  |
| --- | --- |
| Product, Manufacturer and License status |  |
| Is substitution with a safer product practical? Please provide reasons for your answer. |  |
| Indication |  |
| Presentation |  |
| QP release by |  |
| Is the GMO linked to a specific patient?How is this achieved? |  |
| Is there potential for >1 patient to be treated at the same time? |  |

**13.2 – Shipment**

|  |  |
| --- | --- |
| What container is used for shipment? Is dry ice used? |  |
| What are the temperature requirements? |  |
| Specify arrangements for receipt of the GMO |  |

**13.3 – Storage on Site**

|  |  |
| --- | --- |
| Specify arrangements for safe storage of the GMO. |  |
| How long is storage allowed/required? |  |
| Has a suitable location been identified? |  |
| If the GMO is to be stored in Liquid Nitrogen, specify precautions to prevent the release of the GMO during loading or retrieving the product from storage? |  |
| In the event of a breakdown of the storage equipment, detail contingency plans for the transfer to (including the location of) alternative storage |  |
| What security measures are in place? Would you be able to easily and rapidly identify that a sample was missing? Is the storage alarmed? |  |

**13.4 – Preparation/Manipulation**

|  |  |
| --- | --- |
|  Specify arrangements for the safe preparation of the GMO for administration. |  |
| What are the handling requirements? |  |
| Are suitably trained staff available? |  |
| Have suitable facilities/location been identified? (provide specific location details) |  |
| What is the shelf-life following preparation/manipulation? |  |
| Will laboratory preparation of the therapy be required? What facilities will this require (hoods, incubators, centrifuges etc)? |  |
| Will precautions need to be taken against the formation and dissemination of aerosols?If so, what techniques or equipment could give rise to aerosols and how will these be controlled? Will a microbiological safety cabinet be required? Dedicated lab? Negative pressure? Sealed centrifuge buckets etc? |  |
| How will spillages or contaminated equipment be dealt with? |  |
| What are the risks associated with spillage?  |  |
| How will the above identified risks be mitigated? |  |
| Specify arrangements for the safe transport of the GMO to the site of administration.(If the starting product is received and manipulation processes occur at a different site to patient administration, please detail processes of transport to administration site). |  |
| Identify any stages involving transport of the GMO or GMO-contaminated materials within the NHS Board, or between the Board and outside Institutions, and specify how this will be done safely. |  |

**13.5 – Prescription**

|  |  |
| --- | --- |
| How will the ATIMP be prescribed? |  |

**13.6 – Disposal**

|  |  |
| --- | --- |
| What are the arrangements for disposal? |  |

**13.7 – Other Issues**

|  |  |
| --- | --- |
| Are there any other risk considerations to Staff and Public? |  |
| Is so, how will the above identified risks be mitigated? |  |
| What is the reporting process for an Adverse Drug Reaction? |  |
| Is ATIMP Batch Number recorded at each patient visit? |  |
| Are patient information risk mitigation details (e.g. Alert Card/Patient Information Leaflet) available? |  |

|  |
| --- |
| **FOR COMMITTEE USE ONLY** |
| Pharmacy section reviewed by:(include Name and Job Title) |  |
| Date: |  |
| Pharmacy comments (including required actions to be taken prior to sign off): |
|  |
| Date above actions completed (as applicable): |  |
| Pharmacy authorisation for study: | [Signature requiredInsert Full Name and Job Title underneath] |
| Date: |  |

**Section 14: Declarations and Approvals**

**14.1 – To be completed by the PI responsible for this Clinical Research Study**

I confirm that all information contained in this assessment is correct and up to date. Any changes to the research study that alters the information supplied in this assessment will invalidate this assessment and the approval granted to it. If this occurs all work must cease and the changes notified to the ATGM Safety Committee.

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

I undertake to ensure that the containment measures specified in this Risk Assessment are appropriately applied in the conduct of this clinical research study.

I confirm that the information detailed on this risk assessment form has been/will be provided to the relevant persons with responsibility for the clinical care of patients and also to the persons with managerial responsibility for NHS and University of Dundee staff involved in this clinical research study.

|  |  |
| --- | --- |
| Name:  | Title:  |
| Signature:  | Date:  |

**14.2 – Committee Chair Approval**

I confirm that this clinical research study has been unanimously approved by the Committee.

|  |  |
| --- | --- |
| Name:  | Title:  |
| Signature:  | Date:  |

**14.3 – HSE Consent**

*HSE consent/notification is required for projects categorised as Class 2 and above.*

|  |  |
| --- | --- |
| Is HSE notification required for any aspect of this research study? | Yes [ ]  No [ ]   |
| Date HSE consent was given:  | HSE Reference:  |

**14.4 – NHS Biological Safety Officer**

I confirm that I am satisfied with this risk assessment, the arrangements put in place to confirm risk and the facilities proposed for this clinical research study.

|  |  |
| --- | --- |
| Name:  | Title:  |
| Signature:  | Date:  |

**14.5 – Review**

**Scheduled Reviews**

|  |
| --- |
| Review history:The PI responsible for this research study must ensure that this risk assessment remains valid |
|  | Review 1 | Review 2 | Review 3 | Review 4 |
| Due date |  |  |  |  |
| Date conducted |  |  |  |  |
| Conducted by |  |  |  |  |

**Summary Table of Amendments**

|  |  |  |  |
| --- | --- | --- | --- |
| **Risk Assessment Version** | **Date** | **Section Updated** | **Summary of Changes** |
|  |  |  |  |
|  |  |  |  |
|  |  |  |  |

**Submission**

Please submit your competed form, along with the required documents outlined below, to the Secretary of the ATGM Safety Committee at TASCQA@dundee.ac.uk.

• Protocol

• Investigator Brochure/details

• IRAS submission relating to REC

• Relevant publications

• CV of PI and other relevant sub-Investigators

• Evidence of Basic Life Support/Advanced Life Support (BLS/ALS) training (if appropriate) and

• Documents submitted to GTAC with favourable opinion letter (for gene therapy only).

**List of Abbreviations**

ACDP Advisory Committee on Dangerous Pathogens

ATGMSC Gene Modification Safety Committee

ATIMP Advanced Therapy Investigational Medicinal Product

BLS/ALS Basic Life Support/Advanced Life Support

GMO/GMM Genetically Modified Organism/Genetically Modified Microorgansim

GTAC Gene therapy Advisory Committee

HRA Health Research Authority

HSE Health & Safety Executive (HSE)

IRAS Integrated Research Application System

MHRA Medicines & Healthcare products Regulatory Agency

PI Principal Investigator

PPE Personal Protective Equipment

QP Qualified Person

REC Research Ethics Committee

SOP Standard Operating Procedure

TASC Tayside Medical Science Centre

**Appendix 1**

The GMO (Contained Use) Regulations 2014 have introduced a classification system based on the risk of the contained use independent of the purpose of the contained use. The risk classification is based on the four levels of containment for microbial laboratories where Class 1 is of negligible or very low risk.

**Table 1** Containment levels and the corresponding risk classification

|  |  |
| --- | --- |
| Laboratory Containment necessary to control the risk  | GM Risk classification |
| Level 1   | Class 1 |
| Level 1 with the addition of measures from Level 2or Level 2 (without additional measures) | Class 2 |
| Level 2 with the addition of measures from Level 3 or Level 3 (without additional measures) | Class 3 |
| Level 3 with the addition of measures from Level 4 or Level 4 (with or without additional measures) | Class 4 |

Note that the classification is based on the level of containment required to control the risk, not necessarily the level of containment at which the work is planned to be done.