UNIVERSITY HOSPITALS BRISTOL AND WESTON NHS FOUNDATION TRUST

**RISK ASSESSMENT OF PROPOSED ACTIVITIES INVOLVING**

**ADVANCED THERAPY INVESTIGATIONAL MEDICINAL PRODUCTS (ATIMPS) FOR RESEARCH**

**An ATMP is a biological medicinal product that can be classified as one or a combination of the following:**

* **Gene Therapy Medicinal Product (GTMP)**
* **Somatic Cell Therapy Medicinal Product (CTMP)**
* **Tissue Engineered Products (TEP)**

**Directive 2001/83/EC, amended by 2003/63/EC annex 1, Part I**

**Research involving use of the above products will require review and approval from the UHBW ATIMP committee prior to the study commencing at UHBW. There are two types of reviews; proportionate and full review.**

**If you believe your study is eligible for proportionate review only complete sections A, B, C, E and F (*Principal Investigator signature only*).**

**For full review please complete all applicable sections.**

**Once complete please submit this form to** **ResearchApprovals@UHBW.nhs.uk** **who will seek approval from the committee.**

|  |
| --- |
| **SECTION A: DETAILS OF PROPOSED RESEARCH** |

|  |  |
| --- | --- |
| UHBW NHS Trust R&D study reference number: |       |
| Study full title: |  |
| Planned start date: |  |
| Planned end date: |  |
| Location:(e.g. which sites within UHBW) |  |
| Status of regulatory submissions |
| Gene Therapy Advisary Committee (GTAC) |  |
| Health Research Authority (HRA) |  |
| Research Ethics Committee (if not a Gene Therapy trial) |  |
| Medicines & Healthcare Products Regulatory Authority (MHRA) |  |
| Status of any notification to HSE if applicable (reference No.) |       |

|  |  |  |  |
| --- | --- | --- | --- |
| **Principal investigator:** |       | **Position:** |       |
| **Division:** |       |
| **Full postal address:** |       |
| **E-mail address:** |       | **Phone no.:** |       |

|  |  |  |  |
| --- | --- | --- | --- |
| **Alternative contact person:** |       | **Position:** |       |
| **Full postal address:** |       |
| **E-mail address:** |       | **Phone no.:** |       |

**Please note other approvals may also be required prior to study commencement including (but not limited to):**

* **Gene Therapy Advisory Committee,**
* **Medicines and Healthcare products Regulatory Agency (MHRA)**
* **Research Ethics Committee**
* **Health Research Authority**

**Summary of the proposed research (include tasks/activities and frequency/duration):**

**[Provide a summary of the research study]**

**SECTION B: HEALTH & SAFETY**

|  |  |  |
| --- | --- | --- |
| **Substances, machines, tools, processes etc. to be used** | **Hazards identified**  | **Estimated risk to patients, staff and public (Low, Medium, High)**  |
| **1.** |  |  |
| **2.** |  |  |
| **3.** |  |  |
| **4.** |  |  |
| **5.** |  |  |
| **Precautions required to mitigate risk (relate to numbers above):***e.g. use of gloves, face masks, lab coats etc, equipment to be used for safe handling etc, use of fume hoods etc* |
| **Emergency Procedures:***e.g. in case of spillage or contact with skin/eyes etc. Emergency contact numbers etc* |
| **Access restrictions/signage:** |
| **Lone Working:***e.g. any restrictions* |
| **Special Training Requirements:***e.g. required by sponsor* |
| **Storage:***e.g. specific storage requirements (temperature, type of container), where will ATIMP be stored and how, time restrictions etc, refer to relevant SOPs (Sponsor or Trust)* |
| **Waste Disposal:***e.g. requirements and method for disposal, refer to relevant SOPs (sponsor or Trust)* |

|  |  |
| --- | --- |
| Health & Safety section reviewed by:(include Name and job Title) |  |
| Date: |  |
| Health & Safety comments (including required actions to be taken prior to sign off): |
|  |
| Date above actions completed (as applicable): |  |
| Health & Safety authorisation for study: | [Signature requiredInsert Full Name and Job Title underneath] |
| Date: |  |

**SECTION C: PHARMACY (where a GMO it should be consistent with requirements identified in section D)**

1. MANUFACTURE

|  |  |
| --- | --- |
| Product, Manufacturer and License status |  |
| Indication |  |
| Presentation |  |
| QP release by |  |
| Is the ATIMP linked to a specific patient?How is this achieved? |  |
| Is there potential for >1 patient to be treated at the same time? |  |

1. SHIPMENT

|  |  |
| --- | --- |
| What container is used for shipment? |  |
| What are the temperature requirements? |  |
| Is dry ice used? |  |

1. STORAGE AT SITE

|  |  |
| --- | --- |
| How long is storage allowed / required? |  |
| Has a suitable location been identified? |  |

1. PREPARATION / MANIPULATION REQUIRED

|  |  |
| --- | --- |
| What preparation /manipulation of the ATIMP is required? |  |
| 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? |  |
| What are the risks associated with spillage?  |  |
| How will the above identified risks be mitigated? |  |

1. PRESCRIPTION

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

1. DISPOSAL

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

1. OTHER

|  |  |
| --- | --- |
| Are there any other risk considerations to Staff and Public? |  |
| How will the above identified risks be mitigated? |  |
| What is the reporting process for an Adverse Drug Reaction? |  |
| Logging BN and patient details |  |
| Patient information risk mitigation details (e.g. Alert Card/PIL) |  |

|  |  |
| --- | --- |
| 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 D: GENETICALLY MODIFIED ORGANISMS (for studies involving GM only – delete section if not applicable). SACGM guidance should be consulted for help and advice and where prompted:** [**http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/**](http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/) |

**Brief summary of the key features of this risk assessmesnt**

|  |  |
| --- | --- |
| Parent vector details:Also specify ACDP hazard group |       |
| Modified vector: List changes from parent and specify hazard group (take into account any SACGM guidance on reclassification) |       |
| Description of modification. Include source of any inserted material and any control/maintenance sequences included |       |
| Activity classification for a contained genetically modified microorganism (Class 1 – 4).  |       |
| If this considered deliberate release of a GMO and not contained use, provide consent to release references.  |       |
| *In vitro* host cells used and inherent hazards |       |
| Patients involved and route of delivery |       |

|  |
| --- |
| **Facilities in which the proposed activities involving the GMO would take place.**  |
| **Activity**  | **Room No. and designation** | **Description of facilities/ACGM containment level** |
|       |       |       |
|       |       |       |
|       |       |       |

**Detailed Characteristics of Each Component of the Genetic Modification Activity and its Intended Use**

**Full description of the "vector"**

|  |
| --- |
|       |

**Full description of the “insert”; *i.e.* all additional nucleic acid sequences involved**

|  |
| --- |
|       |

***In vitro* recipients of the GMO (if relevant)**

|  |
| --- |
|       |

***In vivo* use of the GMO**

|  |
| --- |
|       |

**Effects of the GMO**

|  |
| --- |
|       |

**Potential hazards of the GMO**

|  |
| --- |
|  |
|  |

**Risks to human health**

|  |
| --- |
|       |
| **Human groups at increased risk from the GMO** |
|       |

**Quantity of the GMO to be used**

|  |  |  |
| --- | --- | --- |
| **Activity and location** | **Volumes to be worked with** | **Concentrations of the GMO to be used** |
|       |       |       |
|       |       |       |
|       |       |       |
|       |       |       |

**Interim Assignment of Containment Conditions**

**to Protect Human Health**

Specify an interim assignment of containment requirements for the work, i.e. containment level that would be required for laboratory work, together with any additional special requirements for the protection of human health and safety(see current HSE/SACGM guidance particularly the sections on work in a clinical setting). Separate consideration should be given to each area or type of procedure in which the GMOs will be handled, including: preparation of the GMO for administration; administration to patients; subsequent care of the patient; and handling of any subsequent samples derived from the patient.

|  |
| --- |
| Complete categorisation for each step of the process.      |

Identification of hazards associated with specific operations, and measures to control the resulting risks. This will be used when completing “Section A: Pharmacy”. Information in this document must be consistent, take into account the classification of the GMO and address the requirements of all applicable regulations.

| **HAZARD** | **COMMENT/ACTION (specify S.O.P if appropriate)** |
| --- | --- |
| Specify arrangements for safe storage of the GMO. |       |
| Specify arrangements for the safe preparation of the GMO for administration. |       |
| Specify arrangements for the safe transport of the GMO to the site of administration. |       |
| Are there any hazards associated with the accidental inoculation of a Health Care Worker with the GMO? Specify precautions to be followed. |       |
| Are there any hazards to Health Care Workers associated with contact with the patients following administration of the GMO? Specify precautions. |       |
| In addition to universal 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? |       |
| 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. |       |
| 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. |       |
| 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 specific safety arrangements required if it is necessary to evacuate the patient in the event of fire. |       |
| Identify any specific safety arrangements required in the event of death of the patient before the end of the treatment period. |       |
| Identify any specific arrangements required in the event of the patient requiring resuscitation following a cardiac arrest or other accute medical emergency |       |
| Specify any health surveillance requirements for staff involved in the work. Has a standard protocol been arranged with Occupational Health to this effect? |       |
| Identify any work procedures likely to generate aerosols, and the control measures will be applied. |       |
| Identify any procedures which will involve sharps, and specify arrangements for their safe use |       |
| Specify the protective clothing and any other personal protective equipment to be used at each stage. |       |
| Identify any stages involving transport of the GMO or GMO-contaminated materials within the NHS Trust, or between the Trust and outside Institutions, and specify how this will be done safely. |       |
| 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. |       |
| Identify any stages of the work or manipulations of the GMO not already covered, which may pose increased risk, and the measures which will be applied to control those risks. |       |

**Emergency procedures**

|  |
| --- |
|       |

**Environmental Considerations**

**Risk to animals, fish, plants etc.**

|  |
| --- |
| Does the work involve a microorganism which is:  |
| * an animal pathogen licensable under the Specified Animal Pathogens Order <http://www.hse.gov.uk/biosafety/sapo.htm>
 | Yes [ ]  No [ ]  |
| * a plant pathogen or pest controlled by the Animal and Plant Health Agency <https://www.gov.uk/guidance/plant-health-controls>
 | Yes [ ]  No [ ]  |
| If you answered yes to any of the above, please provide details and status of any licence application or notification made and attach copies of any licences and approvals |

Specify any identifiable potential hazards to the environment, which might occur IF the genetically modified organism were to be unintentionally released, EITHER from the Trust premises OR following discharge of a treated patient. Classify the potential hazard as Severe, Medium, Low or Negligible.

|  |
| --- |
|  |

In view of the characteristics of the GMO, consider the likelihood of accidental release from Trust premises, and the occurrence of any abovementioned potential harmful effects, if the work were to be performed at the interim containment level specified above. Classify this as High, Medium, Low or Negligible.

|  |
| --- |
|  |

In view of the characteristics of the GMO, consider the likelihood that the GMM will be released to the environment from a treated patient who has been discharged, and lead to the occurrence of any abovementioned potential harmful effects. Should this be considered as a deliberate release of the GMM to the environment?

|  |
| --- |
|       |

Note: Deliberate release of GMOs to the environment will require consent from the Secretary of State for the Enviromnment, Food and Rural Affairs. If a consent has been obtained then this risk assessment must take into account any consent conditions. If consent has not be obtained then an application to Defra/ACRE will be required.

|  |  |
| --- | --- |
| Grade the Overall Risk (= Potential harm x Likelihood) to the environment as High, Medium, Low or Effectively Zero. (See HSE/ACGM Guidance Notes.) |  |

Additional containment measures required to protect the environment

If, in considering the potential for harm to the environment, you have concluded that the Risk to the environment is high or medium, then the containment conditions specified above are inadequate and must be modified to reduce the risk to an acceptably low level.

Indicate below any additional containment facilities or provisions/procedures which will be used in order to meet this requirement (additional to those specified above for the protection of human health).

|  |
| --- |
|       |

**Classification and notification of the work if it involves a contained use (not deliberate release) activity under the GMO (Contained Use) Regulations 2014.**

For a GM microorganism use the containment tables in Annex 1 to derive a class number. For other GMOs state whether the modified organism is more or less harmful to human health than the non-modified equivalent.

Activities with GM micrrorganisms that are Class 2 and above or those involving other GMOs that are more harmful to human health due to the modification will require notification to HSE. All deliberate release activities will instead require consent from the Secretary of State.

Will all the containment measures specified for this class of activity be applied? If not, justify any divergence (consent from HSE will be required for this.)

**Persons who may be affected by the work**

|  |  |
| --- | --- |
| **Personnel involved in work:****(List categories, e.g. Doctors, Nurses, Pharmacists, Laboratory Staff, Porters)** | **Specify any specific information or training to be provided for the listed categories of workers, over and above training and experience normal for such workers.** |
|       |       |
|       |       |
|       |       |

|  |  |
| --- | --- |
| **Non-staff categories who may be affected** | **Information to be provided to this category** |
|       |       |
|       |       |

**Expert Reviewers**

**Please suggest two individuals not connected with the proposed work who would be competent to provide an expert opinion on the suitability of this risk assessment. Ideally at least one expert should be unconnected with either the University of Bristol, or the NHS Trust**

|  |  |  |
| --- | --- | --- |
|  | **Reviewer 1** | **Reviewer 2** |
| **Name** |       |       |
| **Position** |       |       |
| **Address** |       |       |
| **Telephone** |       |       |
| **Fax** |       |       |
| **Email (if known)** |       |       |
| **Justification** |       |       |

**SECTION E: HUMAN TISSUE ACT (HTA) CONSIDERATIONS**

|  |  |
| --- | --- |
| Does the starting material for the ATIMP come from a patient or donor at UHBW? | Yes/No |
| If yes, have you consulted the Designated Individual (DI) at UHBW to review whether the trial and associated processes meet HTA requirements?  |  |

Further information on the Human Tissue Act and the Human Tissue Authority can be found here: <https://www.hta.gov.uk/>

If you need assistance contacting the DI please liaise with the R&D department on 0117 342 0233

**SECTION F: APPLICANT SIGNATURES**

If the proposed research involves Genetically Modified Organisms it must be discussed with the Biological Safety Officer or his/her Deputy.

The Principal Investigator, Divisional Director and Biological Safety Officer should sign below to indicate their acceptance of the following statements.

**Principal Investigator:**

To the best of my knowledge and belief, the information provided in this risk assessment is accurate and complete. If the proposal is approved by the UHBW ATIMP committee (and by the HSE if required), I undertake to ensure that the containment measures specified in this risk assessment are appropriately applied in the conduct of the approved activities.

|  |  |
| --- | --- |
| Principal Investigator |  |
|  |       |       |
| Signature | Print name | Date |

**Biological Safety Officer (for GM only)**

I have read this completed risk assessment and discussed any points requiring clarification with the principal investigator or his appropriate representative. The proposal may now appropropriately be submitted for consideration by the UHBW ATIMP committee.

|  |  |
| --- | --- |
| Biological Safety Officer |  |
|  |       |       |
| Signature | Print name | Date |

**Head of Division**

Subject to the approval of this risk assessment by the UHBW ATIMP committee (and HSE if required), and approval from other relevant bodies if appropriate (e.g. the Gene Therapy Advisory Committee; Medicines and Healthcare Products Regulatory Agency; Research Ethics Committee, HRA), I agree to the conduct of the approved activities in accordance with the indicated containment provisions, within the Division for which I have responsibility.

|  |  |  |  |
| --- | --- | --- | --- |
| Divisional Director |  |  |  |
|  |       |       |
| Signature | Print name | Date |
|  |
| Division |       |

|  |
| --- |
| **SECTION G: Approval by UHBW ATIMP Committee** |

|  |
| --- |
| **This risk assessment of proposed activities involving ATIMPs has been considered by the UHBW ATIMP Committee, of which I am the authorised representative. The approval of HSE is either not required or has been obtained. Any modifications to the risk assessment required have been incorporated into this final version of the document.** |
| **Proportionate review by ATIMP Committee** | **Yes/No** |
| **Signature** |  |
| **Print name** |  |
| **Position** |  |
| **Date** |  |

|  |  |
| --- | --- |
| **Comments** |  |

**Is HSE notification required?**

|  |  |
| --- | --- |
| First Use Notification | Yes [ ]  No [ ]  |
| Individual Activity Notification | Yes [ ]  No [ ]  |
| If yes, date sent |       |
| Date of approval |       |
| HSE Reference number |       |

**ANNEX 1**

**TABLES OF CONTROL MEASURES AND CONTAINMENT LEVELS FOR ‘CONTAINED’ ACTIVITIES INVOLVING GM MICROORGANISMS**

The basic principles of classification are that you:

1. Determine the containment and control measures required by the risk assessment to control the risk of the activity;
2. Where this corresponds to a single containment level this will read across directly to give you the activity class, i.e.level 1 = class 1, level 2 = class 2, etc;
3. Where the measures identified correspond to measures from two different levels of containment the class corresponds to the higher of the two levels.

**\*\*\***

Please consider the table(s) overleaf. Select the appropriate table for the work you are involved in. In most cases this will be **Table 1A** **(Laboratory Activities) as this is most appropriate to a clinical setting**. **Where your project involves the use of GMMs in plant growth facilities or animal facilities, you should consider Table 1B or 1C in conjunction with table 1A.** (In the final column of Tables 1B and 1C "additional" specifies use of that control measure in addition to the measures in Table 1A, while "modification" specifies that this measure shall be substituted for the relevant measure in Table 1A).

**Large scale activities** should be classified using **Table 2.**

Select your control measures. You should place a **X** in the appropriate box on each row to indicate whether that containment measure is required or not.

Determine the corresponding level of containment and hence the class of GMO. Where controls are selected from more than one containment level the Class corresponds to the higher of the containment levels.

**FOR ALL CONTAINMENT TABLES AND FURTHER INFORMATION PLEASE REFER TO THE GUIDANCE TO THE REGULATIONS (L29) OR THE SACGM COMPENDIUM OF GUIDANCE**

[**http://www.hse.gov.uk/pubns/priced/l29.pdf**](http://www.hse.gov.uk/pubns/priced/l29.pdf)

[**http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/**](http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/)

**TABLE 1A: LABORATORY ACTIVITIES**

| CONTAINMENT MEASURES | CONTAINMENT LEVELS |
| --- | --- |
| 1 | 2 | 3 | 4 |
| Laboratory suite: isolation (**note 1**)  | not required | not required | required | required |
| Laboratory: sealable for fumigation | not required | not required | required | required |
| **Equipment** |  |  |  |  |
| Surfaces impervious/easy to clean surfaces | required for any bench | required for any bench | required for any bench and floor | required any bench, floor, ceiling and walls |
| Entry to lab via air lock (**note 2**) | not required | not required | risk assessment identifies requirements | required |
| Negative pressure relative to the pressure of the immediate surroundings | not required | not required | required **except** for activities where transmission does not occure by the airborne route | required |
| Extract and input laboratory air must be HEPA filtered | not required | not required | required for **extract** air **except** for activities where transmission does not occure by the airborne route | required for both input and extract (**note 3**) |
| Microbiological safety cabinet/enclosure | not required | risk assessment identifies requirement | 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 |
| Autoclave | required on site | required in thebuilding | required in laboratory suite (**note 4**) | required in laboratory (double ended) |
| **System of work** |  |  |  |  |
| Access restricted to authorised personnel only | not required | required | required | Required (via airlock key procedure) |
| Biohazard sign on the door | not required | required | required | required |
| Specific measures to control aerosol dissemination  | not required | required so as to minimise | required to so as to prevent | required so as to prevent |
| Shower | not required | not required | risk assessment identifies requirement | required |
| Protective clothing | suitable protective clothing required | suitable protective clothing required | suitable protective clothing required. Risk assessment identifies footwear requirement | complete change of clothing and footwear required before entry/exit |
| Gloves | not required | risk assessment identifies requirement | required | required |
| Efficient control of disease vectors (eg rodents and insects) which could disseminate GMMs | risk assessment identifies requirement | required | required | required |
| **Waste** |  |  |  |  |
| Inactivation of GMMs in effluent from handwashing sinks, showers and similar effluents | not required | not required | risk assessment identifies requirement | required |
| Inactivation of GMMs in contaminated material and waste | required by validated means where and to the extent identified in the risk assessment | required by validated means | required by validated means with waste inactivated in the laboratory suite | required by validated means with waste inactivated in the laboratory |
| **Other measures** |  |  |  |  |
| Laboratory to contain its own equipment | not required | not required | required so far as is reasonably practicable | required |
| An observation window or alternative present so that occupants can be seen | risk assessment identifies requirement | risk assessment identifies requirement | risk assessment identifies requirement | required |
| Safe storage of GMMs | risk assessment identifies requirement | required | required | secure storage required |
| Written records of staff training | not required | risk assessment identifies requirement | required | required |
| CLASSIFICATION | CLASS 1 | CLASS 2 | CLASS 3 | CLASS 4 |

**Notes**

1. In table 1A, 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 preferable by interlocking doors.
3. Where viruses are not retained by the HEPA filters, extra requirements will be necessary for extracted 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