Advanced Therapy Treatment Centres

Midlands-Wales Advanced Therapy Treatment Centre

Example SOP: Handling and Administration of *In vivo* GMO Gene Therapies

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Background

In vivo gene therapies are a type of Advanced Therapy Medicinal Product (ATMP) or Advanced Therapy Investigational Medicinal Product (ATIMP), and organisations are required to have a defined governance process in place for their implementation.

In vivo gene therapies may include genetically modified organisms (GMOs), which have the potential to cause harm to human health and the environment. Therefore specific handling precautions are necessary in accordance with national guidance and regulations. National guidelines on governance requirements for gene therapies advise that this should include, specifically in relation to handling;

- **Local policies** to consider handling of the GMO gene therapy
- A risk assessment of risks of the GMO gene therapy to human health and the environment, including the product, the patient and waste pathways
- Advice on the risk assessment should be obtained from the organisation's biological safety officer (if one is appointed), or designated 'competent persons'. Some organisations may delegate BSO duties to the Genetic Modification Safety Committee (GMSC) as a whole via the representation of staff appointed to the committee.

This SOP considers general principles for the handling and administration of an example *In vivo* GMO gene therapy in a clinical area and should be consulted in conjunction with the MW-ATTC document:

'Non-cellular GMOs: a visual guide'

It will require adaptation to accommodate local procedures or product-specific requirements. It is important that all GMO gene therapies are risk assessed locally by the Trust Genetic Modification Safety Committee.

Note this SOP applies to *in vivo* gene therapies only and does not refer to cellular, ex vivo gene therapies.

For further details consult:

Pan UK Pharmacy Working Group for ATMPs. Gene Therapy Medicinal Products; Governance and Preparation Requirements. Available from:
https://www.sps.nhs.uk/wp-content/uploads/2019/09/PAN-UK-PWG-for-ATMPs-Gene-Therapy-Guidance-issue-2.pdf

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1. Aim

- To ensure safe handling and administration of Genetically Modified Organism (GMO) *in vivo* gene therapies (Class I or II biohazards) to minimise any risk to human health and the environment.

2. Indications for practice

- *In vivo* gene therapies are a type of Advanced Therapy Medicinal Product (ATMP) or Advanced Therapy Investigational Medicinal Product (ATIMP) and may contain GMOs.
- Due to the potential risk to human health and the environment, GMO gene therapies must be carefully handled as set out in the risk assessment undertaken by the Trust Genetic Modification Safety Committee (GMSC).
- This SOP covers the actions required to safely handle and administer Class 1 or 2 in vivo GMO gene therapies in clinical areas. Separate guidance must be sought for ex vivo gene therapies, other settings (eg in Pharmacy aseptic facilities) or for GMOs classified as Class 3 biohazards or above.

3. Authorised personnel/training required

- All staff handling GMO gene therapies must be suitably qualified, trained and must demonstrate competency. They must be aware of and follow the applicable Trust SOPs and the agent specific instructions.
- All staff have a responsibility to report near misses and hazards via the Trust incident reporting system.
- The Trust GMSC, including the Biological Safety Officer, are to advise staff on the handling of in vivo GMO gene therapies.
- Staff who may be pregnant or who are breastfeeding should not handle GMO gene therapies.
- Staff who are immunocompromised or have significant health issues should not handle GMO gene therapies unless a detailed risk assessment has been performed.

4. Procedure for preparation/administration of *in vivo* GMO gene therapies

4.1. Preparation of in vivo GMO gene therapies

- The Trust GMSC must risk assess the optimum location for preparation of the GMO gene therapy in accordance with national guidance and regulations. Information sources to guide this decision include;
- The SACGM Compendium of guidance Part 6: Guidance on the use of genetically modified microorganisms in a clinical setting. **http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/part6.pdf** (see Appendix 1)
- Pan UK Pharmacy Working Group for ATMPs. Gene Therapy Medicinal Products; Governance and Preparation Requirements. Available from: **https://www.sps.nhs.uk/wp-content/uploads/2019/09/PAN-UK-PWG-for-ATMPs-Gene-Therapy-Guidance-issue-2.pdf**
- Product-specific protocols should be used, stipulating preparation steps, any special containment requirements and required personal protective equipment (PPE).
- For preparation of patient–specific doses, a prescription must be available, screened by a suitably trained pharmacist.

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4.2. Transportation of in vivo GMO gene therapies to administering area (if applicable)

- Transportation of GMO gene therapies must only be undertaken by specifically trained and competent staff.
- The chain of custody must be maintained during transport between the preparation and the treatment area and written records maintained. Temperature during transit should ideally also be monitored and recorded, particularly for longer transit periods.
- In vivo GMO gene therapies should be transferred to the treatment area in an appropriate, spill proof, labelled container. For class II biohazards, the container must be labelled with a 'biohazard' label.
- A biohazard spillage kit must be readily available during transportation and a route with minimal footfall should be used where possible.

4.3. Administration of Class 1/2 in vivo GMO gene therapies

- Product-specific instructions must be used for administering the *in vivo* GMO gene therapy. These will stipulate any special containment requirements including personal protective equipment (PPE).
- Class 1 agents may be administered in clinical areas, unless agent specific instructions state otherwise.
- Class 2 agents must be administered in a side room with only essential personnel present. 'Do Not Enter' and 'Biohazard' signs must be placed on the door to the side room to prevent unnecessary entry.
- Further information regarding administration location is available from 'The SACGM Compendium of guidance Part 6: Guidance on the use of genetically modified microorganisms in a clinical setting.' **http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/part6.pdf** (also see Appendix 1).

- **Prior to commencing administration;**
  - Ensure appropriate PPE is worn according to agent specific instructions and universal standard precautions.
  - Ensure that a GMO spillage kit and anaphylaxis kit are available
  - Ensure that appropriate containers/bags/waste bins for waste management are available
  - Ensure that appropriate dressings are available.
  - Ensure that a prescription is available and has been screened by a suitably trained pharmacist.

Administration of in vivo GMO gene therapies;

- Open the transfer container, place the contents onto a disposable mat on a tray to minimise the risk of spillage and damage to product.
- Place an absorbent mat under the body area where the agent will be administered.
- Follow universal standard precautions and use aseptic techniques rigorously. Administer the *in vivo* GMO gene therapy according to the drug protocol and/or product instructions.
- After administration, clean the administration site with an alcohol swab. Cover the site with the chosen dressing in accordance with the protocol, applying pressure to stop bleeding as necessary. Advise the patient to dispose of the dressing as normal unless otherwise specified in the agent specific instructions.
- The patient may leave the room once the administration site is dressed and observation period completed unless otherwise specified.
- Administration is completed once the patient has left and all waste disposed of safely as per Trust GMO Waste Management SOP. Complete administration records and remove signs from the door if applicable on leaving.

Viral shedding

- The risk of viral shedding must be considered in the local GMSC risk assessment
- Where significant shedding is anticipated, further advice should be sought from the Health and Safety Executive / trial sponsor (ATIMPs) or manufacturer (ATMPs)
- Strategies to manage risk of significant shedding include delivering treatment on an in-patient basis until shedding is complete or unlikely to pose a risk, using an appropriate antibiotic or antiviral prior to discharge, or the use of occlusive dressings (disposed of in accordance with GMO waste management procedures).
- Further information on the management of shedding is available from 'The SACGM Compendium of guidance Part 6: Guidance on the use of genetically modified microorganisms in a clinical setting.'

Cleaning procedures

- The area(s) used to prepare and administer the in vivo gene therapy and any non-disposable items must be disinfected as per local policy. This should include use of a viricidal agent (eg Virkon®) or viricidal wipes. Non-disposable items may also be immersed in a viricidal agent such as Chemgene® 10% where appropriate.
- Any spillage of a GMO gene therapy should be managed as per MW-ATTC Example SOP: Management of GMO Spillage or Accidental Exposure in a Clinical Area.

5. Supporting Documents/Further Information

- Further information may be provided in the product specific SOPs, risk assessments, Summary of Product Characteristics and clinical trial protocols as appropriate.

References

The Genetically Modified Organisms (Contained Use) Regulations 2014.
http://www.hse.gov.uk/pubns/books/l29.htm

HSE COSHH homepage: **http://www.hse.gov.uk/coshh/index.htm**

The SACGM Compendium of guidance Part 2: Risk assessment of genetically modified microorganisms (other than those associated with plants) **http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/part2.pdf**

The SACGM Compendium of guidance Part 6: Guidance on the use of genetically modified microorganisms in a clinical setting. **http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/part6.pdf**

HSE homepages on microbiological safety: **http://www.hse.gov.uk/biosafety/index.htm**

The HSE ACGM compendium of Guidance and newsletters at: **http://www.hse.gov.uk/a-z/**

Appendix 1

The following table is adapted from the Health and Safety Executive 'The SACGM Compendium of guidance Part 6: Guidance on the use of genetically modified microorganisms in a clinical setting'. It summarises considerations when assessing the optimum location for the preparation and administration of in vivo GMO gene therapies. Full guidance is available from **http://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/part6.pdf**

Containment measure	Containment Level 1	Containment Level 2
Autoclave	Required on-site	Required in the building
Access restricted to authorised personnel only	Not required	Required
Specific measures to control aerosol dissemination	Not required	Required so as to minimise
Protective clothing	Suitable protective clothing required	Suitable protective clothing required
Gloves	Not required	Required where and to extent the risk assessment shows it is required
Specified disinfection procedures in place	Required where and to extent the risk assessment shows it is required	Required
Surfaces impervious to water and resistant to acids, alkalis, solvents, disinfectants, decontamination agents and easy to clean	Required for bench	Required for bench
Laboratory suite isolation	Not required	Not required
Laboratory: sealable for fumigation	Not required	Not required
Entry to laboratory via airlock	Not required	Not required
Negative pressure relative to pressure of immediate surroundings)	Not required	Required where and to extent the risk assessment shows it is required

Containment measure	Containment Level 1	Containment Level 2
Extract and input air from the laboratory should be HEPA filtered	Not required	Not required
Micro biological safety cabinet/enclosure	Not required	Required where and to extent the risk assessment shows it is required
Shower	Not required	Not required
Efficient control of disease vectors (eg for rodents and insects) which could disseminate GMO	Required where and to extent the risk assessment shows it is required	Required
Safe storage of GMOs	Required where and to extent the risk assessment shows it is required	Required
Inactivation of GMOs in contaminated material and waste	Required by validated means	Required by validated means
Written records of staff training	Not required	Required where and to extent the risk assessment shows it is required