Advanced Therapy Treatment Centres

Midlands-Wales Advanced Therapy Treatment Centre

Example SOP: Management of GMO Spillage or Accidental Exposure in a Clinical Area

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Background

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.

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[1] advise that this should include, specifically in relation to handling;

- Local policies to consider handling of the GMO gene therapy, including dealing with accidents, spillages and other incidents
- 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 (BSO), if one is appointed, or designated 'competent persons'. Some organisations may delegate BSO duties to the committee as a whole via the representation of staff appointed to the GMSC (Genetic Modification Safety Committee).

For further details consult;

[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

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This SOP considers general principles for the management of a Class 1 or 2 GMO gene therapy spillage or accidental exposure in a clinical area. 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.

Example SOP for Management of Class 1 or 2 GMO Gene Therapy Spillage or Accidental Exposure in a Clinical Area

1. Aim

To ensure any spillage of or accidental exposure to Genetically Modified Organism (GMO) gene therapies (Class 1 or 2 biohazards) are managed appropriately to minimise any risk to human health and the environment.

2. Indications for practice

- Gene therapies are a type of Advanced Therapy Medicinal Product (ATMP) or Advanced Therapy Investigational Medicinal Product (ATIMP) and may include GMOs.
- Accidental spillage and/or exposure to a GMO gene therapy may occur when handling. Such untoward incidents must be managed to minimise any risks posed to human health or the environment.
- This SOP covers the actions required to manage spillage or accidental exposure to Class 1 or 2 GMO gene therapies. Separate guidance must be sought on the management of GMO gene therapy spillage outside of this setting (eg in Pharmacy aseptic facilities) or for GMOs classified as Class 3 biohazards or above.
- Further information may be provided in the product specific SOPs, risk assessments, Summary of Product Characteristics and clinical trial protocols as appropriate.

3. Authorised personnel/training required

- All staff handling GMO gene therapies and waste 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 handling GMO gene therapies, have a responsibility to report near misses and incidents via the Trust incident reporting system.
- The Trust GMSC, including the Biological Safety Officer are to advise staff on the management of spillages and incidents of accidental exposure.

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4. Procedure for management of spillage of Class 1 or 2 GMO gene therapy

4.1 GMO gene therapy spill kit

Prior to handling or administering a GMO gene therapy, appropriate PPE must be worn. The GMO spill kit should accompany the GMO gene therapy from the preparation area to the administration area. A spill kit should contain;

- 2x plastic aprons
- 2x disposable gowns
- 2 pairs of gloves
- 2x masks
- 1x safety glasses
- Disposable mat
- Absorbent wipes (e.g. paper towels)
- Yellow clinical waste bag.
- Decontaminent* e.g Duel® (Activator and base solution) (*https://www.tristel.com/uk/cache-products/duel*)

*Several different agents are available for the decontamination of a GMO gene therapy spillage. An example of Duel® activator and base solution is used in this SOP, but alternatives include Virkon® 2%, hydrogen peroxide 6%,1,000 ppm chlorine. The choice of agent should be determined locally by the GMSC, taking into account the irritant nature of some decontamination agents.

4.2 Decontamination of a spillage

A major spill is a potentially serious incident, even if there is no obvious accidental exposure. Examples of a significant spillage include breakage of a container or spillage of whole vials. (Note minor splashes occurring during manipulation still require decontamination of the affected area as described below, but evacuation of the area would not be necessary).

- Staff present during the spillage must request urgent assistance and request for an expert advisor to be contacted if required.
- Staff affected by the spillage should immediately change their gloves and check forearms/clothing/shoes for contamination. If affected, the staff member should remove the PPE or change clothes immediately and undertake any necessary measures for accidental exposure (see Section 5). A separate member of staff must decontaminate the area.
- Suitably trained staff attending the incident must wear protective clothing and eye protection (available in the spillage kit).

- All non-essential personnel and where possible, patients, must leave the contaminated area. A sign must be put on the door to prevent anybody entering the area. If possible no one should re-enter the area for 30 minutes to let potential aerosols settle. (Further estimates of the required period of evacuation may be evaluated locally by considering volume of spillage and room ventilation).
- If a major spillage occurs in a room under positive pressure air filtration, vented to another area, the air filtration system to the room should be temporarily shut-down until any potential aerosols have settled and the area decontaminated. Where the air circulation system cannot be shut-down, evacuation of the area into which the affected room vents, should be considered.
    - Cover the spillage with the absorbent material (eg paper towels) from the spillage kit.
    - Pour sufficient Duel® disinfectant onto the absorbent material to flood and leave for 1 minute. (Note the recommended duration of exposure is agent specific and observing longer exposure times than recommended is not more effective and may damage surfaces)
    - Absorb the liquid with an absorbent cloth/material
    - Thoroughly wash the area using water. Do not use other disinfectants or alcohol, as it is likely to cause frothing or smearing which may be difficult to remove.
    - Dry the area using absorbent cloth, e.g. paper towels.

- When dealing with spillages of cellular (ex-vivo) gene therapies such as CAR T cells, Trust policies for the Infection Control of blood products and management of blood product spillage must also be adhered to.
- Patients and their clinical team should be informed if the spillage affects availability of their treatment.

4.3.Waste management of spillage, spill kit and contaminated materials

- Dispose of the GMO spillage, used contents of spill kit and other disposable items in contact with spillage, in accordance with Trust procedures for the management of GMO waste.
- Treat affected clothes, uniform or bed linen as infectious linen in accordance with Trust policy. Uniform should ideally be laundered on the premises at a minimum of 65^{0}C.

5. Procedure for management of accidental exposure to a Class I or 2 GMO gene therapy

- In general, accidental exposure to Class 1 agents pose a negligible risk. The risk from a Class 2 agent will be low to moderate. Note that decontamination agents may also cause irritant effects if accidental exposure occurs.
- Provide immediate clinical assistance – staff attending should wear suitable protective clothing. Call one of the designated expert advisors (see Section 6) to attend the scene immediately/provide urgent advice if the incident is potentially serious or if in any doubt about its management.

Any accidental exposure of staff or patients not involved in the work.

- Negligible risk for class 1, moderate risk for class 2 agents, contact expert advisor immediately.

Needle stick:

- Potentially serious, contact expert advisor immediately
- For injury with a used needle, also consult the Trust Needlestick Injury Policy.
- Encourage bleeding of wound or puncture site.
- Wash site thoroughly with soap and water then dry area using disposable material, e.g. paper towel.
- Cover area with waterproof dressing.
- Observe in reach of medical attention as directed by the attending medic or expert advisor.

Eye Splash

- Potentially serious, contact expert advisor immediately
- Irrigate eye immediately with sterile eye wash solution or water for at least 3 minutes.
- Observe in reach of medical attention as directed by the attending medic or expert advisor.

Mouth splash

- Potentially serious, contact expert advisor immediately
- Wash out mouth immediately with water repeatedly for at least 3 minutes.
- Observe in reach of medical attention as directed by the attending medic or expert advisor.

Inhalation

- Potentially serious, contact expert advisor immediately
- Observe in reach of medical attention as directed by the attending medic or expert advisor.
- Consider moving the affected person outside to fresh air

Skin Splash (intact skin)

- Wash area thoroughly with soap and water
- Dry using disposable material, e.g. paper towel.
- Keep under observation if known irritant risk or actual evidence of skin becoming irritated.

6. Reporting of near misses or incidents

6.1 Trust Reporting Procedures

- All incidents of spillage or accidental exposure (including hazards and near misses), must be reported according to the Trust Clinical Incident Policy.
- Additional reporting will also be required for gene therapy investigational medicinal products in accordance with clinical trial procedures.
- Contact the Lead ATMP Pharmacist, GMSC Chair or Biological Safety Officer if in doubt if or how to report an incident, hazard or near miss.

6.2 Informing expert advisors

- In addition to Trust incident reporting procedures, report all incidents, near misses or hazards to the following expert advisors as soon as practicably close to the event. **Call one or more of these advisors immediately for serious incidents**;
    - The responsible Principal Investigator / Lead Consultant
    - The Local Biological Safety Officer
    - Chair/ Vice Chair of the GMSC
    - Lead Pharmacist
    - Occupational Health

6.3.Informing other relevant parties

As close to the time of the incident as practical, the Principle Investigator / Lead Consultant should also inform;

- Safety Officers from relevant external organisations e.g. clinical trial sponsor.
- Occupational Health Service (if not already aware)

6.4 Follow up of near misses or incidents

In addition to routine Trust procedures for incident review, all incidents and near misses involving GMO gene therapies must be reviewed by the Trust GMSC and the impact on future GMO gene therapy risk assessments and product specific SOPs/instructions considered. Incidents or near misses involving ex-vivo cellular GMO gene therapies must also be considered by the relevant Quality Management Group detailed in the centre's JACIE accreditation.

7. Acknowledgements

The MW-ATTC wish to thank; Oxford University Hospitals, University Hospital of Wales, University Hospitals Birmingham and University Hospitals Bristol & Weston, for their contributions in sharing their documentation as a basis for this exemplar SOP.

8. 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/