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Midlands-Wales Advanced Therapy Treatment Centre

Non-cellular GMO therapies: a visual guide

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Non-cellular GMO therapies: a visual guide

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Non-cellular GMO therapies: a visual guide

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A visual guide to the preparation, administration and disposal of non-cellular, genetically modified organisms (GMOs), in a clinical setting.

What is shown in this guide?

This guide highlights general principles relevant to working with GMO therapies in clinical areas. Local and product/trial-specific protocols must always be followed.

This document provides a simple visual demonstration of the steps that may be taken to prepare, administer and deal with waste disposal for an example GMO therapy in a clinical trial setting. The example product involves GMO class 1 activities and has been assessed as suitable for preparation in a clinical area. Not all GMO therapies can be prepared in a clinical area; some require preparation in pharmacy aseptic services or another suitable facility.

Protective clothing and waste disposal procedures should always be used as appropriate for the class of GMO being handled, and according to local Genetic Modification Safety Committee (GMSC) risk assessment.

Guidance on Requirements for Gene Therapy Governance and Preparation has been produced by the Pan UK Pharmacy Working Group for ATMPs and includes flowcharts to help decide which products may be suitable for preparation in clinical areas.

https://www.sps.nhs.uk/articles/requirements-for-governance-preparation-of-gene-therapy-pan-uk-pharmacy-working-group-for-atmps/

For more information, refer to the **Pharmacy Working Group guidance document** and to the Midlands-Wales ATTC example SOPs: **Handling and Administration of In vivo GMO Gene Therapies** and **Management of GMO Spillage or Accidental Exposure in a Clinical Area**.

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What are GMOs?

Genetically modified organisms (GMOs) are organisms whose genes have been artificially altered to somehow modify their characteristics. Micro-organisms can be genetically modified to produce a GMO (sometimes referred to as a genetically modified micro-organism, GMM) that can be used therapeutically.

Activities relating to GMOs are classified into one of four classes, based on the risk that they present to human health and the environment. The risk classification is derived from the outcome of a detailed risk assessment and corresponds to an appropriate containment level. Most activities involving GMO therapies will be class 1 or 2.

Containment level 1 is suitable for class 1 activities, for example working with 'replication defective' genetically modified viruses (that lack one or more components necessary to make copies of themselves).

Containment level 2 is required for class 2 activities such as the use of conditionally replicating viruses (that selectively replicate in tumour cells, leading to their destruction, while sparing normal cells).

Most activities involving GMO therapies will be class 1 or 2; refer to local risk assessments.

What are gene therapy medicinal products?

A gene therapy medicinal product is a medicinal product of biological origin that contains recombinant nucleic acid(s) and is administered to patients to regulate, repair, replace, add or delete a genetic sequence. It is one type of a group of medicines known as advanced therapy medicinal products (ATMPs). In most cases, a gene therapy medicinal product will be classified as a GMO.

Gene therapy medicinal products can be divided into two main types:

- **ex vivo gene therapies, whereby cells are genetically modified while they are outside of the body and the modified cells are then administered to the patient;**
- **in vivo gene therapies, whereby a gene delivery vector is directly administered into the patient's body.**

This guide focuses on non-cellular (in vivo) gene therapy medicinal products.

"Preparation" is the process of making the product ready-to-administer. In the example shown on the following pages, no reconstitution is required; the product is simply drawn up into a syringe prior to administration. In some cases, reconstitution activities may occur either in a clinical area or in specialised aseptic facilities.

The example shown is not a cellular medicine. It is important to note that cellular (ex vivo) gene therapy medicinal products (also referred to as gene-modified cell therapies) require preparation and administration by operators who are skilled in handling cellular products; guidance on working with cellular products is outside the scope of this document.

Before undertaking any work relating to GMO therapies:

- **Speak to your local Genetic Modification Safety Committee**
- **Consult local policies and procedures re:**
  - **action in case of inoculation injury involving GMOs,**
  - **action in case of GMO splash or spillage,**
  - **disposal of GMO waste.**

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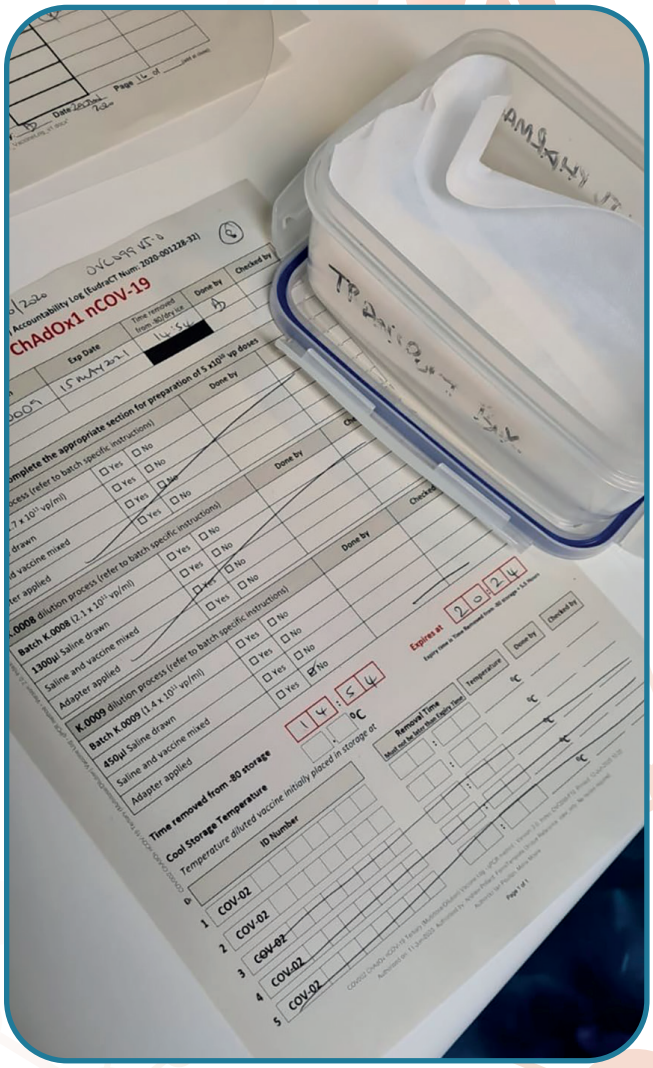
Preparation of GMO therapies in a clinical area

1. GMOs must be prepared in a suitably cleaned room which has been designated for GMO preparation. At the site in these pictures, a sign is placed on the door to ensure no one enters unless they are directly involved (some sites may not require this for Class I GMOs).

2. Documentation is completed to include: vial reference number, date/time taken out of fridge, expiry time. Fridge temperature log is checked to ensure that the cold chain has been maintained. PPE should be donned as appropriate before preparation of product, to include disposable gloves, aprons and visor. A suitable spill kit should be readily available throughout, according to local procedures.



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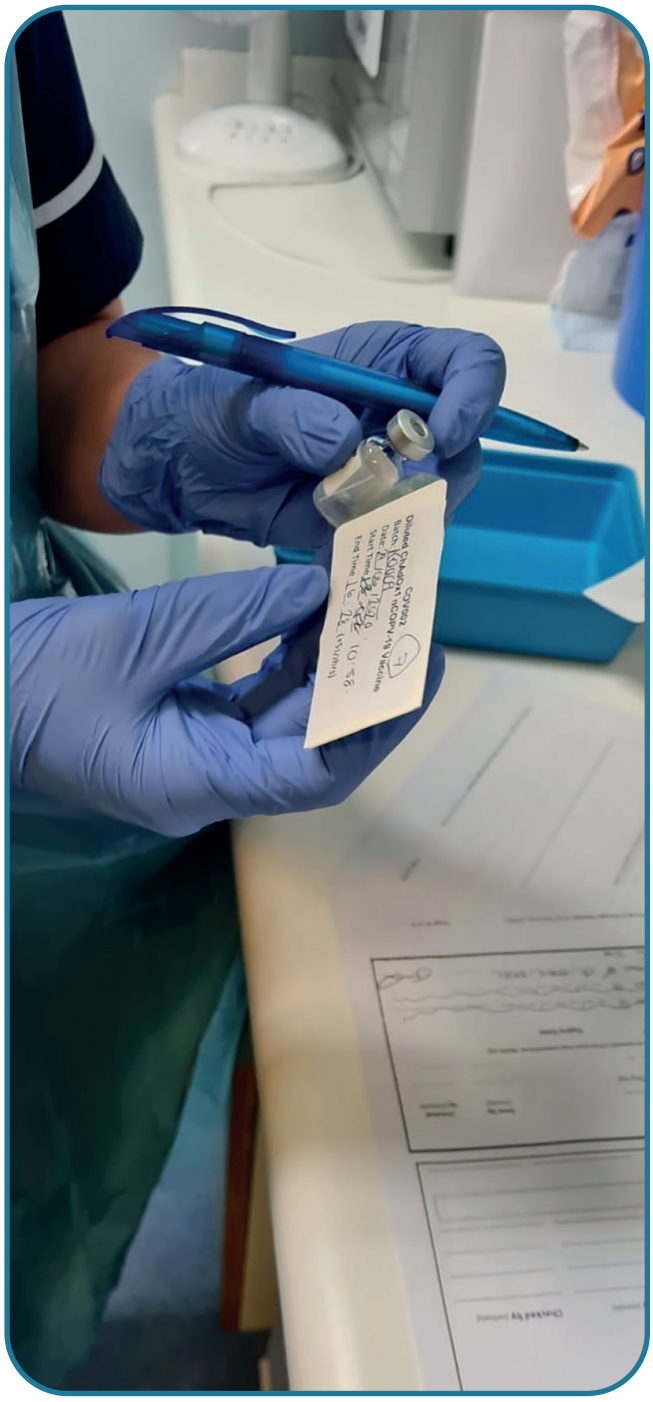
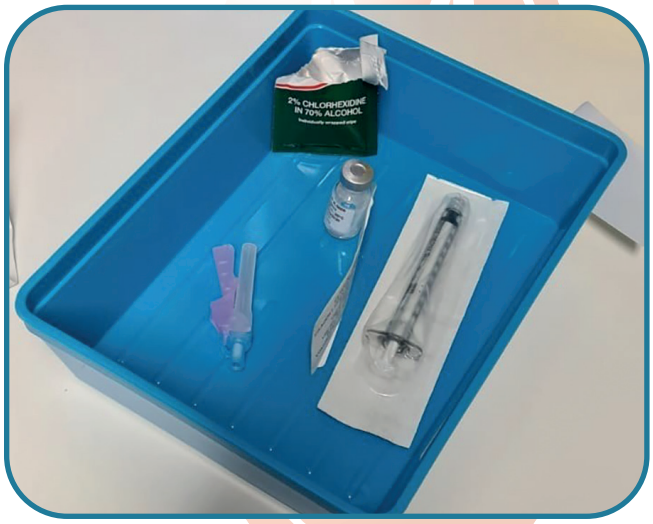
3. Nurse writes details onto label attached to vial (in this example the vial is used for multiple doses).



4. A clean tray is prepared for draw up. The tray has been disinfected using local universal wipes.



5. Nurse draws up the required amount from the vial using the recommended syringe (refer to protocol).

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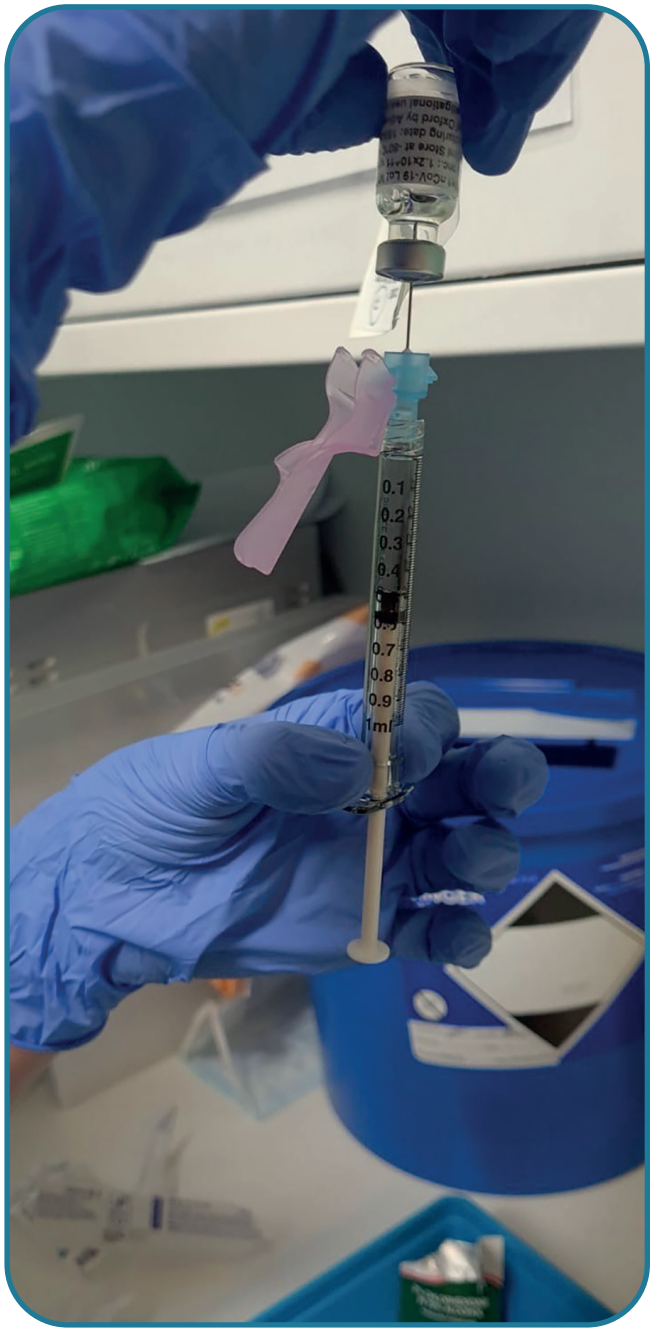
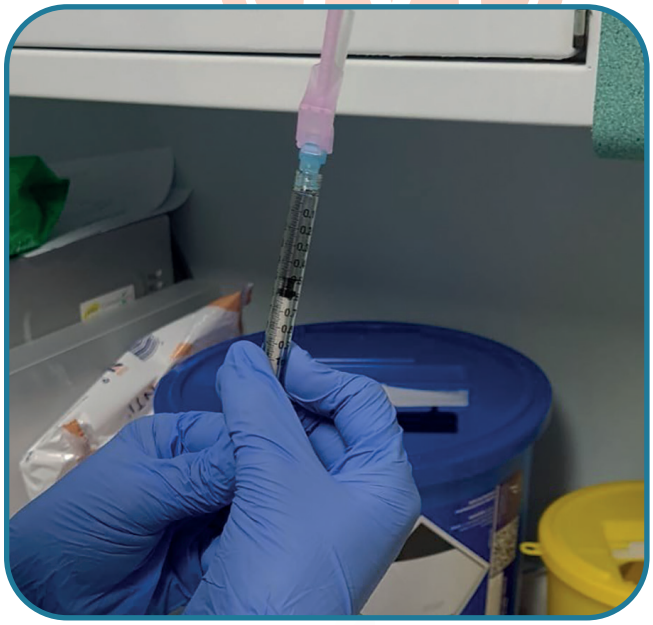
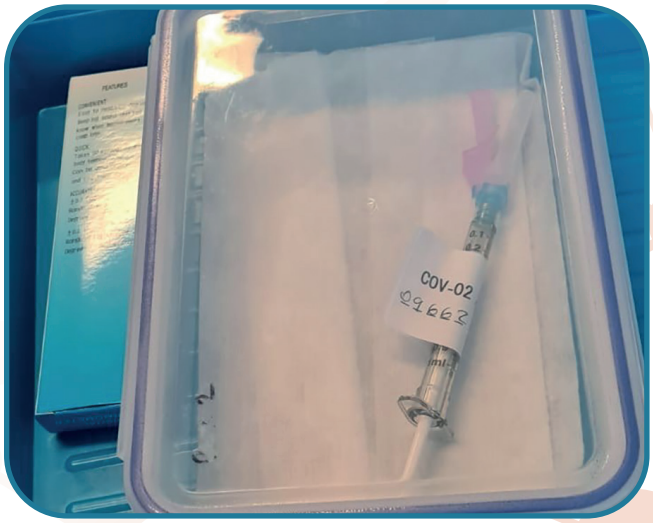
6. The vial may be inverted to maximise usage (does not apply to all products; follow product specific information). Multiple use vials should be returned to the appropriate fridge after the required dose is withdrawn. Single use/empty vials are disposed of in the medicines disposal bin.



7. The nurse checks that the correct volume has been drawn up. Great care must be taken when recapping the syringe to avoid a potential sharps injury. Following preparation work, bench and trays should be disinfected with a virucidal agent (for example Virkon) as per local procedures.



8. The syringe is placed into a safe carrier and transported by suitably trained staff to the nurse who will be carrying out the administration.



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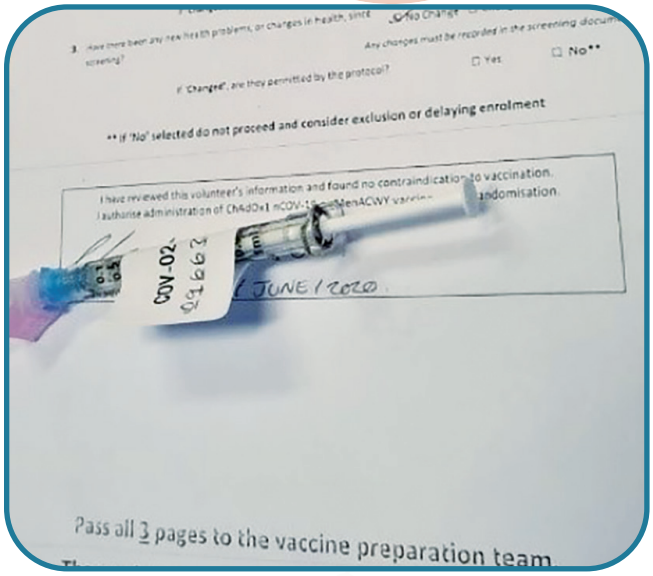
Administration of GMO therapies

9. The administration procedure takes place in an isolated room – no access except to staff directly involved. This may also apply in non COVID-related practice. Be advised by local protocols and procedures or according to trial protocol/ prescription.

10. Pre-procedure observations to be recorded may include: blood pressure, heart rate, temperature. Two nurses need to check details on the prescription and protocol against the syringe and the patient's details.



11. The administration site is cleaned with alcohol wipe. An anaphylaxis pack is to be kept in the room with the patient at all times. A spill kit should also be available nearby. When ready to administer, the needle should be exposed, bevel side up.

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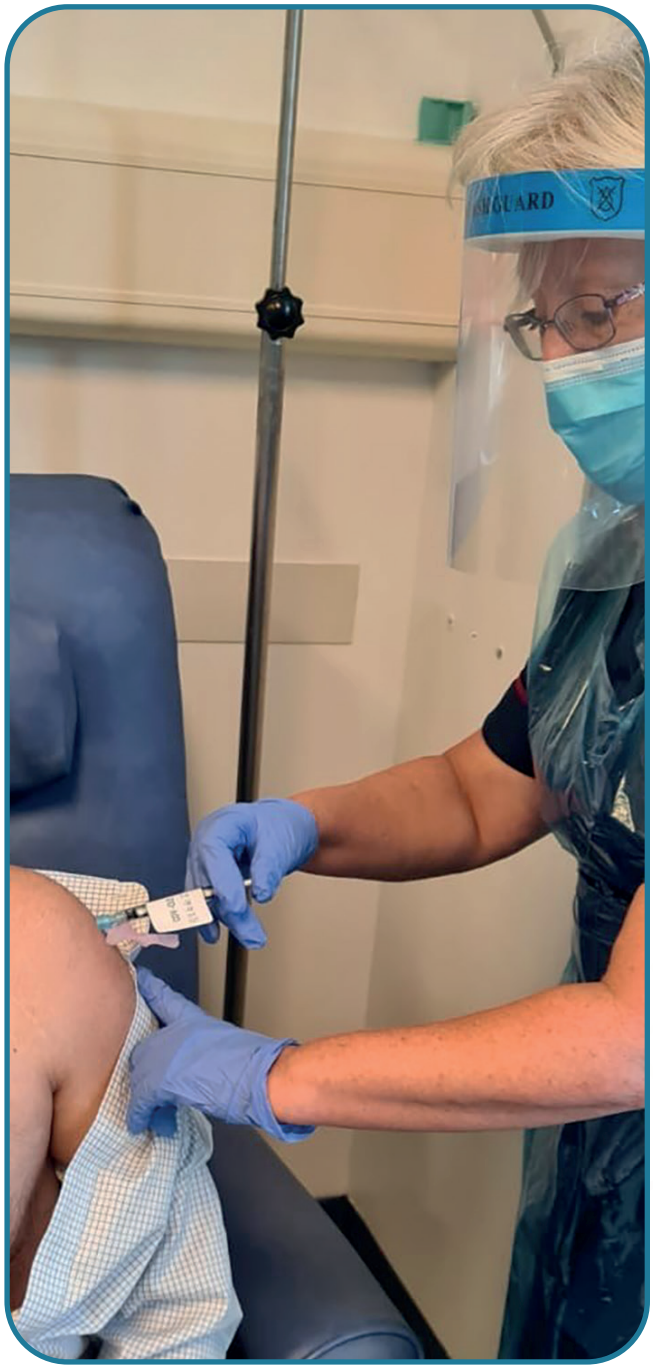
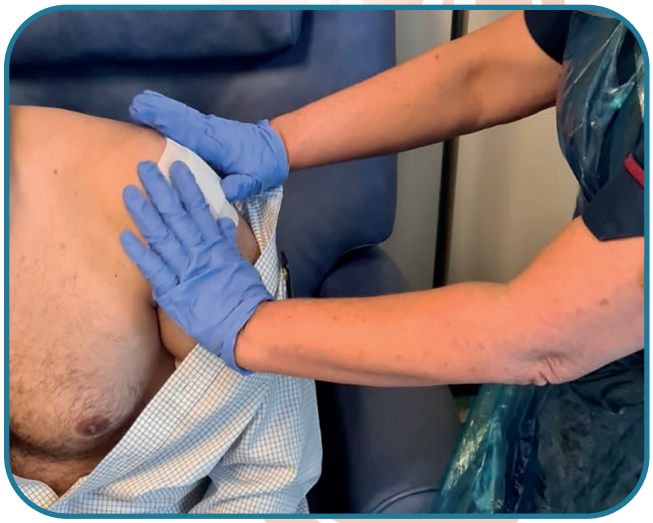
12. GMO is delivered (in this case via IM injection), wearing PPE appropriate to the product. Mask worn due to current COVID-19 measures. Handling of class 1 GMOs usually requires gloves, apron and visor. Some class 2 GMOs may require handling with full sleeved aprons.



13. After administration, the injection site is cleaned with an alcohol swab then covered to prevent shedding of the GMO.



14. Syringe & needle are disposed of in a sharps bin. PPE is disposed of in a bag as per trust protocol. Patient observations are repeated after 15 minutes. Dressing is removed and disposed of in the bag along with PPE. The injection site is checked by the nurse.

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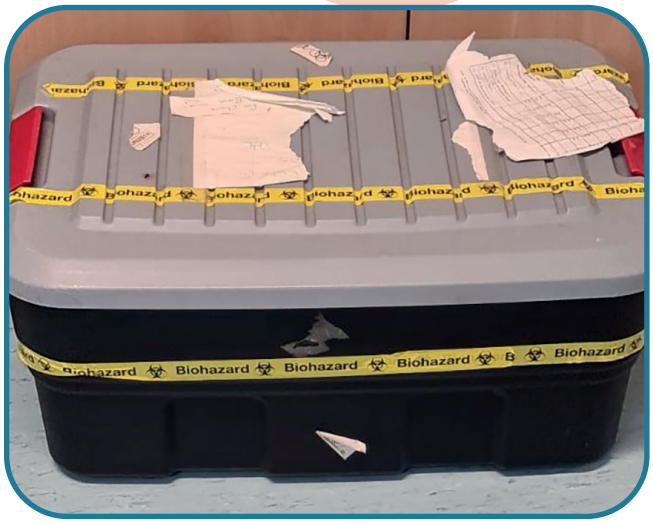
Disposal of GMO therapies

15. The sharps bin is placed into the bag for disposal. The lid of the sharps bin is not fully closed as it may explode in the autoclave. It needs to be open to allow penetration of steam for autoclaving to be fully effective. Air is removed from bag and bag tied off or folded according to local procedures, before placing in a transport case labelled with biohazard tape.

16. In this example, the closed case containing the GMO waste is taken to labs to be autoclaved on-site. There may be other waste disposal options for class I GMO waste that involve sending the waste off-site. Refer to the local GMSC risk assessment.



17. The sealed case is delivered securely to the lab. Care should be taken to take a route avoiding contact with hospital visitors where possible. Signage on the lab door warns of the biohazard.

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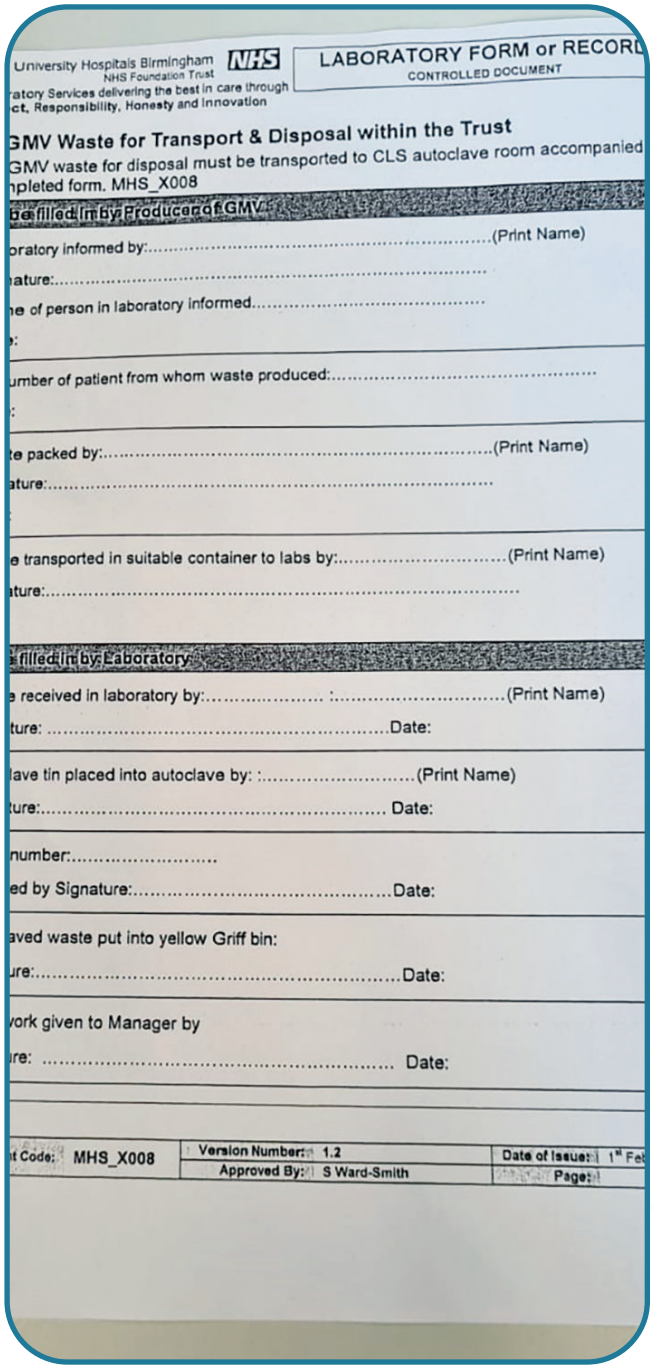
18. GMO waste disposal is fully documented including patient hospital number, staff member responsible for packing the case, and handover to lab staff. Lab staff complete their part and retain the form.



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NHS LABORATORY FORM or RECORD
CONTROLLED DOCUMENT

GMV Waste for Transport & Disposal within the Trust

GMV waste for disposal must be transported to CLS autoclave room accompanied ...npleted form. MHS_X008

...be filled in by Producer of GMV

...oratory informed by:.....(Print Name)
...nature:.....
...me of person in laboratory informed.....
...:
...umber of patient from whom waste produced:.....
...:
...e packed by:.....(Print Name)
...ature:.....
...:
...e transported in suitable container to labs by:.....(Print Name)
...ature:.....

...e filled in by Laboratory

...e received in laboratory by:..... :.....(Print Name)
...ture: .....Date:
...lave tin placed into autoclave by: :.....(Print Name)
...ture:..... Date:
...number:.....
...ed by Signature:.....Date:
...aved waste put into yellow Griff bin:
...ure:.....Date:
...vork given to Manager by
...re: ..... Date:

...t Code: MHS_X008	Version Number: 1.2	Date of Issue: 1st Fe...
	Approved By: S Ward-Smith	Page:

19. The lab technician unpacks the case and places the bags into metal autoclave containers.

20. The containers are shut and placed in the autoclave for inactivation.

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Reflective learning exercise

Consider your responses to the following to check your understanding around GMO therapies. For more information, consult the further reading list below, or speak to your local Genetic Modification Safety Committee (GMSC) or Biological Safety Officer (BSO).

Are you familiar with the four activity classes defined by the GMO regulations? Which is the highest risk, class 1 or class 4?

What do you understand by the term "shedding"? What are the possible implications if a GMO is shed by a patient?

Why might the injection materials, PPE & dressings used for a GMO therapy need to be autoclaved (or otherwise inactivated)?

What is the local policy for dealing with a spill of a GMO?

Further reading

- Health and Safety Executive: What are GMOs? **https://www.hse.gov.uk/biosafety/gmo/whatare.htm**
- Health and Safety Executive: About genetically modified organisms (contained use) **https://www.hse.gov.uk/biosafety/gmo/about.htm**
- Health and Safety Executive: The Genetically Modified Organisms (Contained Use) Regulations 2014. 5th edition, published 2014. **http://www.hse.gov.uk/pubns/books/l29.htm**
- The SACGM Compendium of guidance – Part 6: Guidance on the use of genetically modified microorganisms in a clinical setting **https://www.hse.gov.uk/biosafety/gmo/acgm/acgmcomp/part6.pdf**
- Pan UK Pharmacy Working Group for ATMPs: Requirements for Governance and Preparation of Gene Therapy **https://www.sps.nhs.uk/articles/requirements-for-governance-preparation-of-gene-therapy-pan-uk-pharmacy-working-group-for-atmps/**
- NIHR e-Learning on GMO Vaccines: Governance and Management **https://learn.nihr.ac.uk/course/view.php?id=757**

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