GENE THERAPY - *IN VIVO* GENE THERAPEUTICS – ADMINISTRATION AND HANDLING

PROCEDURE ©

DOCUMENT SUMMARY/KEY POINTS

- The purpose of this procedure is to ensure that *in vivo* gene therapeutics are handled and administered in clinical care settings in compliance with applicable NSW Health and SCHN policies and national regulatory requirements in order to ensure the safety of patients, staff and the environment.
- *In vivo* gene therapeutics must be securely stored under appropriate conditions at all times and personally couriered to the clinical area post-dispensing.
- Staff involved in the handling and administration of *in vivo* gene therapeutics must be trained on the therapy in use, the relevant physical containment (PC) level requirements and be authorised to administer the agent (as applicable). Documented evidence of biosafety training must be available to demonstrate competency. Refer to section on Staff Training.
- All staff involved in the handling and administration of an *in vivo* gene therapeutic must complete and record any occasions of use on the *In Vivo* Gene Therapeutics Administration Log (Appendix).
- The clinical space to be used for administration must be confirmed as appropriate by the treating medical officer in consultation with the responsible Nurse Unit Manager (NUM) or Delegate, with consideration of the patient's condition/care needs, risks associated with the use of the *in vivo* gene therapeutic, risks to other patients or staff and requirements for local storage or reconstitution and access to equipment/supplies.
- Prior to administration, *in vivo* gene therapeutics must be checked in accordance with the SCHN Practice Guideline 2020-043 – Medication Administration.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1st April 2021	**Review Period**: 3 years
Team Leader:	Nurse Unit Manager	**Area/Dept**: Kids Research CHW

Date of Publishing: 8 October 2021 11:47 AM Date of Printing: 8 October 2021

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- Patient and family verbal and/or written education must be delivered by the treating medical officer or delegate prior to administration of the *in vivo* gene therapeutic.
- Personal Protective Equipment (PPE) must be worn as per the requirements for the Therapy.
- A spill kit, appropriate for the therapy in use, must be accessible at all times.
- Two fully qualified staff must remain present until administration of the *in vivo* gene therapeutic has commenced. A medical officer should be present for the first 15 minutes of administration. At least one qualified nursing staff member must remain with the patient during administration for observation of any reaction and vital sign changes.
- *In vivo* gene therapeutics should be administered within 'normal working hours' wherever possible when a full range of specialist expertise, knowledge and support is readily accessible. If not possible to administer during these hours, please ensure appropriate staff will be available to escalate through should they be needed. Administration should take place in a low-foot-traffic area to minimize risk of error and interruption.
- All post-administration care, including requirements for PPE, should follow standard clinical care practices, unless the medical officer nominates that additional safeguards are necessary to protect patients, staff and the environment, in accordance with the Product Information (PI) or equivalent.
- *In vivo* gene therapeutics and all exposed disposable products are to be managed as described in SCHN Procedure – Transport, Waste & Spill Management of Medicinal Products containing GMOs (*Document currently in draft*), unless otherwise specified.

CHANGE SUMMARY

- N/A – New Document
- **8/10/2021** Minor changes:
  - Details added to staff training, product labelling, PPE requirements, and exposure records.
  - Title changed for consistency other Gene Therapy documents and references to related documents added.

READ ACKNOWLEDGEMENT

- **Training/Assessment Required** – Staff responsible for the direct management and care of patients receiving *in vivo* gene therapeutics must read and acknowledge this Procedure, and be trained in the specific requirements of the therapy.
- **All staff handling of *in vivo* gene therapeutics should read and adhere to OGTR mandated training when required**
- All Registered Nurses and Enrolled Nurses employed by SCHN must successfully complete the Mandatory eLearning 'Fundamentals of paediatric medication safety' found in My Health Learning before they can check or administer medications.
- All nursing staff working with *in vivo* gene therapeutics should read and acknowledge NSW Health Policy – Medication Handling in NSW Public Health Facilities.
- Medical staff and Pharmacists should read this document, SCHN 'Medication Administration' ePolicy and NSW Health Policy – Medication Handling in NSW Public Health Facilities.

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Purpose/Scope

The purpose of this procedure is to ensure that *in vivo* gene therapeutics are handled (including transferred/transported) and administered in compliance with applicable NSW Health and SCHN policies and national regulatory requirements in order to ensure the safety of patients, staff and the environment.

The requirements of this Procedure are applicable regardless of whether the *in vivo* gene therapeutic is being used for investigational (e.g. research) or non-investigational (standard of care) purposes and regardless of the regulatory mechanism used to access the therapeutic (e.g. CTA, SAS, CAS, LSDP, Formulary). In all cases, requisite approvals (e.g. HREC/RGO, SCHN Drug Committee/TGA, OGTR) must be obtained prior to the sourcing and use of *in vivo* gene therapeutics in clinical care settings.

Procedures for pharmacy in relation to the receipt, storage, accountability and reconstitution of *in vivo* gene therapeutics (if applicable) are outside the scope of this document. Contact Pharmacy directly for further information if required.

The Procedure must be followed by all staff involved in the handling and administration of *in vivo* gene therapeutics at SCHN. Additionally, staff who are directly involved in handling and administration must acquire and maintain biosafety training appropriate for the therapeutic.

Background

In vivo gene therapeutics are novel, complex and technical products which aim to provide new possibilities for patients with chronic and often fatal conditions. Gene therapy seeks to modify or introduce genes into a patient's body with the goal of durably treating, preventing or potentially even curing disease. *In vivo* gene therapeutics are rapidly developing and may introduce new risks to patients, staff and the environment.

Due diligence must be applied in ensuring that the treating medical officer and care team are aware of the unique profile of the *in vivo* gene therapeutic in use, including any additional safeguards necessary to protect patients, staff and the environment, as defined by the Product Information (PI) or equivalent[1].

In vivo gene therapeutics generally consist of a vector or delivery formulation/system containing a genetic construct engineered to encode a specific therapeutic sequence or protein responsible for the regulation, repair, addition or deletion of a genetic sequence. The active substance is the nucleic acid sequence(s), or genetically modified microorganism(s) or cells. The active substance may be composed of multiple elements.

[1] The type of information available for therapies will vary in accordance with current marketing authorisation/status (e.g. whether it is experimental being administered in the context of clinical research or approved for a given indication). Such information may be in the form of Product Information (PI), Consumer Medicine Information (CMI), Investigator Brochure (IB) and/or Summary of Product Characteristics (SPC).

Staff Training

- Staff involved in the handling and administration of *in vivo* gene therapeutics must be trained on the therapeutic product in use, requirements for working with Genetically Modified Organisms (biosafety training) and be authorised to administer the agent (as applicable). Documented evidence of training must be available to demonstrate competency. Specific biosafety training can be arranged through the Kids Advanced Therapeutics Program Manager.
- In addition, all staff involved in the handling and administration must complete and record any occasions of preparing, handling and/or administering the therapy on the SCHN *In Vivo* Gene Therapeutics Administration Log (Appendix).
- All SCHN medication handling and administration policies must be read and acknowledged by any staff members involved in such actions.

Patient and Family Education

- Patient and family verbal and/or written education must be delivered by the treating medical officer or delegate prior to administration of *in vivo* gene therapy.
- Any education provided to the patient and family must be clearly documented, along with the consent process, in the patient's medical record.
- Education must include:
  - *In vivo* gene therapy - specific information
  - Concomitant medications and fluids
  - Treatment protocol and cycle of treatment (if applicable)
  - Potential side effects and symptom management (acute and chronic)
  - Potential environmental risks related to the *in vivo* gene therapy (e.g. shedding)
  - Waste management (if applicable)
  - Who and when to contact post hospital admission if symptoms/concerns arise
- Patients, parents and/or family members should be provided with an *in vivo* gene therapy record, which includes details of product administration, and contact details of the treating medical officer should the patient receiving the therapy need care in a facility unfamiliar to their medical history.

Procedure

Transfer/Transit

- On notification of dispensing by Pharmacy, the *in vivo* gene therapeutic must be personally couriered by appropriately trained staff to the clinical space to be used for administration of the agent. These agents are currently prepared in a biosafety cabinet at CHW by CHW Pharmacy.
- *In vivo* gene therapeutics must be stored under appropriate conditions as indicated by individual providers at all times during transfer/transit. A key condition is maintenance within a defined temperature range.
- A chain of custody that enables the therapy to be tracked from the point of collection to delivery to the clinical care setting must be maintained at all times by the CHW pharmacy personnel.
- Transfer/transit of the therapy must only occur once the timing of administration of the agent has been confirmed by the medical officer or delegate, in order to avoid any prolonged storage in the clinical space being used for administration.
- *In vivo* gene therapeutics must be packaged and transported in compliance with all requirements of the OGTR - Guidelines for the Transport, Storage and Disposal of GMOs.
- In the event of an incident during transfer/transit, such as the therapy being dropped, crushed, or involved in a collision follow requirements of OGTR and the SCHN Procedure – Transport, Waste & Spill Management of Medicinal Products containing Genetically Modified Organisms.

Clinical Space

- The clinical space to be used for administration must be confirmed as appropriate by the treating medical officer in consultation with the responsible Nurse Unit Manager (NUM) or delegate.
- Consideration should be given to the patient's condition/care needs, any risks associated with the use of the *in vivo* gene therapeutic (including for management of adverse events and/or containment), any requirements for storage or reconstitution in the clinical care setting and access to the necessarily equipment/supplies.
- Due to the risk of acute systemic reaction including anaphylaxis it is required that appropriate resuscitation equipment and medication is readily available by the bedside throughout the entire administration process and post-administration observation period.
- On receipt, the *in vivo* gene therapeutic must be clearly labelled and stored securely in the medication room of the clinical care space preferably in a secure locked cabinet or fridge (if appropriate) when not immediately being administered. No medication is to be left at the bedside.

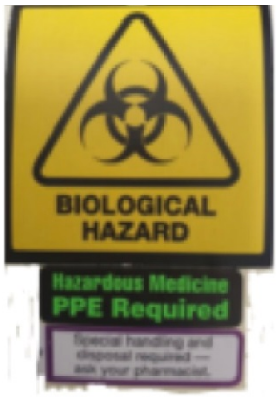
- Any preparation for administration of the *in vivo* gene therapeutic in the clinical care setting must occur:
  - on a medication trolley away from distractions,

    and
  - maintaining an aseptic field when required

    and
  - only by the staff administering with the second checker.

Preparation

- Prior to consent and administration of the gene therapeutic, the specific product must be approved by the appropriate committees including ethics and governance for clinical trial therapeutics, or IPU/formulary approval in a standard of care setting.
- Ensure that the *in vivo* gene therapeutic is checked in accordance with the SCHN Practice Guideline 2020-043 – Medication Administration.
- Gene therapy products will be prepared in aseptically in pharmacy and delivered to the ward area in accordance with any OGTR requirements. Ensure pharmacy is contacted at least 48 hours in advance prior to gene therapy administration to allow for preparation.
- Gene therapy products will be labelled as biohazardous with appropriate stickers identifying them as requiring special precautions when handing and administering. Stickers include:



In Vivo Gene Therapy Administration

- Perform hand hygiene and don PPE as per SCHN guidelines and/or specific product requirements. PPE must include, but is not limited to:
  - A long sleeve gown
  - Gloves
  - Protective eye wear: This can be goggles or protective eyewear with side shields or visors if available
  - Enclosed footwear.

- Ensure long hair is tied back.
- Use a closed system transfer device (CSTD) *where possible* when administering and handling biohazardous medication. Where it is not advised to use a CSTD by the product manufacturer, a risk assessment should be performed in consultation with the institutional biosafety committee.
- Two qualified staff must check the prescribed *in vivo* gene therapy in accordance with the SCHN Practice Guideline 2020 043 – Medication Administration and remain present until the administration has been commenced. Qualified staff members include accredited registered nurses or medical officers. At least one checker must be an RN (Year 2 – 8th year thereafter). A qualified medical officer must remain present for at least 15 minutes for observation of any reaction and vital sign changes, while a qualified nurse must remain with the patient until the administration is completed, unless otherwise specified.
- If not already present, notify the treating medical officer that the infusion is about to commence and ensure that they will be present for the first 15 minutes of the infusion.
- Ensure emergency drug calculations for resuscitation are readily available and emergency medications are prepared and at the bedside should a reaction occur.
- Where an infusion or a syringe pump is used to administer a medication the settings must be checked by a second person.
- *In vivo* gene therapies should be administered within 'normal working hours' when a full range of specialist expertise, knowledge and support is readily accessible. If this is not possible, please ensure appropriate staffing is available should you need to escalate care in an emergency.
- Administration should take place in a low-foot-traffic area to minimize risk of error and interruption.
- All equipment used by the bedside for administration should be cleaned, taken away or discarded appropriately at the end of the procedure. Refer to SCHN Procedure – Transport, Waste & Spill Management of Medicinal Products containing Genetically Modified Organisms.
- It is the expectation that all interventions and clinical assessments are documented clearly in the patient's medical record as per SCHN policy 2016-9052 – Clinical Procedure Safety.

Post-Administration

- All post-administration care, including requirements for PPE, should follow standard clinical care practices, unless the treating medical officer nominates that additional safeguards are necessary to protect patients, staff and the environment, in accordance with the PI or equivalent.
- All staff involved in post-administration care must to be aware of potential risks associated with the *in vivo* gene therapy including side effects and any

notification/escalation pathways applicable. Education resources should be provided prior to assuming care of the patient.

- Any educational resources available should be uploaded to the patient's medical record for easy reference.
- Gene therapy contains GMOs which are used to deliver the therapeutic gene to the patient. The GMO is a viral vector which can be found in bodily fluids for up to 30 days after treatment. This includes vomiting, saliva, urine and faces. Exposure may occur through;
  - removing or inserting catheters
  - handling vomitus, blood, excreta, or fluid drained from body cavities
  - handling bedpans, urinals, emptying urinary catheter bags, colostomy or urostomy
  - vomit bags, wet nappies and incontinence pads, and wet dressing materials
  - handling bed linen or clothing soiled with a patient's waste, or potentially contaminated with the medication
- Staff should wear gloves and follow hand hygiene procedures when handling bodily fluids until 30 days post the gene therapy administration. Appliances that may be contaminated with patient bodily fluids, such as disposable nappies, should be placed into biohazard waste bags which are then tied and discarded of in a clinical waste bin.

Waste Management

- Refer to SCHN Procedure – Transport, Waste & Spill Management of Medicinal Products containing Genetically Modified Organisms.
- Waste should be managed in accordance with the SCHN Policy, unless the treating physician nominates that additional safeguards are necessary to protect patients, staff and the environment, or in accordance with any licencing requirements, the PI or Protocol (for therapies used as part of clinical research).

Spill Management

- A biological spill requires immediate management and must be effectively controlled so as to avoid unnecessary contamination of the environment.
- Ensure that a spill kit, appropriate for the *in vivo* gene therapeutic in use, is accessible in the clinical space at all times.
- Biological spill kits should accompany the product from the point of pharmacy dispensing through to treatment administration in the clinical area.
- In the event of a spill or other incident, pre-, during or post-administration, ensure that the appropriate spill kit is immediately accessed and used.

- Follow the SCHN Procedure – Transport, Waste & Spill Management of Medicinal Products containing Genetically Modified Organisms for detailed information on how to manage spills.
- Ensure that the SCHN Practice Guideline 2006-8324 – Incident Management requirements are followed.

Records of Staff Exposure

- Exposure Records are to be maintained by individual staff members at the time of administration of a hazardous medication. This is done by manual data entry (see appendix 1) using a paper based form.
- On resignation, a copy of the exposure records is available to the exiting staff member on request.
- Biohazardous therapeutic spills or spill equivalents must be reported in IMS+. A spill equivalent event is generally defined as a spill of a substance (i.e. patient waste (vomit, urine, blood, faeces)) that may be contaminated with hazardous medication, and should be managed with a spill kit and full PPE.
- Exposure incidents to hazardous medications must be reported in ims+ and a copy saved in the staff members' personnel file.

Appendices

SCHN In Vivo Gene Therapy Administration Log

Abbreviations

CAS	Compassionate Access Scheme
CHW	The Children's Hospital at Westmead
CMI	Consumer Medicine Information
CSTD	Closed System Transfer Device
CTN	Clinical Trial Notification
CTA	Clinical Trial Approval
EMA	European Medicines Agency
GMO	Genetically Modified Organism
HREC	Human Research Ethics Committee
IB	Investigators Brochure
IBC	Institutional Biosafety Committee

IPU	Individual Patient Use
LSDP	Life Saving Drugs Program
NSW	New South Wales
OGTR	Office of the Gene Technology Regulator
PC	Physical Containment
PI	Product Information
RGO	Research Governance Office
SAS	Special Access Scheme
SCH	Sydney Children's Hospital
SCHN	Sydney Children's Hospitals Network
SmPC	Summary of Product Characteristics
TGA	Therapeutic Goods Administration

References

1. CHW Practice Guideline - Medication Management and Handling - http://webapps.schn.health.nsw.gov.au/epolicy/policy/603
2. EMA - Guideline on the Quality, Non-Clinical and Clinical Aspects of Gene Therapy Medicinal Products [EMA/CAT/80183/2014] - https://www.ema.europa.eu/en/documents/scientific-guideline/draft-guideline-quality-non-clinical-clinical-aspects-gene-therapy-medicinal-products_en.pdf
3. EMA – Guideline on Safety and Efficacy Follow-Up and Risk Management of Advanced Therapy Medicinal Products [EMEA/149995/2008] - https://www.ema.europa.eu/en/guideline-safety-efficacy-follow-risk-management-advanced-therapy-medicinal-products
4. OGTR - Guidelines for the Transport, Storage and Disposal of GMOs - http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/tsd-guidelines-toc
5. SCHN Policy 2016-9052 – Clinical Procedure Safety -
6. http://webapps.schn.health.nsw.gov.au/epolicy/policy/5134
7. SCHN Policy 2018-180 – Environmental Cleaning - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4606
8. SCHN Policy 2013-9044 – Incident Management Policy - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4936
9. SCHN Policy 2017-157 - Infection Prevention and Control - Isolation and Transmission Based Precautions - http://webapps.schn.health.nsw.gov.au/epolicy/policy/3730
10. SCHN Policy 2013-9042 – Infection Control – NSW Ministry of Health - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4427
11. SCHN Policy 2014-9027 - Medication Handling in NSW Public Health Facilities - http://webapps.schn.health.nsw.gov.au/epolicy/policy/3263
12. SCHN Policy 2016-9029 - Personal Protective Equipment for Infection Control - http://webapps.schn.health.nsw.gov.au/epolicy/policy/2609
13. SCHN Policy 2015-9070 – Waste Management - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4701
14. SCHN Practice Guideline 2013-9031 – Hand Hygiene - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4806
15. SCHN Practice Guideline 2006-8324 – Incident Management - http://webapps.schn.health.nsw.gov.au/epolicy/policy/3795
16. SCHN Practice Guideline 2020-043 – Medication Administration - http://webapps.schn.health.nsw.gov.au/epolicy/policy/5024

17. SCHN Procedure 2018-183 – Accountable Medicines Lost or Stolen Report Procedure - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4269
18. SCHN Procedure 2017-226 – Accountable Medicines Audits - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4167/
19. SCHN Procedure - 2019-139 – Clinical Research – Investigational Medicinal Product Accountability - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4631
20. SCHN Procedure 2019-150 - Clinical Research - Investigational Medicinal Product (IMP) Destruction - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4627
21. SCHN Procedure 2019-140 – Clinical Research – Investigational Medicinal Product (IMP) Preparation and Dispensing - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4632/
22. SCHN Procedure 2019-143 – Clinical Research – Investigational Medicinal Product (IMP) Receipt and Storage - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4628
23. SCHN Procedure 2019-144 – Clinical Research – Investigational Medicinal Product (IMP) Temperature Monitoring - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4634/
24. SCHN Procedure 2019-028 – Clinical Research – Staff Roles and Responsibilities - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4624
25. SCHN Procedure 2019-027 - Clinical Research - Staff Qualifications and Training Records - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4623
26. SCHN Procedure - Transport, Waste & Spill Management of Medicinal Products containing Genetically Modified Organisms – *(Document currently in draft)*
27. TGA - The Australian Regulatory Guidelines for Biologicals (ARGB) - https://www.tga.gov.au/publication/australian-regulatory-guidelines-biologicals-argb

Appendices

IN VIVO* GENE THERAPEUTIC ADMINISTRATION LOG									
Name				**Employee Number**					
Department									
EXPOSURE LOG								**CHECKED BY**	
Date *(DD-MMM-YY)*	**Product**	**Dosage** *(Strength/Form)*	**Route of Administration**	**Exposure Time** *(24HR)*	**Activity**	**PPE Used**	**Signature**	**Signature**	**Date** *(DD-MMM-YY)*

*All staff involved in the handling and administration must complete and record any occasions of preparation and administration on the SCHN *In Vivo* Gene Therapeutic Administration Log