Sheffield Teaching Hospitals NHS
NHS Foundation Trust

STANDARD OPERATING PROCEDURE

Study Specific STH 21413

SOP for drug preparation, vaccination procedures (including management of anaphylaxis) and waste management for the following study: A phase II/III study to determine the efficacy, safety and immunogenicity of the candidate coronavirus disease (COVID-19) vaccine ChAdOx1 nCoV-19 (COV002).

SOP Number	STH21413 -01	**Version Number**	2.5
Effective Date	21 Aug 2020	**Author**	Ruth Payne Helen Bowler Gail Mills
Related SOPs	OVC099 COV002 Vaccine Preparation and Storage (University of Oxford Sponsor SOP)		

Approved by (name & role)	Dr Thomas Darton Principal Investigator		**Date**: 20 Aug 2020

Standard Operating Procedure for drug preparation, vaccination procedures (including management of anaphylaxis) and waste management for the following study: A phase II/III study to determine the efficacy, safety and immunogenicity of the candidate coronavirus disease (COVID-19) vaccine ChAdOx1 nCoV-19 (COV002)

This SOP has been written to give study specific guidance to study personnel completing study visits for STH 21413, which is a Phase II/III participant-blinded individually randomised controlled trial to determine the efficacy, safety and immunogenicity of ChAdOx1 nCoV-19 vaccination regime in healthy volunteers at risk of COVID-19. ChAdOx1 nCoV-19 is a genetically modified organism (GMO) and therefore specific procedure relating to management of GMOs will be detailed in this SOP. A GMO risk assessment has been completed for this study with approval for use of ChAdOx1 nCoV-19 given by the local Gene Therapy Research Therapy Safety Group.

Background

This SOP has been produced in accordance with Medicines for Human Use (Clinical Trials) Regulations 2004 and amendments, ICH GCP and The Health Technical Memorandum (HTM 07-01 – Safe Management of Heath care Waste).

This SOP will describe the process of receiving, preparing, administrating and safely disposing of the IMP relating to STH21413. It will also cover procedures to be followed in case of anaphylaxis following vaccination with either the IMP or control vaccine.

Participants will be enrolled and those randomised to IMP will receive a single dose of ChAdOx1 nCoV-19 administered via intramuscular injection at Day 0. Those randomised to the control arm of the study will receive a single dose of the licensed MenACWY vaccine.

Study Vaccines

The IMP is made up of a replication-deficient virus: a type of common cold virus called chimpanzee adenovirus Ox1, or “ChAdOx1”. The virus expresses the structural surface glycoprotein (Spike protein) antigen of the SARS CoV-2 (nCoV-19), with a leading tissue plasminogen activator (tPA) signal sequence.

The ChAdOx1 (Adv Y25 serotype) viral vector is replication deficient as the essential E1 gene region has been deleted so the virus can only propagate in cells expressing E1 functions. The virus is unable to replicate within vaccinated animals or humans.

Spike protein (S) is a type I, trimeric, transmembrane protein located at the surface of the viral envelope, giving rise to spike shaped protrusions from the virion. The S protein’s subunits are responsible for cellular receptor ACE-2 binding via the receptor-binding domain and fusion of virus and cell membranes, thereby mediating the entry of SARS-CoV-2 into the target cells. The S protein has an essential role in virus entry and determines tissue and cell tropism, as well as host range. The roles of the S protein in receptor binding and membrane fusion make it a perfect target for vaccine and antiviral development. ChAdOx1 nCoV-19 expresses a codon-optimised coding sequence for Spike protein from the SARS-CoV-2 genome sequence accession MN908947.

ChAdOx1 nCoV-19 is a genetically modified product and falls under specific regulations. Genetic modification means any alteration of the genetic material of an organism (i.e. DNA or RNA), which does not occur naturally (by mating or recombination) according to the

Genetically Modified Organisms (Contained Use) Regulations (2014). GMO's are assigned a risk classification from 1 – 4, 1 being the lowest risk. The risk classification then correlates to the level of containment required. In this study, the cells are classified as Class 1, requiring containment level 1 for clinical waste.

According to the Health Technical Memorandum (HTM) 07-01 – Safe Management of Health care Waste 2013 Clinical Waste which contains level 1 GMO's should be inactivated by validated means (e.g. disposal via the Trust orange sack disposal route). All staff that come into contact with products containing GMOs should be aware of their use.

Participants who are allocated to the control groups will receive one or two injections of MenACWY vaccine instead of ChAdOx1 nCoV-19. Either of the two licensed quadrivalent protein -polysaccharide conjugate vaccine MenACWY vaccines will be used, i.e.:

- Nimenrix (Pfizer). The licensed posology of this vaccine for those over 6 months of age is a single (0.5ml) intramuscular dose, containing 5mcg each of *Neisseria meningitidis* group A, C, W and Y polysaccharide, each conjugated to 44 mcg tetanus toxoid carrier protein.
- Menveo (GlaxoSmithKline). The licensed posology of this vaccine for those 2 years of age and over is a single (0.5ml) intramuscular dose, containing
    - 10 mcg meningococcal group A polysaccharide, conjugated to 16.7 to 33.3 mcg *Corynebacterium diphtheriae* CRM_{197} protein
    - 5mcg meningococcal group C polysaccharide, conjugated to 7.1 to 12.5 mcg *C. diphtheriae* CRM_{197} protein
    - 5mcg meningococcal group W polysaccharide, conjugated to 3.3 to 8.3 mcg *C. diphtheriae* CRM_{197} protein
    - 5mcg meningococcal group Y polysaccharide, conjugated to 5.6 to 10.0 mcg *C. diphtheriae* CRM_{197} protein

The summary of product characteristics for both vaccines allows for administration of a booster dose if indicated by ongoing risk, therefore allows for the two doses administered to a subset of participants in this study. Similarly, previous receipt of either vaccine (or a plain polysaccharide quadrivalent meningococcal A, C, W and Y vaccine) will not be a contraindication to receiving a further vaccine in this study.

Participants will be blinded as to which injection they are receiving.

Procedure for collecting the active IMP (ChAdOx1 nCoV-19) and Vaccine Accountability

a) Where the ChAdOx1 nCoV-19 batch requires freezer storage

The ChAdOx1 nCoV-19 vaccine will be stored at a nominal temperature of -80°C (+/- 20°C) in a secure freezer in the CRF. Where possible, vaccines will be stored in a secure freezer which does not also house any biological samples. Where this is not possible, vaccines will be stored in the freezer within a sealed rigid box and biological samples being stored in the same freezer will be stored in a different compartment within the freezer and will be double-bagged to reduce the chance of contamination. Vaccines for the clinic session (morning or afternoon) will be transported in a sealed rigid box from the freezer to the vaccine preparation room, where they will be stored at 2 - 8°C in a temperature-monitored fridge. These vials will be documented as removed from the freezer in the ChAdOx1 nCoV-19 primary accountability log. Any vaccines distributed to a vaccine preparation area will be recorded as transferred out from the primary log and into the secondary log, with the same Date/Time details recorded on both logs.

Any member of staff handling the vaccine vials must wear gloves. The IMP will remain in the sealed rigid box within the fridge at all times until ready for dilution/ administration. The IMP will be checked by two qualified research nurses against the prescription, participant and vaccine administration source document before administration, as per STH medicines management policy. The ChAdOx1 nCoV-19 vials are multi-use vials requiring dilution with sterile, refrigerated normal saline for injection as per Sponsor SOP OVC099. This dilution step will be carried out in a mixing vial, a dilution label will be applied to the vial. After withdrawal of a dose of IMP, the mixing vial will be placed into the fridge between uses, also in a sealed box. Each vial transferred to the vaccine preparation room will be documented on the IMP-specific secondary accountability log, and each dose used will be documented on the IMP-specific multi-dose accountability log.

Any unused vaccine remaining in the vial at the end of the clinic session, or if the time since removal from the freezer exceeds 5.5 hours, or if the vial has been left at room temperature for more than an hour before use, will be discarded into a purple-lidded yellow sharps bin and this will be documented on the secondary accountability log.

Transfer of vaccine between sites

Vaccine may be transferred between RHH and NGH sites where necessary to permit sufficient vaccine to be available for the participants attending for vaccination. This process will be carried out in accordance with the Sponsor SOP relating to the IMP.

Vials for a clinic session will be allocated from either RHH or NGH CRF freezer and transported to the CRF at the other site where they can be stored at 2.- 8°C for a maximum of 5.5 hours from leaving the freezer. These vials will be documented as removed from the freezer in the relevant ChAdOx1 nCoV-19 primary accountability log. Any vaccines distributed to a vaccine preparation area will be recorded as transferred out from the primary log and in to the relevant secondary log, with the same Date/Time details recorded on both logs. Any member of staff handling the vaccine vials must wear gloves.

A designated study staff member will collect the vials from RHH or NGH CRF in a wipe-clean sealed rigid box, inside a temperature-monitored validated/approved coolbox which has been prepared for this transfer by either RHH Pharmacy or NGH Pharmacy. This person will then transport the IMP to the cross site CRF in a vehicle under appropriate pre-arranged insurance.

Once in the CRF the IMP will be transferred to the designated temperature-monitored fridge in the vaccine preparation room as per relevant above processes.

b) Where the ChAdOx1 nCoV-19 batch requires refrigerated storage

The ChAdOx1 nCoV-19 vaccine will be stored in refrigerated storage (2-8°C) in a secure location in the pharmacy at both RHH and NGH sites.

On vaccination days, vials for a clinic session (either morning or afternoon) will be allocated from pharmacy and transported to the CRF at the Royal Hallamshire (O floor) or NGH site where they will be stored at 2- 8°C under temperature monitored conditions in a designated fridge. Any member of staff handling the vaccine vials must wear gloves. The vials may be transferred to the CRF by either CRF or Pharmacy staff will transfer the vials from pharmacy in a wipe-clean sealed rigid box, inside a temperature-monitored approved cool-box. This person will then transport the IMP to the CRF. These vials will be documented as removed from the storage in pharmacy in the ChAdOx1 nCoV-19 primary accountability log and documented as received by the CRF for ongoing refrigerated storage prior to use in the secondary accountability log.

Once in the CRF the IMP will be transferred to the designated temperature-monitored fridge in the vaccine preparation room. The IMP will remain at all times in the sealed, rigid box until ready to be drawn. No dilution is required.

Each vial to be prepared ready for dosing will be documented on the IMP-specific secondary accountability log, and an IMP specific tertiary accountability log started. A multidose vial label must be applied. Each dose used will be documented on the IMP-specific multi-dose accountability log. Any unused vaccine remaining in the vial at the end of the time period permitted for IMP storage after first use as specified in the Sponsor vaccine preparation SOP will be discarded into a purple-lidded yellow sharps bin, and this will be documented as required by the Sponsor.

After withdrawal of a dose of IMP, the vial will be placed in a sealed, labelled box and may be stored at room temperature between uses up to the maximum time period specified by the Sponsor. The IMP will be checked by two qualified research nurses against the prescription, participant and vaccine administration source document before administration, as per STH medicines management policy.

Transfer of vaccine between sites

Vaccine may be transferred between RHH and NGH sites where necessary to permit sufficient vaccine to be available for the participants attending for vaccination. This process will be carried out in accordance with the Sponsor SOP relating to the IMP.

Vials for a clinic session will be allocated from either RHH or NGH pharmacy and transported to either the CRF or the pharmacy at the other site depending on whether the vials are needed for immediate use, where they can be stored at 2.- 8°C in the relevant designated temperature-monitored fridge or cold storage. These vials will be documented as removed from the pharmacy in the relevant ChAdOx1 nCoV-19 primary accountability log and recorded as received on the relevant log in either the pharmacy or CRF. Any member of staff handling the vaccine vials must wear gloves.

A designated study staff member will collect the vials from RHH or NGH CRF in a wipe-clean sealed rigid box, inside a temperature-monitored validated/approved coolbox which has been prepared for this transfer by either RHH Pharmacy or NGH Pharmacy. This person will then transport the IMP to the cross site CRF in a vehicle under appropriate pre-arranged insurance.

Procedure for collecting the control vaccine (MenACWY) (both sites) and Vaccine Accountability

A primary vaccine accountability log of MenACWY will be maintained in pharmacy at each trial site. MenACWY will be stored in a locked (or access controlled) refrigerator (2°C – 8°C), as per the SmPC. Vials for each clinic session (morning or afternoon) will be transferred from pharmacy to the CRF at either the RHH or NGH sites in an approved temperature-monitored cool-box. Once received in the CRF they will be stored in a temperature-monitored fridge in the vaccine preparation room. All uses of the MenACWY vaccine will be documented on the secondary vaccine-specific accountability log. Any doses of vaccine that are unused at the end of a clinic session can be kept in the fridge for use in the next clinic session. Vaccine preparation rooms will have limited swipe card access so will remain locked overnight, in addition to the fridge being locked. Any vaccine that is wasted or discarded will also be logged.

Vaccination procedure

1. Ongoing consent and eligibility, including all pre-vaccination procedures as detailed in the protocol will be carried out, and a prescription completed prior to randomisation, as well as the COV002 vaccine record form (supplied by the Sponsor).
2. On receipt of the participant's prescription and vaccine record form, the vaccine preparation nurse will access REDCap to randomise the participant to receive either the IMP or control vaccine.
3. The allocated vaccine will be prepared by the vaccine preparation nurse and administering nurse in the vaccine preparation room.

Preparation of vaccines

At both sites, preparation of the IMP and the MenACWY control vaccine will take place in the vaccine preparation room, to ensure blinding of participants is maintained and wastage of vaccine is limited. Anyone handling the vaccines must wear gloves.

Equipment required may include the following, depending on the batch of IMP in use:

- Sharps bin with lid
- Disinfectant and cleaning cloths (Tristel fuse- can also be used in case of spillage)
- Aprons
- Gloves
- Eye protection
- Clean, sealable rigid box
- 1mL Luer slip syringes with 10 microlitre increments e.g. BD 1mL Plastipak
- Syringes of suitable size for dilution step e.g. BD 1mL/5mL Plastipak
- 5 – 10mL Ampule of sterile normal saline for injection (pre stored at 2-8^{0}C)
- 10mL Internally Sterile Nitrogen Filled Glass Vial (product code VNS10RB) (where required by sponsor SOP dependent on vaccine batch in current use)

- 70% alcohol wipes (e.g. Clinell)
- 21g 11/2" Needles
- Dilution Labels
- 23g 1" Needles
- Sterile absorbent pads

Preparation of the IMP

Where dilution of the IMP is required, to ensure the maximum number of doses are available from each vial of vaccine it will be necessary to perform a single dilution step using pre-chilled (2-8°C) 0.9% saline for injection. To ensure stability of the vaccine once diluted, the vaccine will be stored at 2–8°C with the final dose from the vial being prepared within 5 hours 30 minutes to ensure the final vaccination is administered within six hours of defrosting/removal from -80°C storage.

NB. Dilution of the vaccine does not constitute a manufacturing process and is fully in line with EU GMP Annex 13 under Article 9(2) Directive 2005/28/EC. Further information can be found at:

https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-4/2009_06_annex13.pdf

https://mhrainspectorate.blog.gov.uk/2016/05/20/manufacture-of-investigational-medicinal-products-frequently-asked-questions/ (accessed 25 May 2020).

Dilution and preparation of the IMP will be performed by the vaccine preparation nurse and administering nurse in the vaccine preparation room as per the Sponsor SOP OVC099, 'COV002 Vaccine Preparation and Storage'.

Preparation of the MenACWY vaccine

Preparation of the MenACWY vaccine will also take place in the vaccine preparation room, following manufacturer's instructions for reconstitution and mixing.

The vaccine will be drawn up into a 1 mL syringe, as used for the IMP, as detailed in the Sponsor SOP OVC099, 'COV002 Vaccine Preparation and Storage'.

Administration of the IMP/ control vaccine (MenACWY)

Equipment required:

- Clean Procedure trolley
- Injection tray
- Sharps bin with lid
- Disinfectant and cleaning cloths (Tristel fuse- can also be used in case of spillage)
- Apron
- Gloves
- Eye protection
- Alcohol skin swabs
- Occlusive dressing

1. Ensure that the room for administration is adequately prepared, including equipment to handle spillage, and a couch or bed for use by the participant when being vaccinated if necessary (vaccinations can take place with the participant sat in a chair).

2. Inform the participant of the nature and route of the vaccine and give the opportunity to ask questions and even withdraw their consent (if so desired).

3. The administering nurse (wearing a disposable apron, fluid-resistant surgical mask, clean gloves and protective eyewear) will bring the syringe containing the vaccine to the clinic room and transfer this from the rigid sealable box to the injection tray.

4. The injection should be administered in the deltoid site of the arm (ideally the non-dominant arm).

5. Clean the injection site with an alcohol wipe for 30 seconds and allow to dry completely.

6. Volunteers should be asked to expose the deltoid region and rest their hand on their hip to allow for greater muscle relaxation. Spread the skin taut and insert the needle about 2.5cm below the acromial process at 90^{o}.

7. Administer the vaccine as described by the protocol. Once administered apply an occlusive dressing for 15 minutes (+ 15 minutes).

8. Once the vaccine has been administered, record the time of injection.

9. Dispose all equipment as per waste management guidelines.

Disposal Procedure.

The chosen route for disposal for some of the waste equipment (i.e. needle and syringe) due to its potential to be medicine contaminated, is via incineration, using the hospitals 'Yellow' waste stream. Single use, Icomed rigid plastic containers, which are non – leak bins suitable for the disposal of sharps and which comply with BS7320 approvals will be used. This is also compliant with The Genetically Modified Organisms (controlled use) Regulations 2014 which apply from 1st October 2014.

Other clinical waste associated with the administration of ChAdOx1 nCoV-19 should be disposed of via the Orange STH waste stream for incineration. (e.g. aprons, gloves, occlusive vaccination site dressing).

All members of the research team who will be handling the clinical waste will be responsible for ensuring waste is disposed of correctly.

The safe use and disposal of sharps is a legal requirement under the COSHH (1994) Regulations and General Health and Safety Law. Sharps injuries are avoidable if safe working practice is followed.

Disposal of sharps

Definition

Sharps- A sharp is described as any item that may potentially cut or penetrate the skin. This includes all needles, giving set spikes, cannulae, surgical blades, razors, guide wires stitch cutters, disposable trocar and any glass items. If in any doubt, dispose of the item as a sharp. Please refer to the STHFT Waste Strategy & Policy to ensure the correct disposal of sharps.

Procedure

1. All members of the research team who will be handling the clinical waste will be responsible for ensuring waste is disposed of correctly

2. All members of the research team who will be handling the clinical waste generated during and after the administration of ChAd-MVA will be responsible for ensuring bins designated for the disposal of GMO contaminated sharps by incineration are used. The bin must be EU approved and conform to British Standard 7320 (this number is printed on the front of the sharps bin)

3. A single use, rigid, yellow lidded container will be available in the clinical room used prior to each administration. It is the responsibility of the research nurse who will administer the injection to ensure the appropriate bin is available.

4. All members of the research team are responsible for ensuring the correct size of sharp bin is used. A variety of sizes of sharps bins are available via the Head Porter at the Royal Hallamshire Hospital.

5. Any individual responsible for using sharps must dispose of their used sharps immediately after use.

6. Where sharps are being used, the individual responsible must take the sharps bin the place where the sharp is to be used, not the sharp to the bin. The sharps bin must be carried by the handle when being transported.

7. Any individual responsible for using needles must dispose of single use needles and syringes as a single unit.

8. Any individual responsible for using needles should never re-sheath bend or cut them.

9. All members of the research team are responsible for ensuring that the sharps bins are not filled more than 2/3 full.

10. When the sharps bin is 2/3 full, or at the end of each vaccination day (whichever is sooner) lock the bin.

11. The person responsible for locking the bin must fill in the identification record on the sharps bin.

12. GMO waste should not remain in the clinical department for long periods of time, or in areas accessible by the public, therefore, Porters should be contacted to arrange collection of the clinical waste as soon as possible.

Action to be taken in the event of a sharps injury

STH sharps injury policy should be followed in the event of an unintended sharps injury, including the completion of a datix incident report form.

In addition to a Datix form, the incident should be reported to the research nurse overseeing the clinic session, the PI and the Sponsor.

Disposal of contaminated clinical waste

GMO contaminated clinical waste – This covers any items which are potentially infected and have been in direct patient contact e.g. dressing, swabs, gloves, aprons etc. It must be kept separate to other waste streams such as household and placed in orange clinical waste bags.

Procedure

1. All members of the research team present in the clinical area are responsible for disposing of clinical waste correctly. Please refer to STHFT Waste Strategy & Policy.

2. All members of the research team who will be handling the clinical waste generated during the procedure will be responsible for ensuring that clinical waste bags for the disposal of GMO contaminated waste by autoclaving or incineration are used.

3. Orange clinical waste bags will be used to dispose of any potentially GMO contaminated materials used during the patient visit. It is the responsibility of the research nurse to ensure that the specified clinical waste bags are available.

4. All members of the research team present at the patient visit are responsible for ensuring the contents of the clinical waste are not moved from one container to another.

5. All members of the research team are responsible for ensuring that the clinical waste bags are not filled more than 2/3 full.

6. When the orange clinical waste bag is 2/3 full, or immediately post procedure once all associated clinical waste has been disposed of (whichever is sooner) the bag must be sealed. This is regardless of how much capacity there may be left in the bin. The closure tags provided for all clinical waste bags should be used, which allow traceability back to the department.

7. The individual responsible for emptying the clinical waste bin is responsible for tagging the bag.

8. GMO waste should not remain in a clinical department for long periods of time, or in areas accessible by the public, therefore, Porters should be contacted to arrange collection of the clinical waste as soon as possible.

Action to be taken in the event of a spillage/leakage

1. All members of the research team are responsible for dealing with and disposing of any spilled GMO materials or clinical waste correctly.

2. PPE (i.e. eye protection, gloves and apron) should be worn at all times as per local policy and procedures.

3. Tristel Fuse (STHFT surface disinfectant, which is active against viruses), should be present in each area where a spill might occur (i.e. storage locations in pharmacy and CRF, vaccine preparation room and vaccine administration clinic rooms).

4. In the event of a spillage, any liquids should be soaked up with disposable absorbent materials (such as swabs).

5. The area should be cleaned thoroughly using Tristel fuse.

6. All materials used in cleaning up any spillages should be disposed of as GMO contaminated clinical waste (as above).

Any spillage of ChADOx1 nCoV-19 should be documented on the drug accountability form and the Sponsor should be notified. If a member of staff spills the IMP on their person, they

should wash the area thoroughly using local hand wash available in the clinical area, and report the spillage to the Sponsor.

In the event of any spillage of any IMP a Datix form should be completed in line with STH policy.

Accidental Exposure and Incident Reporting

Address exposure/incidents in the following order:

- Clean any wound/contact
- Clean any spillage/contaminated areas
- Dispose of all materials exposed to GMO according local waste policies
- Observe the individual (discuss with the PI a suitable observation period) and ensure they have access to medical care during this time
- Discuss the incident with senior staff, and if required, the Occupational Health department
- Report the incident by completing a Datix form

Needle stick injuries

1. Encourage bleeding of wound.
2. Wash puncture site thoroughly with soap and water.
3. Dry area using disposable material.
4. Cover with waterproof dressing.

Skin Contact

1. Wash area thoroughly with soap and water.
2. Dry area using disposable material.

Eye splash

1. Irrigate eye immediately with sterile eye wash solution (if available) or water.

Mouth splash

1. Wash out mouth immediately with water several times.

Inhalation

1. Discuss with senior staff, and the Occupational Health department to determine immediate requirements. All staff should be wearing fluid-resistant surgical masks at all times during this study, so inhalation should never occur.

Action to be taken in the event of anaphylaxis following vaccination

There are no universally accepted definitions of anaphylactic and anaphylactoid reactions. Disparate mechanisms can lead to serious symptoms and signs due to sudden activation of mast cells and basophils. The term anaphylaxis is commonly used for hypersensitivity reactions typically mediated by immunoglobulin E (IgE). Anaphylactoid reactions are similar, but do not depend upon hypersensitivity. For simplicity the term anaphylaxis will be used here for both types of reactions

Consider anaphylaxis when clinical picture is suggestive. Signs and symptoms vary with severity and include respiratory difficulties, (shortness of breath and wheeze); oedema, (particularly of the face and may include the airway thus causing stridor), hypotension, arrhythmia and skin rash. Onset is normally rapid (within 20 minutes of precipitant).

All clinic rooms in which vaccines are administered will have an anaphylaxis pack, and there are resuscitation ('crash') trolleys available in each CRF. There will be staff trained in advanced life support (ALS) or basic life support (BLS) and management of anaphylaxis present at all vaccination clinics.

1. ABC approach
2. Shout for help and call for assistance via the emergency phone system by dialling 2222 and requesting the crash team.
3. If the volunteer is sitting in a chair lay them on the floor, if on an examination couch lower the back, this will aid circulation.
4. Administer 0.5ml of 1:1000 adrenaline intramuscularly into the anterior lateral thigh. – Record this time.
5. Administer Oxygen at 15 litres/minutes through a non-rebreathe mask.
6. During the interim period, if not already in place, blood pressure, pulse and respiratory function should be measured.
7. If symptoms persist a second dose of 0.5ml of 1:1000 adrenaline may be administered after 5 minutes have elapsed – Record this time. No further doses of adrenaline may be administered without the direction of a medically qualified person being present.
8. Continue to provide support and reassurance to the patient until instructed otherwise by the crash team.
9. All actions taken must be recorded in the medical notes and incident forms completed.

Further action taken should be at the discretion of the medically qualified staff member present, however guidance should be taken from the Resuscitation Council (UK) guidelines on management of anaphylaxis.

1. Secure intravenous access using 18G or larger cannulas and give fluid challenge of 500- 1000mL of normal saline, if available.
2. The clinician may consider giving chlorphenamine 10mg intramuscularly (antihistamine). This can be given intravenously as a slow bolus over one minute to avoid provoking hypotension.
3. If the reaction is severe the clinician may consider giving hydrocortisone 200mg intramuscularly or slowly intravenously.
4. The on-call medical team attending the emergency will decide on patient placement for ongoing medical care.

If two participants simultaneously experience anaphylaxis, the same processes will apply. There will be adequate medical and nursing cover to deal with this extremely unlikely occurrence.

An anaphylactoid reaction will be reported to the Sponsor as an SAE following standard reporting procedures (i.e. reported within 24 hours).

Appendix 1 Documents Associated with the SOP

Document Name and location	Author
SOP CRF.L110 V2.0 Clinical Waste Management I:\Clinical Research Facility\Shared Documents\SOPs\CRF SOPs (Current)\CRF Laboratory SOPs\SOP CRF.L110 V2.0 Clinical Waste Management.pdf	Emma Goodwin
The Genetically Modified Organisms (controlled use) regulations 2014 http://www.legislation.gov.uk/uksi/2014/1663/contents/made	Health and Safety Executive
Sheffield Teaching Hospitals NHS FT (STH) Waste Management Strategy and Policy. V4.0. 24/06/2015. Issued 30/04/18 http://nww.sth.nhs.uk/NHS/ControlledDocuments/	Ray Wright
The Health Technical Memorandum (HTM) 07-01 – Safe Management of Health care Waste 2013 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/167976/HTM_07-01_Final.pdf	Department of Health
STH Infection Control Guidelines http://nww.sth.nhs.uk/STHcontDocs/STH_CGP/InfectionControl/SheffieldInfectionControlGuidelines.doc	STH Infection Control Team
STH Hand Hygiene Policy http://nww.sth.nhs.uk/STHcontDocs/STH_Pol/ClinicalGovernance/HandHygienePolicy.doc	STH Infection Control Team
COSHH Guidance 1994 http://www.hse.gov.uk/pubns/indg136.pdf	
Infection Prevention and Control Standard Precautions, Prevention of Sharps Injuries and Prevention of Exposure to Blood and Body Fluids Policy V 2.0 07/09/2012 http://nww.sth.nhs.uk/STHcontDocs/STH_Pol/HumanResources/BloodExposurePolicy.doc	Patty Hempshall Alison Redfern Alison Rimmer
Medicines for Human Use (Clinical Trials) Regulations 2004, http://www.legislation.gov.uk/uksi/2004/1031/contents/made	
Infection Prevention and Control Standard Precautions, Prevention of Sharps Injuries and Prevention of Exposure to Blood and Body Fluids Policy V 2.0 07/09/2012 http://nww.sth.nhs.uk/NHS/OccupationalHealth/	Patty Hempshall, Alison Redfern, Alison Rimmer,
Sheffield Teaching Hospitals NHS FT STH Incident Management Policy, http://nww.sth.nhs.uk/STHcontDocs/STH_Pol/HealthAndSafety/IncidentManagementPolicy.doc	Andrew Scott
Sheffield Teaching Hospitals FT (STH) Medicine Code http://nww.sth.nhs.uk/STHcontDocs/STH_Pol/ClinicalGovernance/MedicineCode/MedicineCode_Management.doc	Nicky Thomas
The Royal Marsden Hospital manual of Clinical Nursing Procedures 7th edition 2008.	Lisa Dougherty Sara Lister
CRF SOP for Theatre Waste Disposal for STH 18323, A Phase II Simon Two Stage Efficacy Study of Intracerebral CTXOE03DP in Patients with Stable Paresis of the Arm Following an Ischaemic Stroke. I:\Clinical Research Facility\CRF Projects\Active Projects\MAJID Arshad\STH 18323\Study Documentation\SOPs (Study Specific)	Gail Mills
STH21413 GMO Risk Assessment. STH21413 CRIO Research Management System	CRIO
Prescription template. Pharmacy local network drive	Pharmacy

Appendix 2 SOP revisions and history

SOP number	Effective date	Reason for change	Author
THIS SOP			
2.4	13 Jul 2020	Update required to accommodate supply of IMP batches which can be stored refrigerated rather than frozen and which may not need dilution	Erica Wallis
PREVIOUS SOPs			
2.3	24 June 2020	Clarify arrangements for storage within -80 freezer in the event that co-storage with biological samples is necessary	Erica Wallis
2.2	23 June 2020	Change in storage location of frozen ChAdOx1 vaccine at RHH site	Erica Wallis
2.1	10 June 2020	Clarification of the process for transporting vaccine between hospital sites	Erica Wallis
2	02 June 2020	Removal of specific information relating to quantities of dilutant required for ChAdOx1 vaccine dilution. Replacement with reference of Sponsor SOP	Ruth Payne
1	29 May 2020	Alteration of vaccine preparation to include reference to a dilution step, as described in the Sponsor SOP OVC099, 'COV002 Vaccine Preparation and Storage'.	Ruth Payne