Objective

A new process to follow to enable a SN to facilitate research project: SIGNET: Statins for Improving orGaN outcomE in Transplantation

Changes in this version

Additional action to record the randomisation number on the consent form sticker

Roles

- **SNs -** Identify a potential organ donor and approach for organ donation and research consent/authorisation. Facilitate the SIGNET study.
- **SIGNET trial team -** Facilitate the research study.
- **Recipient Co-ordinator -** receives organ offers, co-ordinates the transplant recipients and mobilises NORS team
- **Transplanting Centres -** transplants organs.
- **NORS team -** performs organ retrieval.
- **Hub Operations -** offers organs and records consents/authorisations and donation outcomes on NTxD

Restrictions

- This SOP is to be followed by a qualified and trained SN-OD. In the event of a SN who is in training, this SOP is to be utilised under supervision.
- Participating hospitals are listed within **DAT3936**

Items Required

Instructions

Please note: SN SIGNET FAQ sheet (INF1586) is also available for information.

SN

The patient is referred as a potential DBD organ donor.

Screen for clinical contraindications for organ donation as per **POL188**.

If there is suitability for organ donation, screen for eligibility for the SIGNET study and confirm this with an ICU doctor:

Inclusion criteria

- Within a participating ICU (check **DAT3936**)
- Confirmed dead by neurological criteria (DBD) or neurological death is suspected and testing is planned.

Exclusion criteria

- Under 18 years
- Planned donation after circulatory death (DCD)
- No consent/authorisation for organ donation
- Known hypersensitivity to simvastatin

Approach/consent/authorisation

If organ donation consent/authorisation is gained, approach for participation in the SIGNET study. Formal consent for SIGNET can be taken pre or post neurological death confirmation. This does not apply to neurological dead patients who are proceeding as a DCD. Stand down on SIGNET if the patient is not subsequently confirmed dead by neurological death criteria. Randomisation into the SIGNET trial must **not** happen until after neurological death has been confirmed.

If the family wish to go home pretesting and not return, they can be given the SIGNET information leaflet to take with them to read if they wish to do so.

Deemed consent/authorisation does not apply to research therefore explicit consent/authorisation must be taken (**SOP5818/SOP5878**). You will need to establish whether this donor would have been unwilling to participate in this research study.

Key information for relatives:

- As you have generously given consent/authorisation for donation of organs for transplantation, your relative is now in a unique position to participate in the SIGNET study.
- Statins are commonly used for people with high cholesterol, but this study will explore another possible function. The SIGNET study aims to investigate whether a statin tablet could improve the condition and function of transplanted organs by reducing inflammation which naturally occurs during neurological death. It is hoped that if this study demonstrates that this is effective then this treatment could potentially help many transplant recipients in the future.

- As part of the study, some patients will receive the medication, and some won't. This is important so that organ outcome comparisons can be made between the two groups. Should your relative be allocated the statin, it will be crushed up and given via the nasal tube that is already in place or, via one that will be put in place to help support successful organ donation. This is given after neurological death is confirmed and will not cause discomfort to your relative. We don't think there are any risks to the donor by taking part in the study.

Give the information sheet to the relatives and ask them to read this fully for further information. If consenting/authorising by telephone, advise that this will be sent to them. Direct the family to the website (www.nhsbt.nhs.uk/SIGNET) if they wish more information.

Record relative consent/authorisation for SIGNET study by initialling other/scheduled purposes specific consent/authorisation section 3b 'yes' box of and inserting the study sticker in the additional notes of the consent/authorisation form (**FRM4281**, **FRM1538**). Also record this in other/scheduled purposes question 3b 'yes' box on DonorPath. Record the randomisation number at the bottom of the consent form sticker.

SIGNET Patient Consent Form Sticker (Version 1.2 dated 04.09.2023)
Study: Statins for Improving orGaN outcomE in Transplantation (NHSBT Study Ref no: 109)

REC No: 21/LO/0412 IRAS: 288722 Sponsor Reference: 9691

Chief Investigators: Professor John Dark and Professor Dan Harvey

Consent for the SIGNET study and the points covered on this sticker are for research purposes only. I have received a relative information leaflet regarding the SIGNET study (version 1.2 dated 04.09.2023) and had an opportunity to discuss it with a qualified member of staff. I give consent/authorisation to my relative's participation in SIGNET and I give permission for the researchers and individuals from the Sponsor and NHS organisation to access my relative's records.

I understand that:

- Participation is voluntary and that I am free to withdraw my relative at any time, without giving any reason, without my relative's medical care or legal rights being affected.
- All information will be anonymised by the allocation of codes and the information will remain confidential and only be used for research.
- Relevant sections of my relative's medical notes and data collected during the trial may be looked at by the trial researchers and individuals from the Sponsor or from the NHS organisation, where it is relevant to my relative taking part in this research.
- My relative's data will be stored on a password protected secure database accessible only by the research team and independent statistician for 5 years following the trial closure.
- Information about my relative's organ donation, which is already provided to NHS Blood and Transplant, will be used for this study.
- Information collected about my relative could also be used to support other research in the future.

Randomisation Number: R _ _ _ _

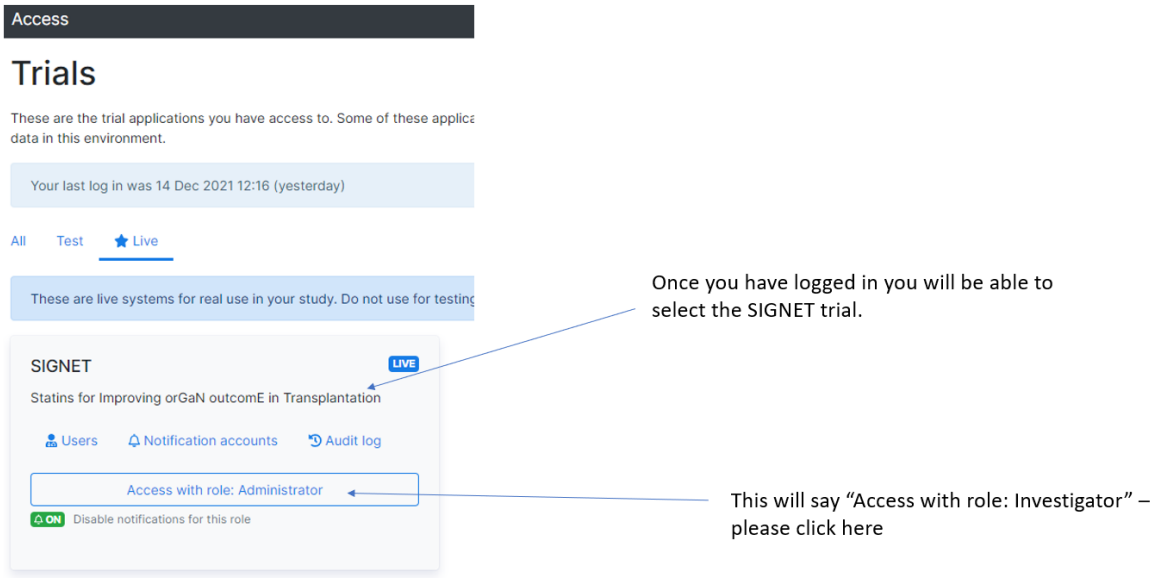
Should the family decline to participate record this on the SN/DFCS handover form and the reason why in the sequence of events section in DonorPath.

Randomisation

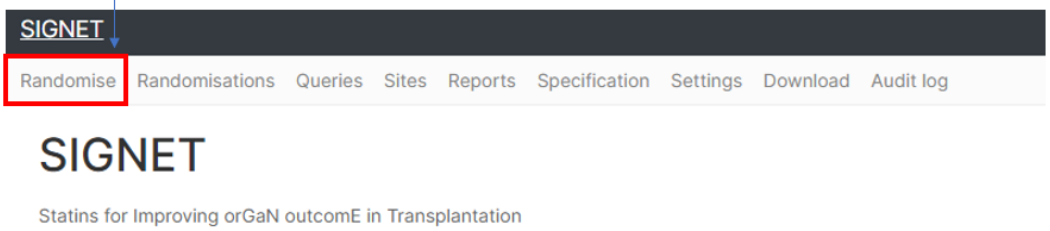
This should be completed as soon as possible following consent/authorisation but not before confirmation of neurological death. This establishes whether the donor will receive standard donor care plus the statin or standard donor care only.

- Firstly, establish if the donor was receiving any statin medication at admission to ICU as this information is necessary for the electronic randomisation.
- Generate the ODT donor number via DonorPath.
- Using your log in details and password, log onto 'Sealed Envelope' at www.sealedenvelope.com
- Use the drop-down box to access SIGNET.
- Complete the questions asked.
- You will receive the participant's randomisation number and allocation. This will be in the form of RXXXX and is to be used on all subsequent study documentation.
- If randomised for standard donor care only, only complete the source data form (SDF). If randomised to receive 80mg of simvastatin, open the SIGNET study pack and record the study participation number on the SDF and the SIGNET consent sticker

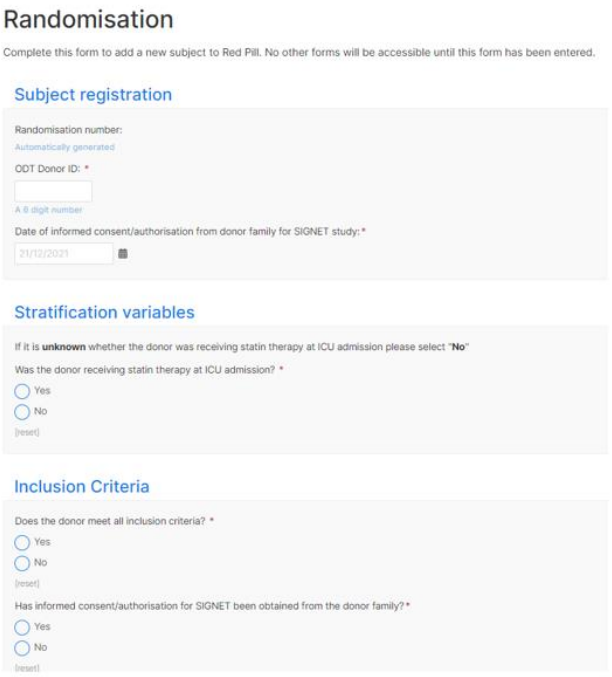
If you are unable to access or use Sealed Envelope, please contact the SIGNET team (SIGNET@nhsbt.nhs.uk or 07764 280175). If outside of working hours, please try accessing Sealed Envelope using a mobile device or using an alternative user account.

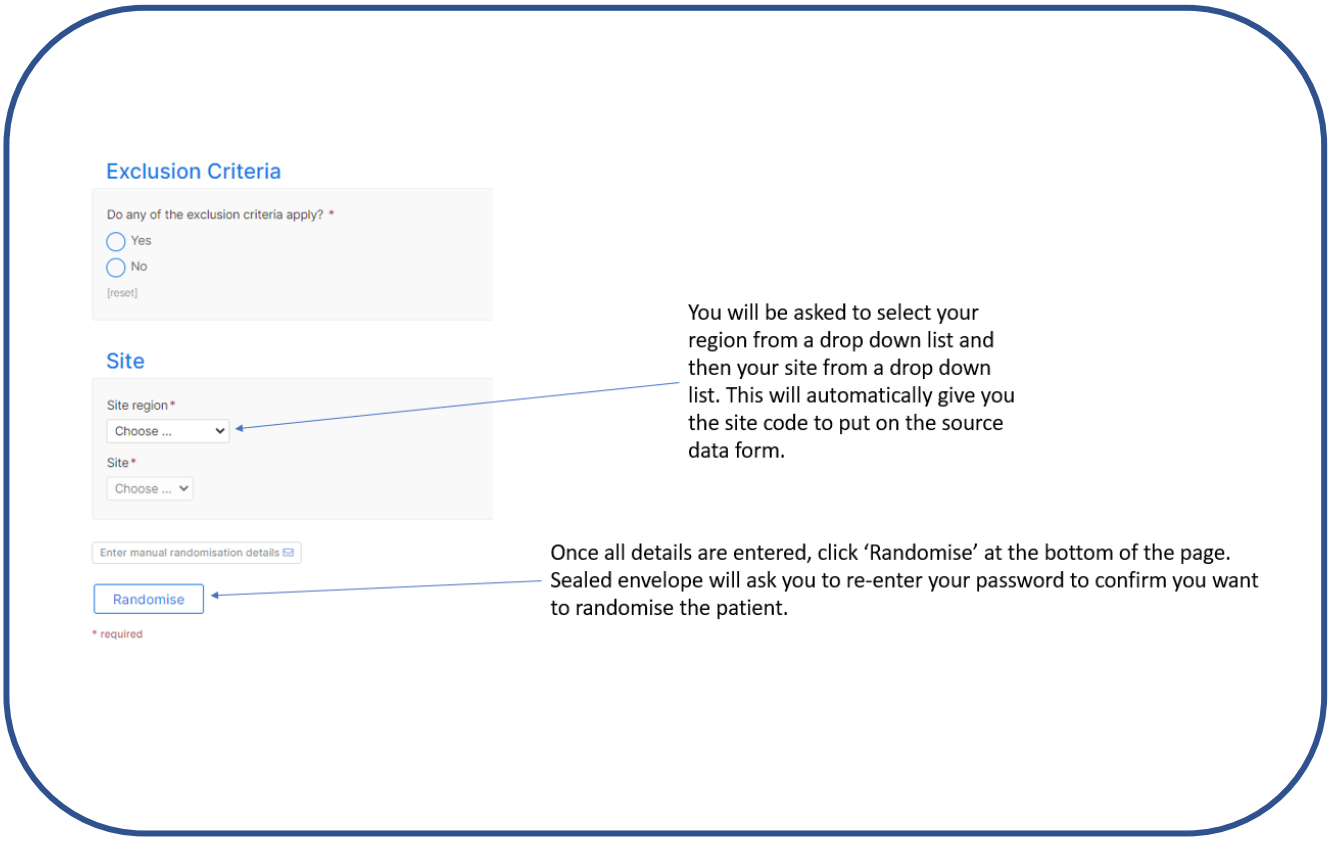


You will now be able to click 'Randomise' to randomise a patient



You will now be asked to answer some questions before you randomise the patient.




Exclusion Criteria
Do any of the exclusion criteria apply? *
Yes
No
[reset]
Site
Site region *
Choose ...
Site *
Choose ...
Enter manual randomisation details
Randomise
* required
You will be asked to select your region from a drop down list and then your site from a drop down list. This will automatically give you the site code to put on the source data form.
Once all details are entered, click 'Randomise' at the bottom of the page. Sealed envelope will ask you to re-enter your password to confirm you want to randomise the patient.

Source Data Form (SDF) information

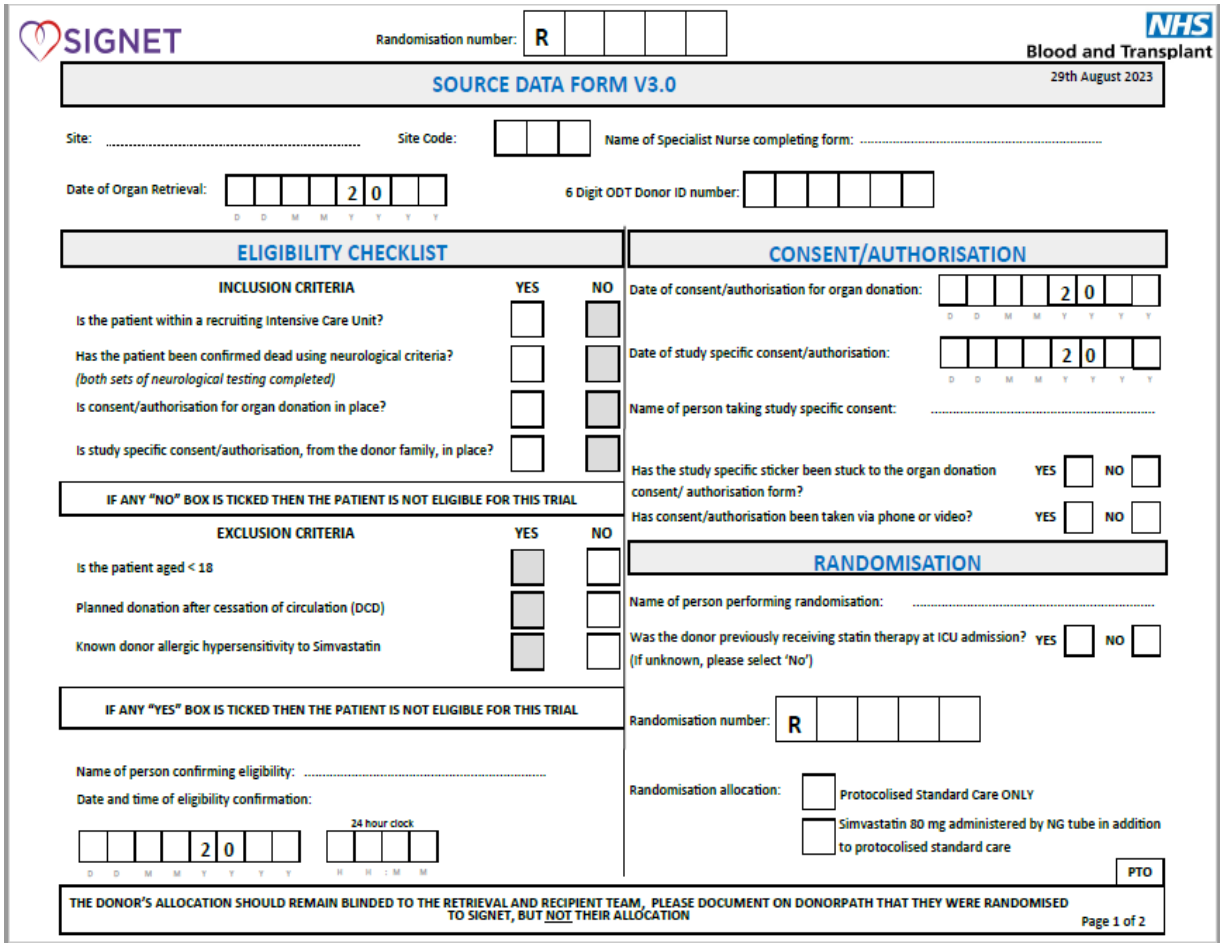
The SDF is a study record of the interventions given and must be completed for each donor that is randomised.

The randomisation number and the site number are generated in the randomisation tool and must be recorded on the form and SIGNET consent sticker

The SN will complete the sections with blue headings.

The ICU doctors and the bedside nurse will document in the intervention section if the donor has been randomised to receive a statin.

If the answer to the first question in the Withdrawal of Consent and Unblinding sections is 'no', then the rest of the questions in these sections do not need to be completed. If unblinding is requested after donation is completed and the form is left in the ICU, the SIGNET study team should be emailed to advise them that this was requested, and the actions taken.



SIGNET

Randomisation number: R

NHS Blood and Transplant

SOURCE DATA FORM V3.0

29th August 2023

Site: ..... Site Code: Name of Specialist Nurse completing form: .....

Date of Organ Retrieval: 2 0 (D D M M Y Y Y Y)

6 Digit ODT Donor ID number:

ELIGIBILITY CHECKLIST

INCLUSION CRITERIA	YES	NO
Is the patient within a recruiting Intensive Care Unit?		
Has the patient been confirmed dead using neurological criteria? *(both sets of neurological testing completed)*		
Is consent/authorisation for organ donation in place?		
Is study specific consent/authorisation, from the donor family, in place?		

IF ANY "NO" BOX IS TICKED THEN THE PATIENT IS NOT ELIGIBLE FOR THIS TRIAL

EXCLUSION CRITERIA	YES	NO
Is the patient aged < 18		
Planned donation after cessation of circulation (DCD)		
Known donor allergic hypersensitivity to Simvastatin		

IF ANY "YES" BOX IS TICKED THEN THE PATIENT IS NOT ELIGIBLE FOR THIS TRIAL

Name of person confirming eligibility: .....

Date and time of eligibility confirmation: 2 0 (D D M M Y Y Y Y) 24 hour clock (H H : M M)

CONSENT/AUTHORISATION

Date of consent/authorisation for organ donation: 2 0 (D D M M Y Y Y Y)

Date of study specific consent/authorisation: 2 0 (D D M M Y Y Y Y)

Name of person taking study specific consent: .....

Has the study specific sticker been stuck to the organ donation consent/ authorisation form? YES NO

Has consent/authorisation been taken via phone or video? YES NO

RANDOMISATION

Name of person performing randomisation: .....

Was the donor previously receiving statin therapy at ICU admission? (If unknown, please select 'No') YES NO

Randomisation number: R

Randomisation allocation:
- Protocolised Standard Care ONLY
- Simvastatin 80 mg administered by NG tube in addition to protocolised standard care

PTO

THE DONOR'S ALLOCATION SHOULD REMAIN BLINDED TO THE RETRIEVAL AND RECIPIENT TEAM, PLEASE DOCUMENT ON DONORPATH THAT THEY WERE RANDOMISED TO SIGNET, BUT NOT THEIR ALLOCATION

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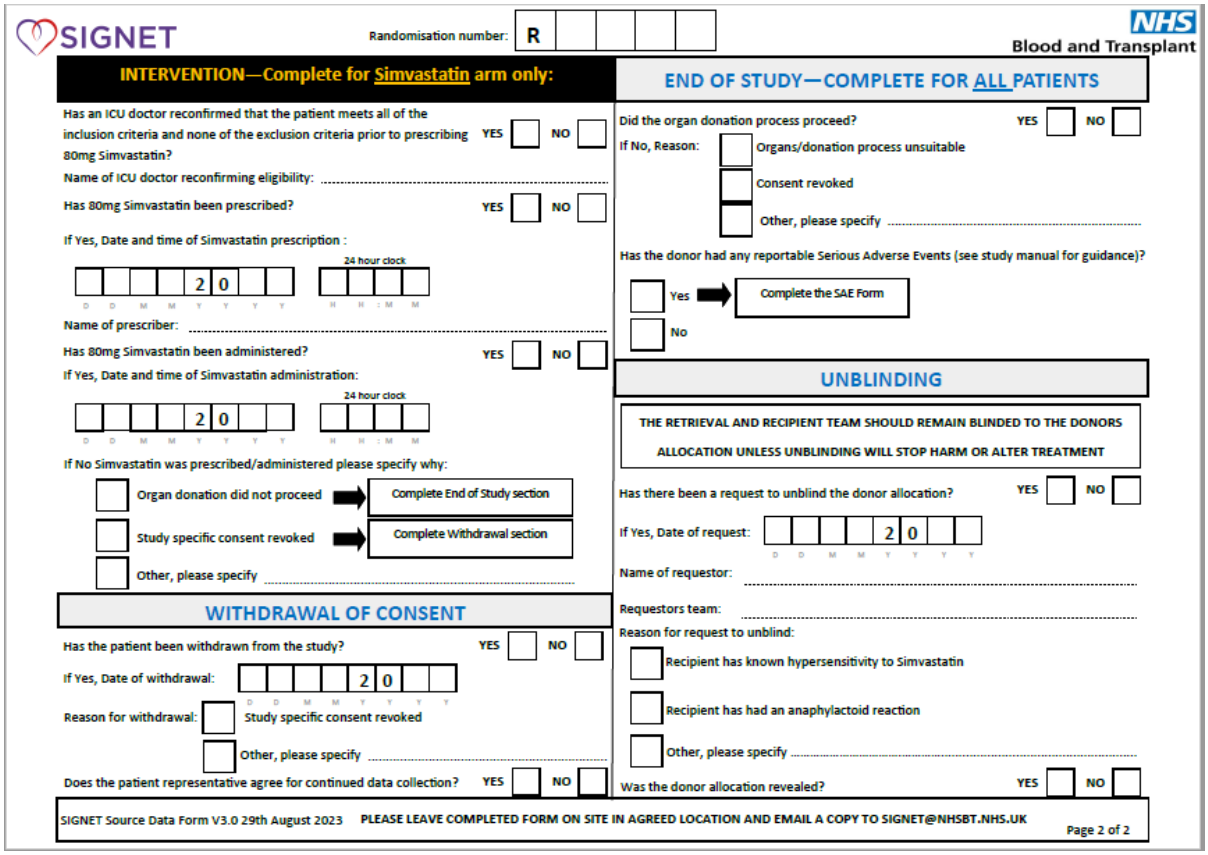


SIGNET

Randomisation number: R

NHS Blood and Transplant

INTERVENTION—Complete for Simvastatin arm only:

Has an ICU doctor reconfirmed that the patient meets all of the inclusion criteria and none of the exclusion criteria prior to prescribing 80mg Simvastatin? YES NO

Name of ICU doctor reconfirming eligibility: .....

Has 80mg Simvastatin been prescribed? YES NO

If Yes, Date and time of Simvastatin prescription :

D D M M Y Y Y Y 2 0 — 24 hour clock H H : M M

Name of prescriber: .....

Has 80mg Simvastatin been administered? YES NO

If Yes, Date and time of Simvastatin administration:

D D M M Y Y Y Y 2 0 — 24 hour clock H H : M M

If No Simvastatin was prescribed/administered please specify why:

- Organ donation did not proceed → Complete End of Study section
- Study specific consent revoked → Complete Withdrawal section
- Other, please specify .....

WITHDRAWAL OF CONSENT

Has the patient been withdrawn from the study? YES NO

If Yes, Date of withdrawal: D D M M Y Y Y Y 2 0

Reason for withdrawal:
- Study specific consent revoked
- Other, please specify .....

Does the patient representative agree for continued data collection? YES NO

END OF STUDY—COMPLETE FOR ALL PATIENTS

Did the organ donation process proceed? YES NO

If No, Reason:
- Organs/donation process unsuitable
- Consent revoked
- Other, please specify .....

Has the donor had any reportable Serious Adverse Events (see study manual for guidance)?

- Yes → Complete the SAE Form
- No

UNBLINDING

THE RETRIEVAL AND RECIPIENT TEAM SHOULD REMAIN BLINDED TO THE DONORS ALLOCATION UNLESS UNBLINDING WILL STOP HARM OR ALTER TREATMENT

Has there been a request to unblind the donor allocation? YES NO

If Yes, Date of request: D D M M Y Y Y Y 2 0

Name of requestor: .....

Requestors team: .....

Reason for request to unblind:
- Recipient has known hypersensitivity to Simvastatin
- Recipient has had an anaphylactoid reaction
- Other, please specify .....

Was the donor allocation revealed? YES NO

SIGNET Source Data Form V3.0 29th August 2023 PLEASE LEAVE COMPLETED FORM ON SITE IN AGREED LOCATION AND EMAIL A COPY TO SIGNET@NHSBT.NHS.UK Page 2 of 2

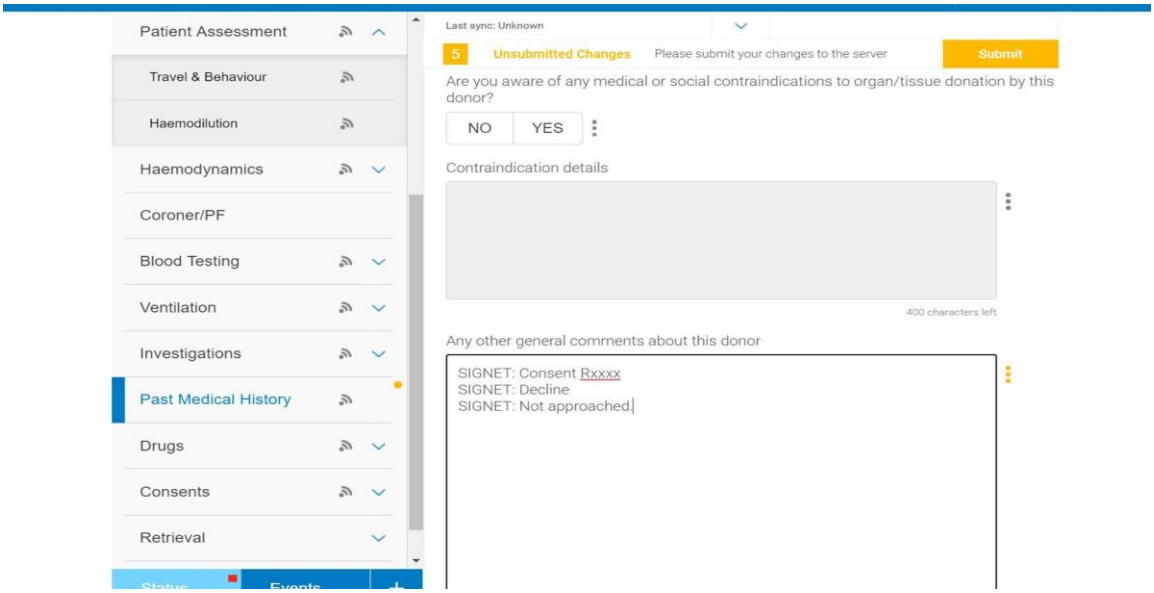
Drug administration and recording

Hand the SDF to an ICU doctor/advanced prescriber and the bedside nurse (BSN). Advise there is an ICU study manual for their information. If the prescriber is not familiar with SIGNET advise them there is a website link on the SIGNET poster to self train if needed. Request a prescription of 80mg simvastatin to be prescribed and administered as per the guide. It **must not** be administered until the patient has undergone neurological death testing and death has been formally confirmed. The ICU doctors should complete the SDF as above.

Check that the statin has been given by the BSN and request that they complete the SDF with accurate timings as these are required for the study data.

SIGNET is a randomised trial which means that the SN/ICU staff may see who has been given the statin, but the NORS team/retrieval centres must not. To maintain this blinding, you must not record that 80mg Statin has been given for the SIGNET study where the transplanting centres are able to visualise it. This will be recorded instead on the SDF which is uploaded onto DonorPath and on the ICU prescription chart.

Record SIGNET study participation as the applicable text below in the past medical history 'other general comments' free text section as either:



This alerts the NORS Team and recipient centre that this drug may have been given.

Should the recipient centre wish for emergency unblinding, they are able to do so by contacting the ICU or an SN/TM/RM via Hub Operations. The uploaded SDF on DonorPath can be accessed for the recipient centre by OTDT if this information is required.

Donation process

Register the donor with Hub Operations including consent/authorisation for SIGNET study number 109.

Continue donor characterisation and ensure the donor management is supported using the OTDT donor care bundle.

If organs are placed for transplant and the donation proceeds to theatre, advise the NORS team of SIGNET participation at SN/NORS handover but there is no participation required from them.

Do not advise the NORS team whether the donor received simvastatin or not.

Post donation

Upload the completed SDF to DonorPath and email a copy to the SIGNET team at SIGNET@nhsbt.nhs.uk with the subject heading: 'Confidential SIGNET Source Data Form'.

Check **DAT3936**/ regional handbook/ local study manual for instructions where to leave the paper form on site.

Complete post donation notes in the hospital records including SIGNET participation.

SN/DFCS handover form completion:

If telephone consent/authorisation has been taken, initial the specific study box and write SIGNET in the additional information section for DFCS to send out the relative's information sheet.

Document SIGNET in the specific studies box to indicate participation.

Please Note:

All incidents should be reported via the ODT Clinical Governance pathway following standard procedure.

Highlight this to the PI and central study team – copy and paste the clinical governance text and email to SN, Embedded specialist nurse and PI (details in **DAT3936**)

⊖ End of Procedure

Definitions

- **BSN** – Bedside Nurse
- **DBD** – Donation following Brainstem Death
- **DCD** – Donation following Circulatory Death
- **DFCS** – Donor Family Care Services
- **ICU** – Intensive Care Unit
- **NORS** – National Organ Retrieval Service
- **NTxD** – National Transplantation Database
- **ODT** – Organ Donation and Transplantation
- **SDF** – Source Data Form
- **SN** – Specialist Nurse (including SR)

Related Documents/Reference

- **DAT3936** – SIGNET: Statins for Improving orGaN outcomE in Transplantation
- **FRM1538** – Authorisation – Solid Organ and Tissue Donation
- **FRM4281** – Consent – For Organ and/or Tissue Donation
- **INF1586** – SIGNET specialist Nurse Frequently Asked Questions
- **POL188** – Clinical Contraindications to approaching families for possible organ donation
- **SOP5818** – Organ and Tissue Donation Consent Manual
- **SOP5878** – Organ and Tissue Donation Authorisation Manual