A multi-centre, randomised, controlled trial evaluating the effects of early high-dose cryoprecipitate in adult patients with major trauma haemorrhage requiring major haemorrhage protocol (MHP) activation

CRYOSTAT-2

EARLY CRYOPRECIPITATE IN TRAUMA

Case Report Forms

Final version 2.0

08 November 2019

COMPLETION GUIDELINES

Clinical Trial Medical Notes Retention Form

To be completed by the research team at the point of patient enrolment and randomisation. This form is for **site use only** and must be retained in the CRF, as source data for audit purposes. **Do NOT send to NHSBT CTU.**

Subsequent Case Report Forms, from FORM 1 onwards should be completed and sent to NHSBT CTU as required.

ELIGIBILITY

All inclusion criteria must be YES and all exclusion criteria must be NO for the patient to be eligible.

Eligibility will be checked by a delegated clinician for the trial.

If the patient is deemed eligible then the patient can be entered into the trial according to the emergency waiver.

STUDY TIMELINES

- Patient must be entered into the trial and had the intervention no more than 3 hours from injury
- Patients randomised to the early cryoprecipitate arm to receive 3 pools, infused as rapidly as possible within 90 minutes from arrival in ED.
- If **>90 minutes**, cryoprecipitate can still be administered **up to 3 hours from injury**.

Final version 2.0
08 November 2019

COMPLETION GUIDELINES

Clinical Trial Medical Notes Retention Form

Randomisation Procedure

1. Open the secure randomisation box containing the sealed envelopes
2. Take the first randomisation envelope available in the box (i.e. the one with the lowest sequential number, RXXXXX).
3. On the back of the envelope, the name of the person opening the envelope and their signature should be recorded, followed by the date and time the envelope was opened to confirm that the next available and lowest numbered envelope of the batch has been taken, and there is no evidence of tampering.
4. On the front of the envelope, complete the patients initials, date of birth and hospital number on the envelope prior to opening. If initials and date of birth are not known, document the unique identifiers used at your participating hospital for identifying unknown patients.
5. Complete the enrolment log (stored at the back of the randomisation box) to document which envelope has been selected.
6. Break the seal on the envelope to reveal a card containing the randomisation number and allocation: either early cryoprecipitate + standard major haemorrhage **OR** Standard major haemorrhage protocol only.
7. Check the randomisation number on the card matches the one printed on the front of the envelope.
8. Email confirmation of the randomisation to NHSBT CTU using the 'Confirmation of Randomisation' form in the CRF.
9. Return the form envelope containing the card to the box, but place it at the back of the box to avoid any errors in randomisation.

The allocation must be reported on the CRF.

A patient is randomised once an opaque sealed randomisation envelope is opened. The randomisation number printed on the envelope is the patient's unique identifier for the trial, and should be recorded on all applicable documents.

Please ensure the confirmation of randomisation (page 7) is emailed to CRYOSTAT2@nhsbt.nhs.uk

Patient Name: .....

Date of Birth | | | | | | | | | (D D M M Y Y Y Y)

CLINICAL TRIAL MEDICAL NOTES RETENTION FORM
COMPLETE AT PATIENT ENROLMENT - DO NOT SEND TO NHSBT CTU

Hospital Number: | | | | | | | | | | |

Hospital Name: .....

Site Number: | | |

Sponsor: **QMUL**

Principal Investigator Name: ..... Contact Number: .....

Research Fellow/Nurse Name: ..... Contact Number: .....

Eligibility Confirmation:

I can confirm the patient meets the following eligibility criteria and has been entered into the CRYOSTAT 2 trial *(Tick box)*: ☐

Inclusion criteria:

1. The participant is judged to be an adult (according to local practice, e.g. 16 years or older in UK) and has sustained severe traumatic injury

2. The participant is deemed by the attending clinician to have on-going active haemorrhage

AND REQUIRES:

3. Activation of the local major haemorrhage protocol for management of severe blood loss

AND HAS STARTED or HAS RECEIVED:

4. at least one unit of any blood component

Exclusion criteria:

A patient will not be eligible for this study if he/she fulfils one or more of the following criteria:

1. The participant has been transferred from another hospital
2. The trauma team leader deems the injuries incompatible with life
3. More than 3 hours have elapsed from the time of injury (taken as time of the 999 call if unknown by medical team).

Delegated clinician confirming eligibility & emergency waiver:

Clinician Name (print) | Signature

Date and time eligibility & enrolment confirmed

				2	0		

D D M M Y Y Y Y

24 hour clock

H H : M M

Patient Name: .....

Date of Birth | | | | | | | | | (D D M M Y Y Y Y)

CLINICAL TRIAL MEDICAL NOTES RETENTION FORM
COMPLETE AT PATIENT ENROLMENT - DO NOT SEND TO NHSBT CTU

Date and time randomisation envelope opened | | | | | 2 | 0 | | | (D D M M Y Y Y Y) 24 hour clock | | | | (H H M M)

This patient has been randomised to receive *(tick applicable box)*

3 pools of early cryoprecipitate within 90 minutes of arrival in ED <u>in addition to the</u> standard major haemorrhage protocol ☐

Or

Standard major haemorrhage protocol ONLY ☐

This is the patient's unique identifier for the trial

| R | | | | | |

Please use on all patient specific study related documents

Date and time cryoprecipitate infusion started | | | | | 2 | 0 | | | (D D M M Y Y Y Y) 24 hour clock | | | | (H H M M)

Number of pools given: ☐ If < 3 pools given provide reason: .....

If randomised to the early cryo arm, was it given within 90 minutes of arrival in ED? ☐ Yes ☐ No

If No, specify reason: .....

Form completed by (Name) | Date Form Completed | Time 24 hour clock | Contact Number

| | | | | 2 | 0 | | | (D D M M Y Y Y Y) | | | | (H H M M) | |

COMPLETION GUIDELINES

Confirmation of Randomisation

This should be emailed to NHSBT CTU at **CRYOSTAT2@nhsbt.nhs.uk** as soon as possible after randomisation.

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NHS Blood and Transplant

Final version 2.0
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CONFIRMATION OF RANDOMISATION

Please send to NHSBT CTU
via email as soon as possible

Sender: ..... Date sent: | | | | | 2 | 0 | | | (D D M M Y Y Y Y)

Study site: ..... Site Number | | | |

To: **CRYOSTAT2@nhsbt.nhs.uk**

This is to confirm Randomisation to the CRYOSTAT 2 Trial

Does the patient meet the eligibility criteria? ☐ Yes ☐ No

Has the patient been entered with emergency waiver? ☐ Yes ☐ No

Randomisation number: | R | | | | | |

Randomisation ☐ Early Cryo arm — **3 pools of Early Cryoprecipitate in addition to standard major haemorrhage protocol**

☐ Standard arm — **Standard major haemorrhage protocol only**

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

Name of person performing randomisation: .....

Please ENSURE the enrolment log has been updated in the Randomisation box

COMPLETION GUIDELINES

ELIGIBILITY

All inclusion criteria must be YES and all exclusion criteria must be NO for the patient to be eligible.

Eligibility will be checked by a member of the research or clinical team.

If the patient is deemed eligible the patient can be entered into the trial according to the emergency waiver procedures.

Eligibility MUST be recorded in CRYOSTAT 2 Study medical notes retention form which MUST be retained in the patient's medical notes or in the case of electronic patient records, in the CRF, as source data for audit purposes.

STUDY TIMELINES

(1) Patients must be entered into the trial and had the intervention no more than 3 hours from injury.

(2) Patients randomised to the early cryoprecipitate arm to receive 3 pools, infused as rapidly as possible within 90 minutes from arrival in ED.

(3) It is still permissible to start the early cryoprecipitate infusion up to 3 hours from the time of injury.

(4) If more than 3 hours from injury have elapsed the study cryoprecipitate must not be started.

Randomisation Number

R | | | | | |

Participant Initials

| | | |

Site Number

| | | |

SCREENING: ELIGIBILITY CHECKLIST

INCLUSION CRITERIA	YES	NO
(1) The participant is judged to be an adult (according to local practice, e.g. 16 years or older in UK) and has sustained severe traumatic injury	☐	☐
(2) The participant is deemed by the attending clinician to have on-going active haemorrhage *AND requires:*	☐	☐
(3) Activation of the local major haemorrhage protocol for management of severe blood loss	☐	☐
(4) Has started or has received at least one unit of any blood component	☐	☐

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

EXCLUSION CRITERIA	YES	NO
(1) Has the participant been transferred from another hospital?	☐	☐
(2) Does the trauma team leader deem the injuries incompatible with life?	☐	☐
(3) Has more than 3 hours elapsed from the time of injury (taken as time of the 999 call if unknown by medical team).	☐	☐

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

Name of person confirming eligibility: .....

Clinician Name (print)

Clinician Signature

Date Form Completed

				2	0		
D	D	M	M	Y	Y	Y	Y

COMPLETION GUIDELINES

PRE-HOSPITAL INFORMATION

Q3: Date and time of injury: Taken from the time of the 999 call, if unknown.

Q4: Date and time of arrival at Emergency Department: To be recorded from the patient's medical admission record (if not available, to be taken from ambulance records).

Date and time of arrival at ED is considered **Day 1** and all subsequent time points should be measured in a 24 hour clock from this time point.

For example
Date of arrival at ED: 01/01/2017
Time of arrival: 18.00
6 hours from arrival: 00.00
24 hours from arrival: 02/01/2017 18.00

Day 28 from arrival (+/- 4 days) (This allows 28 FULL days from arrival at ED)
29/01/2017, 18.00

BLOOD COMPONENTS, IV FLUIDS FROM TIME OF INJURY TO ARRIVAL AT EMERGENCY DEPARTMENT.

Q6-9: Please record the TOTAL number of blood component units and TOTAL volumes administered from time of injury to arrival at ED.

A unit will be considered to be 'administered' within the specified time period if the infusion has been started.

Randomisation Number: R [ ][ ][ ][ ][ ]

Participant Initials: [ ][ ][ ]

Site Number: [ ][ ][ ]

PRE-HOSPITAL INFORMATION

Patient Details

1. Age (years) [ ][ ]

2. Sex: [ ] Male [ ] Female

3. Date and time of injury: [ ][ ][ ][ ][2][0][ ][ ] (D D M M Y Y Y Y) 24 hour clock [ ][ ][ ][ ] (H H : M M)

4. Date and time of arrival at ED: [ ][ ][ ][ ][2][0][ ][ ] (D D M M Y Y Y Y) 24 hour clock [ ][ ][ ][ ] (H H : M M)

5. Injury type: [ ] Blunt [ ] Penetrating

Blood components, IV fluids and tranexamic acid from time of injury to arrival in ED

6. Number of RBC units: [ ][ ] Units

7. Number of FFP units: [ ][ ] Units

6. a) Number of Red Blood Cell & Plasma units: (For applicable sites only) [ ][ ] Units

8. Total volume of Crystalloids: [ ][ ][ ][ ] mls

9. Total volume of Colloids: [ ][ ][ ][ ] mls

10. Was a Tranexamic Acid bolus administered pre-hospital? [ ] Yes [ ] No

Clinician Name (print)

Clinician Signature

Date Form Completed: [ ][ ][ ][ ][2][0][ ][ ] (D D M M Y Y Y Y)

COMPLETION GUIDELINES

RANDOMISATION

Q1: A patient is randomised once the randomisation envelope is opened. Please record on the clinical trial medical notes retention form for audit purposes.

Please ensure confirmation of randomisation is emailed to
CRYOSTAT2@nhsbt.nhs.uk

Q4-Q6: To be taken from medical notes (first available observations recorded in ED)

PROCEDURES IN EMERGENCY DEPARTMENT

Q7: Patients will receive tranexamic acid as part of the standard major haemorrhage protocol. If the patient has not received tranexamic acid for any reason, they are still eligible for the trial and cryoprecipitate administration is permissible. If applicable, record the reason why the patient did not receive tranexamic acid.

CRYOSTAT 2: Form 3

Randomisation Number: R

Participant Initials:

Site Number:

RANDOMISATION

Randomisation

1. Date and time of randomisation: D D M M Y Y Y Y (2 0) — 24 hour clock: H H : M M

2. Name of person randomising: .....

3. Randomisation number: R

Please email completed Confirmation of Randomisation Form to NHSBT CTU

Patient Observations upon Arrival at ED

4. Blood pressure: Systolic / Diastolic mmHg

5. Glasgow Coma Score:

6. Heart rate: bpm

PROCEDURES IN EMERGENCY DEPARTMENT

7. If a Tranexamic Acid bolus was not given in prehospital, was it given to the patient in ED? ☐ Yes ☐ No ☐ N/A

8. Is the patient on any anticoagulant drugs? ☐ Yes ☐ No

9. If Yes, tick all that apply:
- ☐ Warfarin
- ☐ Rivaroxaban
- ☐ Apixaban
- ☐ Dabigatran
- ☐ Edoxaban
- ☐ Betrixaban
- ☐ LMWH
- ☐ Other , Specify: .....

10. If Yes, Have the antidote(s) been administered to the patient? ☐ Yes ☐ No

11. If Yes, tick all that apply:
- ☐ Idarucizumab
- ☐ Andexanet
- ☐ Prothrombin Complex Concentrate
- ☐ Other , Specify .....

Clinician Name (print)

Clinician Signature

Date Form Completed: D D M M Y Y Y Y (2 0)

COMPLETION GUIDELINES

Please read before completing FORM 4

Q1: If patient has died, please ensure that you tick YES and complete relevant section of this form before proceeding to completing a study completion form AND an SAE form.

SECTIONS 1 and 2

PLEASE ONLY ANSWER THE CORRECT SECTION RELEVANT TO THE ALLOCATION OF THE PATIENT

If the patient is randomised to the STANDARD MAJOR HAEMORRHAGE PROTOCOL ONLY arm, complete SECTION 1.

If the patient is in the EARLY CRYOPRECIPITATE arm, complete SECTION 2.

Section 1- Q4: This relates to the first transfusion of cryoprecipitate only so if 4 pools were given but within two separate major haemorrhage packs, please only record the first dose of Cryoprecipitate, i.e. 2 pools. If 4 pools were given altogether, please record 4 pools.

Section 2- Q9: Please ensure a reason is given if a patient in the EARLY CRYOPRECIPITATE arm is given less than 3 pools of cryoprecipitate.

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CRYOSTAT 2: Form 4

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Randomisation Number: R | | | | | |

Participant Initials: | | |

Site Number: | | |

CRYOPRECIPITATE ADMINISTRATION

1. Has the patient died? ☐ Yes → If yes, complete the relevent section of this form, STUDY COMPLETION Form and SAE Form ☐ No

Section 1 - Complete for STANDARD MHP arm only:

2. Was Cryoprecipitate administered to the patient? ☐ Yes ☐ No

3. Date and time first transfusion of cryoprecipitate was started | | | | | 2 | 0 | | | (D D M M Y Y Y Y) 24 hour clock | | | | (H H : M M)

4. Number of pools given: ☐

Section 2 - Complete for EARLY CRYO arm only

5. Date and time first transfusion of Cryoprecipitate was started | | | | | 2 | 0 | | | (D D M M Y Y Y Y) 24 hour clock | | | | (H H : M M)

6. If Cryoprecipitate was not administered, specify reason:
☐ No active bleeding identified
☐ Patient died
☐ Other

7. If other, specify: .....

8. Number of pools given: ☐ 9.If < 3 pools given provide reason: .....

10. Was Cryoprecipitate given within 90 minutes of arrival in ED? ☐ Yes ☐ No

11. If No, specify reason: .....

Clinician Name (print) | Clinician Signature | Date Form Completed | | | | | 2 | 0 | | | (D D M M Y Y Y Y)

COMPLETION GUIDELINES

BLOOD COMPONENTS AND IV FLUIDS

Q5-10: Please record the TOTAL number of blood component units AND TOTAL volumes administered from arrival in emergency department.

A unit will be considered to be administered within the specified time period if the infusion has been started

If the patient has died within the 24 hour period following arrival in ED Q3 –12 still need to be completed. Please record total blood component units and IV fluids given between the time of patient arrival in ED and the time of death.

CRYOSTAT 2: Form 5

Randomisation Number: R | | | | | |

Participant Initials: | | |

Site Number: | | |

6 HOURS FROM ARRIVAL IN EMERGENCY DEPARTMENT

1. Has the patient had a thromboembolic event or serious transfusion related adverse reaction? ☐ Yes ➡ If yes, complete relevant SAE Form ☐ No

2. Has the patient died? ☐ Yes ➡ If yes, complete STUDY COMPLETION and SAE Form ☐ No

24 HOURS FROM ARRIVAL IN EMERGENCY DEPARTMENT

Medications

3. Was a Tranexamic Acid infusion given to the patient? ☐ Yes ☐ No

4. If No, specify reason: .....

Blood components and IV fluids in hospital:

5. Number of RBC units: | | Units

6. Number of FFP units: | | Units

7. Number of Cryoprecipitate units (pooled bags): | | Units

8. Number of Platelet units: | | Units

9. Total volume of Crystalloids: | | | | mls

10. Total volume of Colloids: | | | | mls

11. Has the patient had a thromboembolic event or serious transfusion related adverse reaction? ☐ Yes ➡ If yes, complete relevant SAE Form ☐ No

12. Has the patient died? ☐ Yes ➡ If yes, complete STUDY COMPLETION and SAE Form ☐ No

Clinician Name (print) | Clinician Signature | Date Form Completed: | | | | 2 | 0 | | |

D D M M Y Y Y Y

COMPLETION GUIDELINES

STUDY COMPLETION FORM

To be completed for ALL patients at either study day 28 (+/- 4 days), discharge or death, whichever is soonest.

Injury Severity Score (ISS)

Please use the injury severity scores provided by TARN and transcribe onto the CRF in questions 5-13 on FORM 6.

Q1: Date of assessment should be day 28 (+/- 4 days), discharge or death, whichever is soonest. For those discharged or died before day 28 (+/-4 days) then the date of assessment is the date of discharge or death.

Q17: Please complete the hospital stay form **whether or not the patient has been discharged from hospital**. This is in order to record ward transfers up until study day 28. The hospital stay form is in FORM 7.

Randomisation Number: R | | | | | |

Participant Initials: | | |

Site Number: | | |

STUDY COMPLETION FORM

Study Day 28 (+/- 4 days), day of discharge or death (whichever is sooner)

1. Date of assessment: | | | | | 2 | 0 | | | (D D M M Y Y Y Y)

2. Was the Health Questionnaire EQ-5D-5L completed? ☐ Yes ☐ No ➡ Complete Forms 8 and 9 ☐ N/A

3. If form 8 and 9 were not completed, specify reason: .....

4. Was the GOS completed? ☐ Yes ☐ No ➡ Complete Form 10

Injury severity score:

5. Head AIS ☐
6. Face AIS ☐
7. Chest AIS ☐
8. Abdomen AIS ☐
9. Spine AIS ☐
10. Pelvis AIS ☐
11. Limbs AIS ☐
12. Other ☐

13. Total Injury Severity Score: | |

14. Were measures for thromboprophylaxis used? ☐ Yes ☐ No

15. If Yes, tick all that apply:
- Anti-embolic Stockings ☐
- Pharmacological ☐
- Intermittent Pneumatic Compression Device ☐
- Other ☐

Specify: .....

16. Has the patient had a thromboembolic event or serious transfusion related adverse reaction? ☐ Yes ☐ No → If yes, complete relevant SAE Form

17. Has the patient been discharged from hospital? ☐ Yes ☐ No → COMPLETE HOSPITAL STAY Form

18. Survival status of patient: ☐ Alive OR ☐ Dead ➡ Complete SAE Form for all DEATHS

Clinician name (print) | Clinician Signature | Date Form Completed | | | 2 | 0 | | | (D D M M Y Y Y Y)

COMPLETION GUIDELINES

HOSPITAL STAY FORM

Q1-3: Please record date/time the patient was first admitted to ICU (level 3)/HDU (level 2)/ward (level 1).

Q4-6: Use this section for instances where a patient transitions back up the scale of care intensity e.g. step down from Level 3 to 2 and then patient deteriorates and is escalated back to Level 3.

Level 1: Patients at risk of their condition deteriorating, or those recently relocated from higher levels of care, whose needs can be met on an acute ward with additional advice and support from the critical care team.) e.g. WARD bed.

Level 2: Patients requiring more detailed observation or intervention including support for a single failing organ system or post-operative care and those 'stepping down' from higher levels of care.) e.g. High Dependency environment (HDU).

Level 3: Patients requiring advanced respiratory support alone or monitoring and support for two or more organ systems. This level includes all complex patients requiring support for multi-organ failure.) e.g. Intensive Care Unit (ICU).

Q7: Calculate the total number of ventilator days (rounded up) from arrival to date of assessment (form 6).

Q8:Calculate the total length of hospital stay in total days (rounded up) from arrival to date of assessment (form 6).

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CRYOSTAT 2: Form 7

NHS Blood and Transplant

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Randomisation Number: R | | | | | |

Participant Initials: | | |

Site Number: | | |

HOSPITAL STAY FORM

Study day 28 (+/- 4 days) day of discharge or death (whichever is sooner)

Hospital Stay and Discharge

	Date (D D M M Y Y Y Y)	Time 24 hr clock (H H : M M)	Tick box if N/A
1. Admitted to critical care unit requiring Level 3 care			
2. Admitted to (or remained in) critical care requiring Level 2 care			
3. Admitted to ward (Level 1 care)			
For patient requiring re-admission to critical care:			
4. Admitted to critical care unit requiring Level 3 care			
5. Admitted to (or remained in) critical care unit requiring Level 2 care			
6. Admitted to ward (Level 1 care)			

7. Total ventilator days: | | Days

8. Total length of hospital stay: | | Days

Hospital Discharge

9. Date of discharge: | | | | 2 0 | | | (D D M M Y Y Y Y) | | N/A

N/A if in-patient or died

10. Discharge to the following location:

- Home
- Nursing home / rehabilitation facility
- Another hospital — Hospital name: .....
- Other — Specify: .....

Clinician Name (print) | Clinician Signature | Date Form Completed (D D M M Y Y Y Y)

COMPLETION GUIDELINES

HEALTH QUESTIONNAIRE: EQ-5D-5L AT DISCHARGE OR DAY 28 (+/- 4 days) whichever is sooner

Research teams should administer the standard PROMS questionnaire to CRYOSTAT-2 patients during the trial in order to avoid duplication.

Patients should complete the PROMS questionnaire if they have regained capacity or information obtained from the responsible clinician if the patient has not regained capacity, according to local policy.

Once the PROMs questionnaire has been completed, please **transcribe** the EQ-5D-5L score onto FORM 8, and record the unique Q identifier printed on the PROMS questionnaire onto the relevant field in the CRF. This is a unique identifier attributed to each patient and will allow the Trauma Audit & Research Network to flag CRYOSTAT 2 patients when following them up at six months post injury.

Please remember to complete **ALL** the patients unique identifiers for follow up on the electronic spreadsheet provided to each site.

Please complete Date of assessment as the date the EQ-5D-5L questionnaire was completed.

Randomisation Number

R | | | | | |

Participant Initials

| | | |

Site Number

| | | |

HEALTH QUESTIONNAIRE
EQ-5D-5L AT DISCHARGE or DAY 28 (+/- 4 days) whichever is sooner

Q | | | | | | | | |

Date of assessment: | | | | | 2 | 0 | | |
D D M M Y Y Y Y

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY:

I have no problems in walking about..... ☐
I have slight problems in walking about..... ☐
I have moderate problems in walking about..... ☐
I have severe problems in walking about..... ☐
I am unable to walk..... ☐

SELF- CARE:

I have no problems washing or dressing myself..... ☐
I have slight problems washing or dressing myself..... ☐
I have moderate problems washing or dressing myself..... ☐
I have severe problems washing or dressing myself..... ☐
I am unable to wash or dress myself..... ☐

USUAL ACTIVITIES: *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities..... ☐
I have slight problems doing my usual activities..... ☐
I have moderate problems doing my usual activities..... ☐
I have severe problems doing my usual activities..... ☐
I am unable to do my usual activities..... ☐

PAIN / DISCOMFORT:

I have no pain or discomfort..... ☐
I have slight pain or discomfort..... ☐
I have moderate pain or discomfort..... ☐
I have severe pain or discomfort..... ☐
I have extreme pain or discomfort..... ☐

ANXIETY / DEPRESSION:

I am not anxious or depressed..... ☐
I am slightly anxious or depressed..... ☐
I am moderately anxious or depressed..... ☐
I am severely anxious or depressed..... ☐
I am extremely anxious or depressed..... ☐

COMPLETION GUIDELINES

Research teams should administer the standard PROMS questionnaire to CRYOSTAT-2 patients during the trial in order to avoid duplication.

Patients should complete the PROMS questionnaire if they have regained capacity or information obtained from the responsible clinician if the patient has not regained capacity, according to local policy.

Once the PROMs questionnaire has been completed, please **transcribe** the EQ-5D-5L score onto FORM 9, and record the unique Q identifier printed on the PROMS questionnaire onto the relevant field in the CRF. This is a unique identifier attributed to each patient and will allow the Trauma Audit & Research Network to flag CRYOSTAT 2 patients when following them up at six months post injury.

Please remember to complete **ALL** the patients unique identifiers for follow up on the electronic spreadsheet provided to each site.

Please complete Date of assessment as the date the EQ-5D-5L questionnaire was completed.

Randomisation Number: R

Participant Initials

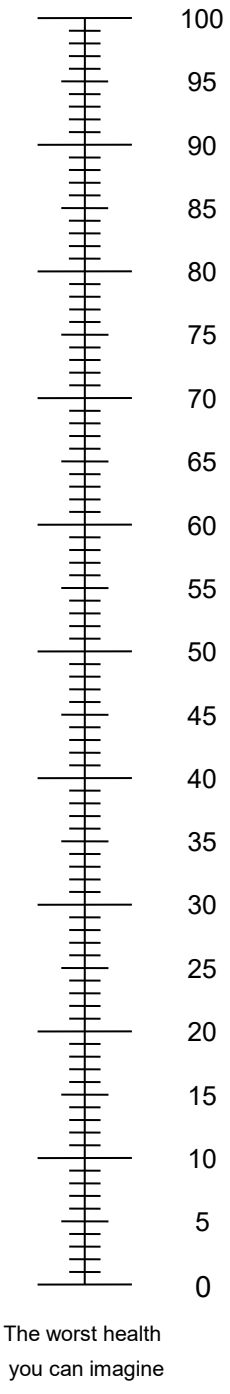
Site Number

HEALTH QUESTIONNAIRE: EQ-5D-5L

Date of assessment: 2 0 (D D M M Y Y Y Y)

Q

- Transcribed from the PROMS Questionnaire
- This scale is numbered from 0 to 100
- 100 means the best health you can imagine
  0 means the worst health you can imagine
- Mark an **X** on the scale to indicate how the patients health is TODAY
- Now please write the number the patient marked on the scale in the box below



THE PATIENTS HEALTH TODAY =

COMPLETION GUIDELINES

The Glasgow outcome scale (GOS) should be collected by the research team upon DISCHARGE or DEATH or DAY 28, (+/- 4 days) whichever is sooner.

The GOS is a global scale for functional outcome that rates patient status into one of five categories:

The scale consists of five outcome categories:

Low disability/Good recovery
Moderate disability
Severe disability
Persistent vegetative state
Death

Please tick the box which best describes the patient's condition as of NOW

CRYOSTAT 2: Form 10

Randomisation Number: R | | | | | |

Participant Initials: | | |

Site Number: | | |

GLASGOW OUTCOME SCALE AT DISCHARGE or DEATH or DAY 28 (+/- 4 days) whichever is sooner

Date of assessment: | | | | | 2 | 0 | | |
D D M M Y Y Y Y

Please tick ONE applicable box

1. **Low disability/Good recovery**: Light damage with minor neurological and psychological deficits (able to live independently, able to return to work or school) ☐

2. **Moderate disability**: No need for assistance in everyday life employment is possible but may require special equipment. (able to live independently, unable to return to work or school) ☐

3. **Severe disability**: Severe injury with permanent need for help with daily living (able to follow commands, unable to live independently) ☐

4. **Persistent vegetative state**: Severe damage with prolonged state of unresponsiveness and a lack of higher mental functions (unable to interact with the environment, unresponsive) ☐

5. **Death**: Severe injury or death without recovery of consciousness ☐

COMPLETION GUIDELINES

The emergency waiver at study entry provides permission for data collection for 5 days post-randomisation. A professional or personal consultee **OR** patient signed informed consent should be sought as soon as possible within the 5 day window.

CRFs should not be sent to the CTU unless a consultee declaration **OR** patient signed informed consent is in place.

Q1, 2 and 4. Please select **all levels** of consent obtained for this patient.

Q3. Approaching the patient includes face-to-face discussions, telephone calls or letters. Any attempts to approach the patient for consent should be documented in the patient notes. If the patient has not responded to attempts to gain consent, please provide more details in Q6 about the attempts made.

Q4. If the answer is No, please complete Q5 and provide a summary in Q6.

Q6. Please explain why the patient has not been approached for consent and/ or why patient informed consent has not been obtained and document any attempts to obtain patient signed informed consent. If patient signed informed consent has been obtained please mark this box as N/A. If a patient has given verbal consent but has not given patient signed informed consent, please document this in Q6.

Randomisation Number: R | | | | | |

Participant Initials: | | |

Site Number: | | |

LEVEL OF CONSENT FORM

1. Professional Consultee — YES ☐ NO ☐ If No, specify: .....

   If Yes, date consultee signed | | | | | 2 | 0 | | | (D D M M Y Y Y Y)

2. Personal Consultee — YES ☐ NO ☐ If No, specify: .....

   If Yes, date consultee signed | | | | | 2 | 0 | | | (D D M M Y Y Y Y)

3. Has the patient been approached? YES ☐ NO ☐ → *If No, go to Q6*

   If Yes, date patient was first approached | | | | | 2 | 0 | | | (D D M M Y Y Y Y)

   If Yes, how many attempts to gain consent have been made? | |

   If Yes, has the patient responded? YES ☐ → *If Yes, go to Q4* NO ☐ → *If No, go to Q6*

4. Has the patient provided Signed Patient Informed Consent? YES ☐ NO ☐ *If No, go to Q5*

   If Yes, date patient signed | | | | | 2 | 0 | | | (D D M M Y Y Y Y)

   YES NO

   If Yes, has the patient initialled box 7 on the patient informed consent form? ☐ ☐

   If Yes, has the patient initialled box 9 on the patient informed consent form? ☐ ☐

5. If No to Q4, has the patient declined to consent? *Give more details in Q6* ☐ ☐

6. Please provide an explanation if patients have not been approached and/or do not have signed informed consent in place

Clinician Name (print) | Clinician Signature | Date Form Completed | | | 2 | 0 | | | (D D M M Y Y Y Y)

COMPLETION GUIDELINES

Record SAEs from randomisation until hospital discharge or Study Day 28 and if death occurs

Q1: Always use the same SAE description/diagnosis for the event on the follow up forms for cross-referencing. SAE name:
The event indicated should be the thromboembolic event that has led to the serious transfusion related adverse event/reaction. **IN THE EVENT THAT DEATH IS THE OUTCOME, 'DEATH' SHOULD NOT BE INDICATED AS THE TITLE IN THIS SECTION. THE *EVENT LEADING TO DEATH* SHOULD CONSTITUTE THE 'SAE NAME'**

Q2: Record start date of SAE. If SAE occurs intermittently at the same frequency and intensity, the start date can be date of the first occurrence.

Q7: Definitions:
Pulmonary embolus (PE)/Deep Vein Thrombosis (DVT): there must be clinical symptoms and definitive radiological evidence as follows:

DVT (of the limbs or other significant veins i.e. portal vein): All DVTs to be reported on the SAE form Accepted methods of diagnosis include:
- compression ultrasound
- venography
- CT scan/MR venogram if more proximal leg veins or abdominal veins involved

Pulmonary Embolus (PE): Accepted methods of diagnosis include:
- CT – pulmonary angiogram (CTPA)
- Ventilation-Perfusion scan (V/Q or Q scan as per local guidelines)
- SPECT scan

Myocardial Infarction (MI): evidence of myocardial necrosis in a clinical setting consistent with myocardial ischaemia. Under these conditions presence of one of the following criteria meets the diagnosis of MI:

- Detection of rise of troponin with at least one value above the 99th percentile of the ULN, plus evidence of myocardial ischaemia with at least 1 of the following:
  - symptoms of ischaemia.
  - ECG changes indicative of new ischaemia [ST-T changes, or LBBB]
  - development of pathological Q waves in ECG
  -imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
- Sudden, unexpected cardiac death, often with cardiac symptoms, and accompanied by new ECG changes, but before blood tests could be taken or death occurred before the appearance of cardiac biomarkers in the blood
- Pathological findings of acute MI.

Ischaemic Stroke: Clinical report of brain imaging consistent with an ischaemic stroke in association with new onset focal or generalised neurological deficit (defined as deficit in motor, sensory or co-ordination function).

Q11: Classify the status of the SAE at the time of reporting. Those marked with an asterisk also require the date/time of resolution to be completed.

Randomisation Number: R

Participant Initials

Site Number

SERIOUS ADVERSE EVENT (SAE) FORM

Type of report: *(Please tick one box only)*

Initial ☐ Follow up 1 ☐ Follow up 2 ☐ Follow up 3 ☐ Follow up 4 ☐

1. SAE Name: .....

2. Date and time of SAE onset: 2 0 (D D M M Y Y Y Y) 24 hour clock (H H : M M)

3. Name of Hospital: .....

4. Sex: ☐ Male ☐ Female 5. Age: ☐☐ Years

6. Date and Time of randomisation: 2 0 (D D M M Y Y Y Y) 24 hour clock (H H : M M)

7. Please classify the SAE under one of the following: *(Please tick one box only)*

- ☐ Pulmonary embolus
- ☐ Ischaemic Stroke
- ☐ Death → Complete question 8
- ☐ DVT
- ☐ Myocardial Infarction
- ☐ Other occlusion of any other artery

8. If DEATH, Date and Time of Death: 2 0 (D D M M Y Y Y Y) 24 hour clock (H H : M M)

9. Primary cause of death:

- ☐ Uncontrolled bleeding
- ☐ Myocardial infarction
- ☐ Stroke
- ☐ Pulmonary embolism
- ☐ Other
- ☐ Multi-organ failure
- ☐ Multiple injury
- ☐ Traumatic brain injury
- ☐ Sepsis

10. If Other, Specify: .....

E-mail SAEs report within 24 hours to Serious_Adverse_Events@nhsbt.nhs.uk

11. Status of SAE: *(Please tick one box only)*

☐ Resolved* ☐ Worsening ☐ Fatal* ☐ Resolved with sequelae* ☐ Ongoing

12. *Date and time of SAE resolution: 2 0 (D D M M Y Y Y Y) 24 hour clock (H H : M M)

Clinician Name (print) | Clinician Signature | Date Form Completed: 2 0 (D D M M Y Y Y Y)

COMPLETION GUIDELINES

This form MUST be completed alongside FORM 11- Serious Adverse Event (SAE) form (Page 31) as it provides vital details required for the CTU when they are formally escalating the event.

Please complete this form at the same time as the SAE form and send directly to the NHSBT CTU as **soon as possible**.
As a maximum timescale, please return via email within 5 working days of the identification of the event to **serious_adverse_events@nhsbt.nhs.uk**.

SAE name: The thromboembolic event that has led to the serious transfusion related adverse event/reaction. **IN THE EVENT THAT DEATH IS THE OUTCOME, 'DEATH' SHOULD NOT BE INDICATED AS THE TITLE IN THIS SECTION. THE *EVENT LEADING TO DEATH* SHOULD CONSTITUTE THE 'SAE NAME'**

Definition of a Serious Adverse Event (SAE) or
Serious Transfusion related Adverse Reaction

Respectively, any adverse event, adverse transfusion reaction or unexpected adverse transfusion reaction that:

1. Results in death
2. Is life-threatening*
3. Requires hospitalisation or prolongation of existing hospitalisation**
4. Results in persistent or significant disability or incapacity

*The term 'life-threatening' in the definition of 'serious' refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
**Hospitalisation is defined as an inpatient admission, regardless of length of stay, even if the hospitalisation is a precautionary measure for continued observation. Hospitalisations for a pre-existing condition (including elective procedures that have not worsened) do not constitute an SAE.

Type of report
Please use this section to indicate whether this is the first (initial), or follow up (1,2,3 or 4) SAE form that has been submitted.

Q1: Please enter a brief but descriptive title for the SAE. Always use the same SAE description/diagnosis as in the SAE form (FORM 11) for cross-referencing.

Q2: Record start date of Serious Adverse Event ensuring that it matches the date on the SAE form (FORM 11).

Randomisation Number: R | | | | | |

Participant Initials: | | |

Site Number: | | |

SERIOUS ADVERSE EVENT (SAE) NARRATIVE FORM

Type of report: *(Please tick one box only)*

Initial ☐ Follow up 1 ☐ Follow up 2 ☐ Follow up 3 ☐ Follow up 4 ☐

1. Serious Adverse Event Description/Diagnosis: .....

2. Date and time of SAE onset: | | | | | 2 | 0 | | | (D D M M Y Y Y Y) 24 hour clock | | | | | (H H : M M)

3. Describe SAE: *(Include manifestation and progression of event. Continue on a separate sheet if necessary)*

.....

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.....

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4. Treatment / Tests given:

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.....

5. Outcome: *(Including death if applicable)* .....

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.....

.....

Completed SAE Narrative Form 12 must be sent to the NHSBT CTU within 5 working days of identification of the event.
E-mail: Serious_Adverse_Events@nhsbt.nhs.uk

Clinician Name (print) | Clinician Signature | Date Form Completed | | | | | | 2 | 0 | | | (D D M M Y Y Y Y)

COMPLETION GUIDELINES

Record SAEs from randomisation until hospital discharge or Study Day 28 and if death occurs

Q1: Always use the same SAE description/diagnosis for the event on the follow up forms for cross-referencing. SAE name:
The event indicated should be the thromboembolic event that has led to the serious transfusion related adverse event/reaction. **IN THE EVENT THAT DEATH IS THE OUTCOME, 'DEATH' SHOULD NOT BE INDICATED AS THE TITLE IN THIS SECTION. THE *EVENT LEADING TO DEATH* SHOULD CONSTITUTE THE 'SAE NAME'**

Q2: Record start date of SAE. If SAE occurs intermittently at the same frequency and intensity, the start date can be date of the first occurrence

Q7: Definitions:
Pulmonary embolus (PE)/Deep Vein Thrombosis (DVT): there must be clinical symptoms and definitive radiological evidence as follows:

DVT (of the limbs or other significant veins i.e. portal vein): All DVTs to be reported on the SAE form Accepted methods of diagnosis include:

- compression ultrasound
- venography
- CT scan/MR venogram if more proximal leg veins or abdominal veins involved

Pulmonary Embolus (PE): Accepted methods of diagnosis include:

- CT – pulmonary angiogram (CTPA)
- Ventilation-Perfusion scan (V/Q or Q scan as per local guidelines)
- SPECT scan

Myocardial Infarction (MI): evidence of myocardial necrosis in a clinical setting consistent with myocardial ischaemia. Under these conditions presence of one of the following criteria meets the diagnosis of MI:

- Detection of rise of troponin with at least one value above the 99th percentile of the ULN, plus evidence of myocardial ischaemia with at least 1 of the following:
  - symptoms of ischaemia.
  - ECG changes indicative of new ischaemia [ST-T changes, or LBBB]
  - development of pathological Q waves in ECG
  -imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
- Sudden, unexpected cardiac death, often with cardiac symptoms, and accompanied by new ECG changes, but before blood tests could be taken or death occurred before the appearance of cardiac biomarkers in the blood
- Pathological findings of acute MI .

Ischaemic Stroke: Clinical report of brain imaging consistent with an ischaemic stroke in association with new onset focal or generalised neurological deficit (defined as deficit in motor, sensory or co-ordination function).

Q11: Classify the status of the SAE at the time of reporting. Those marked with an asterisk also require the date/time of resolution to be completed.

Randomisation Number: R

Participant Initials

Site Number

SERIOUS ADVERSE EVENT (SAE) FORM

Type of report: *(Please tick one box only)*

Initial ☐ Follow up 1 ☐ Follow up 2 ☐ Follow up 3 ☐ Follow up 4 ☐

1. SAE Name: .....

2. Date and time of SAE onset: D D M M Y Y Y Y (2 0) — 24 hour clock H H : M M

3. Name of Hospital: .....

4. Sex: ☐ Male ☐ Female 5. Age: ☐☐ Years

6. Date and Time of randomisation: D D M M Y Y Y Y (2 0) — 24 hour clock H H : M M

7. Please classify the SAE under one of the following: *(Please tick one box only)*

- ☐ Pulmonary embolus
- ☐ Ischaemic Stroke
- ☐ Death → Complete question 8
- ☐ DVT
- ☐ Myocardial Infarction
- ☐ Other occlusion of any other artery

8. If DEATH, Date and Time of Death: D D M M Y Y Y Y (2 0) — 24 hour clock H H : M M

9. Primary cause of death:

- ☐ Uncontrolled bleeding
- ☐ Myocardial infarction
- ☐ Stroke
- ☐ Pulmonary embolism
- ☐ Other
- ☐ Multi-organ failure
- ☐ Multiple injury
- ☐ Traumatic brain injury
- ☐ Sepsis

10. If Other, Specify: .....

E-mail SAEs report within 24 hours to Serious_Adverse_Events@nhsbt.nhs.uk

11. Status of SAE: *(Please tick one box only)*

☐ Resolved* ☐ Worsening ☐ Fatal* ☐ Resolved with sequelae*
☐ Ongoing

12. *Date and time of SAE resolution: D D M M Y Y Y Y (2 0) — 24 hour clock H H : M M

Clinician Name (print) | Clinician Signature | Date Form Completed: D D M M Y Y Y Y (2 0)

COMPLETION GUIDELINES

This form MUST be completed alongside FORM 11- Serious Adverse Event (SAE) form (Page 31) as it provides vital details required for the CTU when they are formally escalating the event.

Please complete this form at the same time as the SAE form and send directly to the NHSBT CTU as **soon as possible**.
As a maximum timescale, please return via email within 5 working days of the identification of the event to **serious_adverse_events@nhsbt.nhs.uk**.

SAE name: The thromboembolic event that has led to the serious transfusion related adverse event/reaction. **IN THE EVENT THAT DEATH IS THE OUTCOME, 'DEATH' SHOULD NOT BE INDICATED AS THE TITLE IN THIS SECTION. THE *EVENT LEADING TO DEATH* SHOULD CONSTITUTE THE 'SAE NAME'**

Definition of a Serious Adverse Event (SAE) or Serious Transfusion related Adverse Reaction

Respectively, any adverse event, adverse transfusion reaction or unexpected adverse transfusion reaction that:

1. Results in death
2. Is life-threatening*
3. Requires hospitalisation or prolongation of existing hospitalisation**
4. Results in persistent or significant disability or incapacity

*The term 'life-threatening' in the definition of 'serious' refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
**Hospitalisation is defined as an inpatient admission, regardless of length of stay, even if the hospitalisation is a precautionary measure for continued observation. Hospitalisations for a pre-existing condition (including elective procedures that have not worsened) do not constitute an SAE.

Type of report
Please use this section to indicate whether this is the first (initial), or follow up (1,2,3 or 4) SAE form that has been submitted.

Q1: Please enter a brief but descriptive title for the SAE. Always use the same SAE description/diagnosis as in the SAE form (FORM 11) for cross-referencing.

Q2: Record start date of Serious Adverse Event ensuring that it matches the date on the SAE form (FORM 11).

Randomisation Number: R | | | | | |

Participant Initials: | | |

Site Number: | | |

SERIOUS ADVERSE EVENT (SAE) NARRATIVE FORM

Type of report: *(Please tick one box only)*

Initial ☐ Follow up 1 ☐ Follow up 2 ☐ Follow up 3 ☐ Follow up 4 ☐

1. Serious Adverse Event Description/Diagnosis: .....

2. Date and time of SAE onset: | | | | | 2 | 0 | | | (D D M M Y Y Y Y) 24 hour clock | | | | | (H H : M M)

3. Describe SAE: *(Include manifestation and progression of event. Continue on a separate sheet if necessary)*

.....

.....

.....

.....

4. Treatment / Tests given:

.....

.....

.....

5. Outcome: *(Including death if applicable)* .....

.....

.....

.....

Completed SAE Narrative Form 12 must be sent to the NHSBT CTU within 5 working days of identification of the event.
E-mail: Serious_Adverse_Events@nhsbt.nhs.uk

Clinician Name (print) | Clinician Signature | Date Form Completed: | | | | | 2 | 0 | | | (D D M M Y Y Y Y)

COMPLETION GUIDELINES

This form should be completed in the event of a Serious Transfusion Related Adverse Event/reaction.

Definition of a Serious Transfusion Related Adverse Event/reaction

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a participant or clinical trial subject to whom a blood component has been administered.
Transfusion Related Adverse Reaction or Event	Any untoward and unintended response to a transfused blood component.
Serious Transfusion related Adverse Reaction	Respectively any adverse event, adverse transfusion reaction or unexpected adverse transfusion reaction that: results in death is life-threatening* requires hospitalisation or prolongation of existing hospitalisation** results in persistent or significant disability or incapacity

*The term 'life-threatening' in the definition of 'serious' refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
**Hospitalisation is defined as an inpatient admission, regardless of length of stay, even if the hospitalisation is a precautionary measure for continued observation. Hospitalisations for a pre-existing condition (including elective procedures that have not worsened) do not constitute an SAE.

Type of report

Please use this section to indicate whether this is the first (initial), or follow up (1,2,3 or 4) SAE form that has been submitted and ensure the date fields are completed..

Reason for transfusion related adverse event/reaction

When reporting grade of Acute Haemolytic transfusions, please indicate which grade using the following 'Serious Hazards of Transfusion' (SHOT) guidance: https://www.shotuk.org/wp-content/uploads/SHOT-Definitions-Update-2017-FINAL-2.pdf retrieved 12th June 2017.

SEVERITY GRADES FOR HAEMOLYTIC TRANSFUSION REACTIONS			
1 = DAT without haemolysis	**2 = Mild**	**3 = Moderate**	**4 = Severe**
Not SHOT reportable	*2 of the following:* • Falling haemoglobin • Positive DAT • Spherocytes	• Falling haemoglobin • Rise in bilirubin • ± positive DAT • ± spherocytes	• Falling haemoglobin • Rise in bilirubin • Renal impairment • ± positive DAT • ± spherocytes

Randomisation Number: R

Participant Initials

Site Number

SERIOUS TRANSFUSION RELATED ADVERSE EVENT

Record Serious Transfusion Related AEs occurring from Randomisation to Study Completion

Did the Transfusion related SAE lead to death? ☐ No ☐ Yes → If **Yes**, also complete an SAE **FORM 11** AND Narrative **FORM 12**

Type of report: *(Please tick one box only)*

Initial ☐ Follow up 1 ☐ Follow up 2 ☐ Follow up 3 ☐ Follow up 4 ☐

Serious Transfusion Related Adverse Event Name: .....

Date and start time of transfusion: 2 0 _ _ (D D M M Y Y Y Y) _ _ : _ _ (H H : M M)

Relates to transfusion of : *(Please insert number of units of each component in the*

☐☐ Red Blood Cells ☐☐ Platelets

☐☐ Fresh Frozen Plasma ☐☐ Cryoprecipitate

Reason for transfusion related adverse event:

☐ Acute Haemolytic transfusion **If Yes, Grade:** Grade 1 ☐ Grade 2 ☐ Grade 3 ☐ Grade 4 ☐

☐ Febrile non-haemolytic transfusion

☐ Transfusion associated acute lung injury

☐ Transfusion related circulatory overload

☐ Anaphylaxis/severe allergic

☐ Incorrect blood component transfused

☐ Other, specify: .....

Causal relationship to trial transfusion: *(Please tick one box only)*

☐ Definite ☐ Probable ☐ Possible ☐ Unlikely ☐ Not related

Is this a known (i.e. expected) adverse transfusion related reaction?

☐ Yes, expected ☐ No, not expected**

**Note: Any unexpected transfusion complications will require expedited reporting as a suspected unexpected serious transfusion related adverse reaction

Completed Form must be sent to the NHSBT CTU within 24 hours of identification of the event. E-mail: Serious_Adverse_Events@nhsbt.nhs.uk

Clinician Name (print) | Clinician Signature | Date Form 2 0 _ _ (D D M M Y Y Y Y)

COMPLETION GUIDELINES

This form MUST be completed alongside FORM 13- Serious Transfusion Related Adverse Event form (Page 39) and provides vital details required for the CTU when they are formally escalating the event.

Please complete this form at the same time as the SAE form and send directly to the NHSBT CTU as soon as possible. As a maximum timescale, please return via email within 5 working days of the identification of the event to **serious_adverse_events@nhsbt.nhs.uk**.

Definition of a Serious Transfusion Related Adverse Event

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a participant or clinical trial subject to whom a blood component has been administered.
Transfusion Related Adverse Reaction or Event	Any untoward and unintended response to a transfused blood component.
Serious Adverse Event (SAE) or Serious Transfusion related Adverse Reaction	**Respectively any adverse event, adverse transfusion reaction or unexpected adverse transfusion reaction that: results in death is life-threatening* requires hospitalisation or prolongation of existing hospitalisation** results in persistent or significant disability or incapacity**
Unexpected Adverse Transfusion Reaction	An adverse reaction, the nature or severity of which is not consistent with the known reactions to transfusion of a blood component (in the case of this trial, cryoprecipitate).

*The term 'life-threatening' in the definition of 'serious' refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
**Hospitalisation is defined as an inpatient admission, regardless of length of stay, even if the hospitalisation is a precautionary measure for continued observation. Hospitalisations for a pre-existing condition (including elective procedures that have not worsened) do not constitute an SAE.

Type of report
Please use this section to indicate whether this is the first (initial), or follow up (1,2,3 or 4) SAE form that has been submitted.

Q1: Please enter a brief but descriptive title for the SAE. Always use the same SAE description/diagnosis as in the Serious Transfusion Related Adverse Event form (FORM 13) for cross-referencing.

Q2: Record start date of Serious Transfusion Related Adverse Event ensuring that it matches the date on the Serious Transfusion Related Adverse Event form (FORM 13) for cross referencing.

Randomisation Number: R | | | | | |

Participant Initials: | | |

Site Number: | | |

SERIOUS TRANSFUSION RELATED ADVERSE EVENT NARRATIVE FORM

Type of report: *(Please tick one box only)*

Initial ☐ Follow up 1 ☐ Follow up 2 ☐ Follow up 3 ☐ Follow up 4 ☐

1. Transfusion Related SAE
Description/Diagnosis: .....

2. Date and time of Transfusion Related SAE onset: | | | | | 2 | 0 | | | (D D M M Y Y Y Y) 24 hour clock | | | | (H H : M M)

3. Describe Transfusion Related SAE:
(Include manifestation and progression of event. Continue on a separate sheet if necessary)

.....

.....

.....

.....

4. Treatment / Tests given:

.....

.....

.....

5. Outcome: *(Including death if applicable)* .....

.....

.....

.....

Completed Transfusion related SAE Narrative Form 14 must be sent to the NHSBT CTU within 5 working days of identification of the event.
E-mail: Serious_Adverse_Events@nhsbt.nhs.uk

Clinician Name (print) | Clinician Signature | Date Form Completed | | | | | 2 | 0 | | | (D D M M Y Y Y Y)

COMPLETION GUIDELINES

Please complete FORM 15 for any patient who was withdrawn from the trial prior to study day 28 irrespective of the reason for withdrawal. If patient died prior to study day 28, do not complete FORM 15, please complete FORM 6—7, & 11—12

Reasons for withdrawal from the study may include;

- withdrawal by clinician due to a serious adverse event or adverse event
- withdrawal by clinician due to other medical complication
- withdrawal of patient/patient representative consent for study follow up to study day 28

It is unlikely that a patient will be withdrawn from study treatment due to the emergency nature of the trial; however; in these circumstances it is important to follow the patient up and collect their data up to study day 28 wherever possible. If the patient/patient representive does not consent for their data to be collected post withdrawal, please indicate on this form.

Please give as much information as possible as to the reason for withdrawal.

Randomisation Number

R | | | | | |

Participant Initials

| | | |

Site Number

| | | |

STUDY WITHDRAWAL FORM

1. Date and time of withdrawal: | | | | | 2 | 0 | | | (D D M M Y Y Y Y) 24 hour clock | | | | (H H : M M)

2. Withdrawal request made by:

Patient ☐

Patient Representative ☐

Independent Clinician ☐

Other ☐

3. If other, please specify: .....

4. What reason was given for withdrawal?

.....

.....

.....

5. Does the patient agree for continued follow up and data collection?

☐ Yes ☐ No

Clinician Name (print) | Clinician Signature | Date Form Completed

| | | | | | | | | (D D M M Y Y Y Y)

COMPLETION GUIDELINES

General Information

Form Completion:
Each form will be printed on two copies of no carbon required (NCR) paper. Please complete the top (white) copy of the form, which will transfer automatically to the bottom (yellow) copy. **Use this writing shield underneath the yellow copy to avoid contamination of ink onto subsequent forms**.

Please complete the CRF in black ink. Please ensure all answers are clear and legible. All questions must be completed as specified. Any question that is unknown (UK), not done (ND), not applicable (NA) should be recorded as such on the CRF.

Each form includes a header where the patient identification details will be recorded. The Randomisation Number is assigned once the sealed envelope is opened. This is the patient's unique identifier for the trial and should be used on all study related documents relating to the patient.

Participant's Initials should be in the format [AAA] or [A-A].

All dates should be completed as DDMM20YY. Enter empty fields as 0 e.g. 4th May 2015 as 04/05/2015. Do not leave blank and do not use -, X, / or other characters.

All times should be completed as HH:MM using the 24 hr clock and enter empty fields as 0 e.g. 3pm is entered as 15:00. Do not leave blank and do not use -, X, / or other characters.

For numerical entries, enter leading zeros to complete all boxes for a 3 box field e.g. 027.

Any data incorrectly recorded on the CRF must be crossed through with a single line and correct value entered to the side. All corrections must be initialled and dated by the individual making the changes.

Each form will require a declaration of completion signed by the delegated individual completing the CRFs to confirm the data collected is a true and accurate reflection of the patient's medical notes and source data.

On completion of each CRF, please tear off the white copy and send with a CRF transmittal form to:
Rupa Sharma,
Data Manager
NHSBT Clinical Trials Unit
Long Road
Cambridge, CB2 0PT

Please do NOT send the yellow copy of each form. They must reside in the CRF booklet for audit purposes.

Confirmation of Randomisation forms MUST be scanned/emailed immediately to:
cryostat2@nhsbt.nhs.uk .

SAE forms MUST be scanned/emailed immediately to:
Serious_Adverse_Events@nhsbt.nhs.uk