

Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

Please enter a short title for this project (maximum 70 characters)

SWiFT - Study of Whole blood in Frontline Trauma

1. Is your project research?

☒ Yes ☐ No

2. Select one category from the list below:

- ☒ Clinical trial of an investigational medicinal product
- ☐ Combined trial of an investigational medicinal product and an investigational medical device
- ☐ Clinical investigation or other study of a medical device
- ☐ Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice
- ☐ Basic science study involving procedures with human participants
- ☐ Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
- ☐ Study involving qualitative methods only
- ☐ Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)
- ☐ Study limited to working with data (specific project only)
- ☐ Research tissue bank
- ☐ Research database

If your work does not fit any of these categories, select the option below:

☐ Other study

2a. Is this a commercially sponsored Phase 1 or Phase 1/2a trial involving healthy volunteers?

☐ Yes ☒ No

2b. Will the study involve the use of any medical device without a UKCA/CE UKNI/CE Mark, or a UKCA/CE UKNI/CE marked device which has been modified or will be used outside its intended purposes?

☐ Yes ☒ No

2c. Please answer the following question:

Is this trial subject to advice from the Expert Advisory Group on Clinical Trials and the Commission on Human Medicine prior to authorisation from MHRA?

☐ Yes ☒ No

2d. Please answer the following question:

Is this a trial of a gene therapy medicinal product?

☐ Yes ☒ No

2e. Please answer the following question(s):

a) Does the study involve the use of any ionising radiation? ☐ Yes ☒ No

b) Will you be taking new human tissue samples (or other human biological samples)? ☐ Yes ☒ No

c) Will you be using existing human tissue samples (or other human biological samples)? ☐ Yes ☒ No

3. In which countries of the UK will the research sites be located?(Tick all that apply)

- ☒ England
☐ Scotland
☐ Wales
☐ Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

- ☒ England
☐ Scotland
☐ Wales
☐ Northern Ireland
☐ This study does not involve the NHS

4. Which applications do you require?

- ☒ IRAS Form
☒ Medicines and Healthcare products Regulatory Agency (MHRA) – Medicines
☒ Confidentiality Advisory Group (CAG)
☐ Her Majesty's Prison and Probation Service (HMPPS)

4a. Will you be seeking data from Hospital Episode Statistics (HES) or the Secondary Uses Service (SUS)?

☐ Yes ☒ No

5. Will any research sites in this study be NHS organisations?

☒ Yes ☐ No

5a. Are all the research costs and infrastructure costs (funding for the support and facilities needed to carry out the research e.g. NHS support costs) for this study provided by a NIHR Biomedical Research Centre (BRC), NIHR Applied Research Collaboration (ARC), NIHR Patient Safety Translational Research Centre (PSTRC), or an NIHR Medtech and In Vitro Diagnostic Co-operative (MIC) in all study sites?

Please see information button for further details.

☐ Yes ☒ No

Please see information button for further details.

5b. Do you wish to make an application for the study to be considered for NIHR Clinical Research Network (CRN) Support and inclusion in the NIHR Clinical Research Network Portfolio?

Please see information button for further details.

☒ Yes ☐ No

The NIHR Clinical Research Network (CRN) provides researchers with the practical support they need to make clinical studies happen in the NHS in England e.g. by providing access to the people and facilities needed to carry out research "on the ground".

If you select yes to this question, information from your IRAS submission will automatically be shared with the NIHR CRN. Submission of a Portfolio Application Form (PAF) is no longer required.

6. Do you plan to include any participants who are children?

☒ Yes ☐ No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

☒ Yes ☐ No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the Confidentiality Advisory Group to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

☐ Yes ☒ No

9. Is the study or any part of it being undertaken as an educational project?

☐ Yes ☒ No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

☐ Yes ☒ No

11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?

☒ Yes ☐ No

Integrated Research Application System
Application Form for Clinical trial of an investigational medicinal product**IRAS Form (project information)**

Please refer to the E-Submission and Checklist tabs for instructions on submitting this application.

The Chief Investigator should complete this form. Guidance on the questions is available wherever you see this symbol displayed. We recommend reading the guidance first. The complete guidance and a glossary are available by selecting [Help](#).

Please define any terms or acronyms that might not be familiar to lay reviewers of the application.

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
SWiFT - Study of Whole blood in Frontline Trauma

Please complete these details after you have booked the REC application for review.

REC Name:
South Central - Oxford C

REC Reference Number:
22/SC/0072

Submission date:
28/02/2022

PART A: Core study information**1. ADMINISTRATIVE DETAILS****A1. Full title of the research:**

A Multi-Centre Randomised Controlled Trial of the Clinical and Cost Effectiveness of Pre-Hospital Whole Blood Administration versus Standard Care for Traumatic Haemorrhage

A3-2. National coordinating investigator (for a multicentre trial) or principal investigator (for a single centre trial)

- ☒ National coordinating investigator
☐ Principal investigator

Given name	Laura
Family name	Green
Qualification (MD...)	MBBS, MRCP, FRCPATH, MD (Res), FRCP, MSc.
ORCID ID	0000 0003 4063 9768
Institution name	NHS Blood and Transplant & Bart's Health NHS Trust
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Fax	

** This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.*

A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project?

This contact will receive copies of all correspondence from REC and HRA/R&D reviewers that is sent to the CI.

	Title Forename/Initials Surname
	Miss Emma Laing
Address	NHSBT Clinical Trials Unit
	Long Road
	Cambridge
Post Code	CB2 0PT
E-mail	emma.laing@nhsbt.nhs.uk
Telephone	07471147868
Fax	

A5-1. Research reference numbers. Please give any relevant references for your study:

Applicant's/organisation's own reference number, e.g. R & D (if available):	21-102-GEN
Sponsor's/protocol number:	v1.0
Protocol Version:	1.0
Protocol Date:	25/02/2022
Funder's reference number (enter the reference number or state not applicable):	Not Applicable
Project website:	www.nhsbt.nhs.uk/swift

Registry reference number(s):

The UK Policy Framework for Health and Social Care Research sets out the principle of making information about research publicly available. Furthermore: Article 19 of the World Medical Association Declaration of Helsinki adopted in 2008 states that "every clinical trial must be registered on a publicly accessible database before recruitment of the first subject"; and the International Committee of Medical Journal Editors (ICMJE) will consider a clinical trial for publication only if it has been registered in an appropriate registry. Please see guidance for more information.

International Standard Randomised Controlled Trial Number (ISRCTN):

ClinicalTrials.gov Identifier (NCT number):

European Clinical Trials Database (EudraCT) number: 2021-006876-18

Additional reference number(s):

Ref.Number	Description	Reference Number

A5-2. Is this application linked to a previous study or another current application?

☐ Yes ☒ No

Please give brief details and reference numbers.

2. OVERVIEW OF THE RESEARCH

To provide all the information required by review bodies and research information systems, we ask a number of specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.

A6-1. Summary of the study. Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. Where the research is reviewed by a REC within the UK Health Departments' Research Ethics Service, this summary will be published on the Health Research Authority (HRA) website following the ethical review. Please refer to the question specific guidance for this question.

Major trauma kills more than 5,400 people every year in the UK and uncontrolled bleeding accounts for a large proportion of these deaths, with approximately 20% occurring in the first 24 hours and 40% occurring within the first 30 days. The overall cost to NHS for managing major trauma is estimated to be £150 million per annum and blood transfusion makes up around 12% of this cost.

Blood transfusion is a life-saving treatment in the management of bleeding patients until bleeding is controlled in hospital, typically delivered through different blood components (red blood cells, plasma and platelets). These components are derived from a whole blood donation and are stored in separate bags (units). There are challenges in carrying separate blood products, such as additional weight in kit bags, and transfusing multiple blood products at the scene can delay transport to hospital. Most UK Air Ambulance Services carry red blood cells and plasma to transfuse pre-hospital. However, a pre-hospital transfusion strategy has not been established and practice varies across the country. This trial aims to investigate if carrying and transfusing two units of whole blood instead of four units (two red blood cells and two plasma) leads to better outcomes for patients and reduces costs.

A6-2. Summary of main issues. Please summarise the main ethical, legal, or management issues arising from your study and say how you have addressed them.

Not all studies raise significant issues. Some studies may have straightforward ethical or other issues that can be identified and managed routinely. Others may present significant issues requiring further consideration by a REC, HRA, or other review body (as appropriate to the issue). Studies that present a minimal risk to participants may raise complex organisational or legal issues. You should try to consider all the types of issues that the different reviewers may need to consider.

ETHICAL CONSIDERATIONS

The primary ethical issue related to this study concerns the enrolment of severely injured patients who are unable to consent for themselves, and where a patient representative or relative may not be immediately available, or who are in a state of mind such that they would be able to digest and comprehend the nature of the research study.

Patients with serious injuries who are treated pre-hospital are assessed by the attending Air Ambulance Service. At the time of treatment these patients will not be in a position to be approached about the study. Some patients will be unconscious and those who are not will usually be in pain, distress and under the influence of medication. When patients are transferred to Emergency Departments, relatives are usually not available immediately and it can take hours or days to identify patients and/or contact any next of kin. We propose to use an emergency waiver of consent in accordance with that outlined within UK law (the The Medicines for Human Use (Clinical Trials: Amendment No. 2) Regulations 2006). The consent process is described in full in section A30. The procedure we will use is an established method of consent in clinical trials for incapacitated emergency patients.

If a participant dies before any form of informed consent has been obtained, we will not actively seek consent from the family. We will adopt a similar approach to previous and ongoing emergency care studies, by placing information in publicly accessible locations and in sites likely to be visited by relatives of the deceased (hospitals, GP surgeries, the offices of the Registrars of Births and Deaths). This will be in the form of a poster. This allows relatives to make an individual decision as to whether to seek further information on whether their relative was part of the trial, at a time of their choosing. This approach was discussed and supported by the NHSBT Patient and Public Advisory Group, as they saw clear justification for it.

TRIAL CATEGORISATION

Although blood components (whole blood, fresh frozen plasma and red blood cells) are not IMPs, several of the participating Air Ambulance services carry freeze-dried plasma (LyoPlas), which is an IMP. LyoPlas is permitted in the

control arm and because of this, the SWiFT trial is classified as a CTIMP (Type A - risk no higher than that of standard medical care).

PARTICIPANT FOLLOW UP & CONFIDENTIALITY

(1) Pre-hospital data: Initial patient identifying data and treatment given will be passed to the treating Emergency Department on arrival at hospital. It will also be retained by the attending Air Ambulance Service, which is standard practice to obtain patient outcomes to inform patient care.

(2) In hospital data: Participant follow up in hospital will be coordinated by the local research teams and data entered onto an online case report form using a unique patient identifier. Only participant initials, gender and age will be captured on the trial database in addition to this unique identifier. Each Research Team has an established process for maintaining participant confidentiality and anonymity. Research staff within the participating hospitals will have access to patient identifiable data, for the purpose of data collection.

The site Research Team will be responsible for keeping a log of all participants for identification purposes. NHSBT Clinical Trial Unit Trial Managers/Monitors will have access to personal data on-site, only for monitoring purposes.

(c) Data obtained from other sources: Data will be requested from the Trauma Audit and Research Network (TARN) and the Intensive Care Audit and Research Centre (ICNARC) for details of patient care in hospital up to 90 days from injury. This may be before or after death or discharge from hospital. There will be a data sharing agreement between NHSBT CTU and the third parties to ensure adherence with the appropriate guidance and laws.

3. PURPOSE AND DESIGN OF THE RESEARCH

A7. Select the appropriate methodology description for this research. Please tick all that apply:

- ☐ Case series/ case note review
- ☐ Case control
- ☐ Cohort observation
- ☐ Controlled trial without randomisation
- ☐ Cross-sectional study
- ☐ Database analysis
- ☐ Epidemiology
- ☐ Feasibility/ pilot study
- ☐ Laboratory study
- ☐ Metanalysis
- ☒ Qualitative research
- ☐ Questionnaire, interview or observation study
- ☒ Randomised controlled trial
- ☐ Other (please specify)

A8. Type of medicinal trial:

- ☐ Clinical trial of an unlicensed investigational medicinal product
- ☐ Clinical trial of a licensed medicinal product in new conditions of use (different from those in the SmPC, i.e. new target population, new dosage schemes, new administration route, etc.)
- ☒ Clinical trial of a licensed medicinal product used according to the SmPC
- ☐ Other (please specify)

A9. Phase of medicinal trial: (Tick one category only)

Human pharmacology (Phase I) ☐ Yes ☒ No

- Therapeutic exploratory trial (Phase II) ☐ Yes ☒ No
- Therapeutic confirmatory trial (Phase III) ☒ Yes ☐ No
- Therapeutic use trial (Phase IV) ☐ Yes ☒ No

A10. What is the principal research question/objective? Please put this in language comprehensible to a lay person.

The primary objective is to determine whether pre-hospital leukocyte-depleted whole blood transfusion is better than standard care (component transfusion) in reducing the proportion of participants who experience death or massive transfusion (defined as needing 10 or more units of blood components) at 24 hours.

A11. What are the secondary research questions/objectives if applicable? Please put this in language comprehensible to a lay person.

- All-cause mortality at 6 hours, 24 hours, 30 days and 90 days
- Morbidity up to 30 days: i.e. number of organ failure free days, and number of days in ICU and hospital.
- Hospital resource use up to 30 days, discharge or death, including organ failure free days, time spent in intensive care and total in-patient stay, blood components and additional haemostatic agents received
- The cost-effectiveness of pre-hospital whole blood administration versus standard care for traumatic haemorrhage
- Health-related quality of life at 90 days
- Health, social and wider care resource use up to 90 days
- Safety

A12. What is the scientific justification for the research? Please put this in language comprehensible to a lay person.

Early blood transfusion improves survival in patients with life-threatening bleeding, but the optimal transfusion strategy in the pre-hospital setting has yet to be established. Although there is some evidence of benefit with the use of whole blood, there have been no randomized controlled trials exploring the clinical and cost effectiveness of pre-hospital administration of whole blood versus component therapy for bleeding trauma patients in the UK setting.

In 2019 we conducted a survey of UK Air Ambulances (18 of 22 services responded). In this survey, 82% stated that whole blood would be their preferred component followed by leukocyte depleted red cells and plasma in one bag (65%), and red blood cells + thawed fresh frozen plasma + platelets (30%). All those who responded said that they would like to see a randomized controlled trial being done, before the wider implementation of whole blood in the NHS. In a stakeholder meeting in July 2020, with representatives from all air ambulance services in the UK, most participants stated that they would support a clinical trial.

Therefore, it is essential for patients, healthcare professionals and blood services that the clinical and cost effectiveness of pre-hospital whole blood transfusion is evaluated in a large trial before its widespread implementation in NHS. A national programme of whole blood production would necessitate significant changes in the current manufacturing processes for blood services, in order to provide appropriate support for hospitals. Whole blood production could potentially affect the supply of blood components required to treat other patients, as a unit of whole blood cannot be used to manufacture other components. However, it could also be argued that early transfusion of whole blood may reduce the need for further blood component transfusion when patients arrive at hospital, due to earlier control of bleeding. The proposed study would enable us to evaluate all of these parameters, along with the clinical and cost effectiveness of whole blood versus standard care in the pre-hospital environment.

A13. Please summarise your design and methodology. It should be clear exactly what will happen to the research participant, how many times and in what order. Please complete this section in language comprehensible to the lay person. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.

STUDY DESIGN

A randomised-controlled trial of pre-hospital whole blood versus red blood cells and plasma (non-blinded), for the treatment of major traumatic haemorrhage.

TYPE OF PARTICIPANT TO BE STUDIED

Patients (of any age) who require blood transfusion in the pre-hospital setting, for the treatment of major traumatic haemorrhage.

SETTING

Pre-Hospital Emergency Medicine.

RANDOMISATION

Randomised boxes containing the trial intervention (either 2 units of whole blood or 2 units of red blood cells and 2 units of plasma) will be prepared in advance by the Transfusion Laboratory Teams. The boxes will be supplied to the participating Air Ambulance Services. If they attend a patient who has suffered major trauma and requires blood transfusion, the team will open the trial intervention box and administer the contents to the patient, in accordance with standard local blood transfusion protocols. The time that the box was opened will be recorded and referred to as the randomisation time for the purposes of follow-up data collection.

Informed consent will not be obtained prior to the initiation of treatment, due to the life-threatening nature of the patient's condition. Patients will be enrolled under an emergency waiver of consent, and informed consent will be sought (either directly from the participant, if they have capacity, or via a representative) as soon as practically possible.

TREATMENT

The intervention arm will be up to 2 units of whole blood (www.transfusionguidelines.org/red-book/annex-3/a3-6-whole-blood-leucocyte-depleted-for-clinical-studies). The control arm will be up to 2 units of red blood cells and up to 2 units of plasma (this is the current standard of care for the participating Air Ambulance Services). The plasma used in the control arm will either be fresh-frozen plasma (FFP) or LyoPlas (freeze-dried plasma). LyoPlas is classified as an IMP as it involves a manufacturing process. All other products used in this trial are blood components and fall under The Blood Safety and Quality Regulations.

If bleeding continues after the trial intervention(s) have been administered, participants will receive further treatment as per standard of care.

FOLLOW-UP OF PARTICIPANTS

Patients will be reviewed as per standard clinical care. Data will be collected for the trial, for the secondary outcome measures, up to 90 days post-randomisation.

SAFETY REPORTING

Serious adverse events will be documented and reported up to 14 days post-treatment. The protocol lists events which are excluded from reporting (i.e. those which are recognised complications and consequences of major trauma).

QUALITATIVE RESEARCH

Alongside the randomised controlled trial, an 'Implementation Study' will be conducted. This will assess the acceptability and implementation of the intervention (whole blood). In this sub-study, qualitative methods will be used, involving interviews and focus groups with operational staff, patient representatives and blood donors.

A14-1. In which aspects of the research process have you actively involved, or will you involve, patients, service users, and/or their carers, or members of the public?

- ☒ Design of the research
- ☒ Management of the research
- ☐ Undertaking the research
- ☐ Analysis of results
- ☒ Dissemination of findings
- ☐ None of the above

Give details of involvement, or if none please justify the absence of involvement.

The NHSBT Patient & Public Advisory Group (PPAG) has been integral to the overall project since a group of patients and the public met in 2021 to meet the Trial team. At this meeting we explored their opinions on consent for emergency care trials. The group also reviewed the patient information and consent documents.

A member of the NHSBT PPAG sits on the Trial Steering Committee, alongside an expert service user, who will meet every six months to review the progress of the trial. They will be an integral part of contributing to the trial publications and will take part in the dissemination process once the results are published.

A14-2. Have you tested the acceptability of using patient identifiable data in this study without consent?

Please give details.

Patient identifiable data (NHS number, date of birth) are required to perform linkage to the Trauma Audit and Research Network (TARN) and Intensive Care National Audit and Research Centre (ICNARC) datasets. We are seeking approval from the Confidentiality Advisory Group (CAG) to perform this linkage in the sub-set of patients for whom consent cannot be obtained. For example, patients who die after admission to hospital (before consent can be obtained), or those who are discharged prior to any form of consent being obtained.

NHSBT Clinical Trials Unit also coordinated the CRYOSTAT-2 Trial (IRAS 201735) which was supported by the CAG for the use of section 251 where signed informed consent was not possible. The SWiFT trial is the same patient population and is expected to incur similar challenges in obtaining signed consent.

This has also been extensively discussed by the Trial Management Group.

4. RISKS AND ETHICAL ISSUES**RESEARCH PARTICIPANTS****A15. What is the sample group or cohort to be studied in this research?**

Select all that apply:

- ☐ Blood
- ☐ Cancer
- ☐ Cardiovascular
- ☐ Congenital Disorders
- ☐ Dementias and Neurodegenerative Diseases
- ☐ Diabetes
- ☐ Ear
- ☐ Eye
- ☐ Generic Health Relevance
- ☐ Infection
- ☐ Inflammatory and Immune System
- ☒ Injuries and Accidents
- ☐ Mental Health
- ☐ Metabolic and Endocrine
- ☐ Musculoskeletal
- ☐ Neurological
- ☐ Oral and Gastrointestinal
- ☐ Paediatrics
- ☐ Renal and Urogenital
- ☐ Reproductive Health and Childbirth
- ☐ Respiratory
- ☐ Skin
- ☐ Stroke

Gender:

Male and female participants

Lower age limit: 0

Years

Upper age limit:

No upper age limit

A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).

Inclusion Criteria:

- (1) Patient (of any age) who has suffered a traumatic injury.
- (2) Attended by a participating Air Ambulance Service (AAS) clinical team.
- (3) Requires pre-hospital blood transfusion to treat major traumatic haemorrhage.

A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).

Exclusion criteria:

- (1) No intravenous or intraosseous access
- (2) Knowledge that patient will object to being given blood transfusion for any reasons
- (3) Blood already administered on-scene, prior to arrival of the participating Air Ambulance team

RESEARCH PROCEDURES, RISKS AND BENEFITS**A18. Give details of all non-clinical intervention(s) or procedure(s) that will be received by participants as part of the research protocol. These include seeking consent, interviews, non-clinical observations and use of questionnaires.**

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days)
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Assessment of eligibility	1	0	1 minute	Attending Air Ambulance Service clinicians
Enrolment (opening the study box)	1	0	1 minute	Attending Air Ambulance Service clinicians
Assessment of capacity to consent	1	0	5 minutes	Treating hospital research team
Consent process (either via participant or legal representative)	1	0	30 minutes	Treating hospital research team
Withdrawal process (if required)	1	0	10 minutes	Treating hospital research team
Follow-up data collection, up Day 90	1	0	45 minutes	Treating hospital research team
Administer quality of life and health resource use questionnaires at Day 90	1	0	35 minutes	Treating hospital research team

A19. Give details of any clinical intervention(s) or procedure(s) to be received by participants as part of the research protocol. These include uses of medicinal products or devices, other medical treatments or assessments, mental health interventions, imaging investigations and taking samples of human biological material. Include procedures which might be received as routine clinical care outside of the research.

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?

3. Average time taken per intervention/procedure (minutes, hours or days).
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Transfusion of pre-hospital blood components (either two units of whole blood, or two units of red cells + two units of plasma)	1	1	20 minutes	Attending Air Ambulance Service clinicians

A20. Will you withhold an intervention or procedure, which would normally be considered a part of routine care?

☐ Yes ☒ No

A21. How long do you expect each participant to be in the study in total?

90 days

A22. What are the potential risks and burdens for research participants and how will you minimise them?

For all studies, describe any potential adverse effects, pain, discomfort, distress, intrusion, inconvenience or changes to lifestyle. Only describe risks or burdens that could occur as a result of participation in the research. Say what steps would be taken to minimise risks and burdens as far as possible.

When compared to blood component therapies, several systematic reviews have shown that the safety profile of WB transfusion is comparable to the blood component therapy currently used as part of standard of care for treatment of bleeding. There is therefore no evidence to suggest that WB transfusion results in higher risk to the patient than the current standard of care. The known risks associated with blood transfusion are provided below:

- (1) FAHR (Febrile, allergic, and hypotensive reactions) formerly known as Acute transfusion reactions (ATR), that could result in shock or cardiac arrest. Allergic reactions are rare (8 per 1 million units issued), resulting mainly in urticaria (skin rash), although pulmonary hypertension (high blood pressure caused by a narrowing of the blood vessels in the lungs) and systemic hypotension (low blood pressure) may occur. Serious allergic reactions (anaphylaxis) are very rare. There have been 25 reported cases of anaphylaxis in the UK over a period of 6 years.
- (2) HTR Acute or Delayed (Haemolytic Transfusion Reactions), acute or delayed.
- (3) PTP (Post Transfusion Purpura)
- (4) UCT (Uncommon and new complications of transfusion not fitting any other category)
- (5) TA-GvHD (Transfusion -associated Graft versus Host Disease). The risk is very small to non-existent, as in the UK we do not allow provision of blood transfusion to recipients from relatives where this risk is higher.
- (6) TACO (Transfusion-Associated Circulatory Overload)
- (7) TAD (Transfusion-Associated Dyspnoea)
- (8) TRALI (Transfusion-Related Acute Lung Injury). TRALI is thought to be caused by certain antibodies present in the plasma of donors who have been pregnant in the past. To minimise the risk of TRALI, the UK blood supplier have agreed to use male donors only for supplying plasma or whole blood, and since 2009 TRALI has not been reported with plasma anymore.

However, serious adverse transfusion reactions are rare. Any instances will be reported via the national Serious Hazards of Transfusion (SHOT) system, reported to the Data Monitoring Committee and reviewed by the Trial Management Group.

In this trial, the transfusion of blood components will be initiated due to the life-threatening nature of the bleeding, and the potential risks of transfusion are considered in light of this.

A23. Will interviews/ questionnaires or group discussions include topics that might be sensitive, embarrassing or upsetting, or is it possible that criminal or other disclosures requiring action could occur during the study?

☒ Yes ☐ No

If Yes, please give details of procedures in place to deal with these issues:

It is possible that patients may be upset when completing the quality of life questionnaires if they have life altering

injuries.

A24. What is the potential for benefit to research participants?

It is not yet known whether participants will benefit from participation in the study, and this is made clear in the Patient Information Sheets. We hope that the trial will be able to show that transfusion of whole blood may stop bleeding sooner, thereby limiting further transfusion exposure and improving the survival rate at 24 hours.

Participants might gain benefit from enhanced data collection and event monitoring. This is a recognised potential benefit of research participation.

A25. What arrangements are being made for continued provision of the intervention for participants, if appropriate, once the research has finished? May apply to any clinical intervention, including a drug, medical device, mental health intervention, complementary therapy, physiotherapy, dietary manipulation, lifestyle change, etc.

Not applicable. Participants will not receive any additional intervention.

A26. What are the potential risks for the researchers themselves? (if any)

There are potential risks in initiating the consent process with patients or relatives who are abusive and threaten violence. In these cases it is not appropriate for research teams to approach the patient.

RECRUITMENT AND INFORMED CONSENT

In this section we ask you to describe the recruitment procedures for the study. Please give separate details for different study groups where appropriate.

A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used? For example, identification may involve a disease register, computerised search of GP records, or review of medical records. Indicate whether this will be done by the direct healthcare team or by researchers acting under arrangements with the responsible care organisation(s).

Potential participants will be screened for eligibility by attending Air Ambulance Service clinicians (direct care team). The Air Ambulance team will notify the team at the receiving hospital if the patient has been enrolled into the SWiFT trial and provide the relevant randomisation number.

The PI and Research Team at the receiving hospital will become responsible for the consent process and follow-up data collection. The majority of data will be collected on the electronic Case Report Forms, and all participant data will be pseudo-anonymised (referred to by the participant's trial ID number).

Additional data, which is routinely collected by the Trauma Audit and Research Network (TARN) and the Intensive Care National Audit and Research Centre (ICNARC), will be used. Once informed consent has been obtained, patient identifiable data will be securely provided to NHSBT CTU by the Research Team. This will allow for linkage to the TARN and ICNARC datasets. Data Sharing Agreements will be put in place between NHSBT and TARN/ICNARC to detail the data transfer procedure.

We are seeking approval from the Confidentiality Advisory Group to perform linkage of data for patients without consent (i.e. patients who die before informed consent can be obtained, or patients where consent could not be obtained for another reason) under the provisions of Section 251 of the National Health Service Act 2006.

A27-2. Will the identification of potential participants involve reviewing or screening the identifiable personal information of patients, service users or any other person?

☐ Yes ☒ No

Please give details below:

Only members of the patient's existing clinical care team will have access to patient records in order to identify potential participants.

A28. Will any participants be recruited by publicity through posters, leaflets, adverts or websites?☐ Yes ☒ No**A29. How and by whom will potential participants first be approached?**

The attending Air Ambulance Service are responsible for assessing eligibility for the trial and study entry via the Emergency Waiver.

These participants (when they have regained capacity) or their parent/legal guardian or personal legal representative will be approached at the earliest appropriate opportunity by a member of the research team at the treating hospital, but this may be some days after admission to hospital.

As the intervention will already have been administered, consent will be sought for the ongoing collection of follow-up data.

A30-1. Will you obtain informed consent from or on behalf of research participants?☒ Yes ☐ No

If you will be obtaining consent from adult participants, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos, or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section 6, and for children in Part B Section 7.

If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.

When a participant regains capacity to give consent, full information will be provided to them and they will be asked to sign a consent form agreeing to their continuation in the study. It will be explained to the participant that they have already received the study treatment. For any participant who is enrolled but does not regain capacity during the study follow up period, or who did not have capacity prior to being injured, a parent/legal guardian or legal professional representative will be approached at the earliest opportunity and no later than the 90 day follow-up point.

In the event that a participant dies during the study, if appropriate, an opinion regarding the participant's likely wishes will be sought from a personal consultee as described above. In some situations, where a participant's death occurs soon after hospital admission, there may be no opportunity for contact between the research team and the personal consultee prior to the participant's death. In this instance, we recognise that approaching a personal consultee to ask their opinion is likely to be distressing and without benefit.

In this circumstance the local clinician in charge of the participant's care will access and anonymise the data to be provided to the study teams. These procedures will be conducted in accordance with the Access to Health Records Act 1990. Although we will not approach a personal consultee to seek their opinion when a participant dies before any contact has been made with the research team, in all other cases we will make every effort, to inform relatives that the participant was entered into the trial.

In the rare event that a participant is found to be below 16 years of age after the point of entry, consent will be obtained from the participant's Parent/Guardian and assent will be sought from the child if and when sufficiently recovered.

If you are not obtaining consent, please explain why not.

We know that there will be some circumstances where it will not be possible to gain informed consent from a participant or an appropriate legal representative. For example, for patients who die after admission to hospital (before consent can be obtained), or those who are discharged prior to any form of consent being obtained. In these circumstances, we intend to apply section 251 for data linkage (subject to approval from the Confidentiality Advisory Group).

Please enclose a copy of the information sheet(s) and consent form(s).

A30-2. Will you record informed consent (or advice from consultees) in writing?☒ Yes ☐ No

A30-3. Why is it not practicable for either the researcher's organisation, or the current holder of the information required by the researcher, to seek or obtain patient consent for proposed use of patient identifiable information?

Research teams at participating centres will make every effort to obtain signed informed consent from patients or their legal representative (if the patient lacks capacity). However, we recognise that in some cases it will not be possible to obtain informed consent. In a previous trial in a similar setting, CRYOSTAT-2 trial (IRAS: 210735), there was a significant proportion of patients where informed consent could not be obtained (28%). Although we expect this to be lower in this trial (because the trial is a CTIMP and therefore consent given by a representative of the patient is legally valid), we believe that there will still be a significant proportion of patients affected.

Missing data from these participants will affect the primary outcome analysis, and therefore jeopardise the quality of the research. It is important that we conduct high-quality research and participants themselves would also expect this of us. As such in order to deliver this trial, we cannot exclude the data from these participants.

A31. How long will you allow potential participants to decide whether or not to take part?

Participants will be approached after the initial period of resuscitation and immediate care is complete. They will be given information regarding the trial and allowed appropriate time to decide if they wish to continue to take part in the study.

They will be clearly informed that if they would like time to consider their ongoing participation, discuss it with relatives/friends or an independent advocate, they can take as much time as they need to decide. The research team at the treating hospital will revisit this with the patient when appropriate.

A32. Will you recruit any participants who are involved in current research or have recently been involved in any research prior to recruitment?

- ☐ Yes
☐ No
☒ Not Known

If Yes, please give details and justify their inclusion. If Not Known, what steps will you take to find out?

It is highly unlikely that those enrolling to SWiFT will be aware if a participant is already enrolled in a clinical trial. Where a SWiFT participant is subsequently found to have been participating in a concurrent trial or is being considered for enrolment into another trial, the site must notify the SWiFT CIs, who will in turn liaise with the CI for the other trial to determine whether co-enrolment is permitted.

A33-1. What arrangements have been made for persons who might not adequately understand verbal explanations or written information given in English, or who have special communication needs?(e.g. translation, use of interpreters)

If a patient, personal legal representative or parent/legal guardian does not understand English sufficiently to understand the trial and what is involved, local arrangements for translation services should be used.

A34. What arrangements will you make to ensure participants receive any information that becomes available during the course of the research that may be relevant to their continued participation?

If the Trial Management Group become aware of any relevant information, participant information sheets and consent forms will be updated as needed and submitted to the HRA/REC/MHRA for review. The PIs and Research Teams at each site will be asked to disseminate the information to their participants (and re-consent if required). As it may not be possible to reach all participants, information will also be posted on the study website.

NHSBT Clinical Trials Unit has procedures in place to implementing urgent safety measures and temporary halts to recruitment, if these should be required.

CONFIDENTIALITY

In this section, personal data means any data relating to a participant who could potentially be identified. It includes pseudonymised data capable of being linked to a participant through a unique code number.

Storage and use of personal data during the study

A36. Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)? (Tick as appropriate)

- ☒ Access to medical records by those outside the direct healthcare team
- ☐ Access to social care records by those outside the direct social care team
- ☒ Electronic transfer by magnetic or optical media, email or computer networks
- ☒ Sharing of personal data with other organisations
- ☐ Export of personal data outside the EEA
- ☒ Use of personal addresses, postcodes, faxes, emails or telephone numbers
- ☐ Publication of direct quotations from respondents
- ☐ Publication of data that might allow identification of individuals
- ☐ Use of audio/visual recording devices
- ☐ Storage of personal data on any of the following:
 - ☐ Manual files (includes paper or film)
 - ☒ NHS computers
 - ☐ Social Care Service computers
 - ☐ Home or other personal computers
 - ☒ University computers
 - ☐ Private company computers
 - ☐ Laptop computers

Further details:

Research teams at treating hospitals will access medical records for data collection and safety reporting purposes.

Patient identifiable information (date of birth and NHS number) will be securely transferred by treating hospitals to NHSBT CTU. These records will then be securely transferred to TARN and ICNARC for patient matching to obtain detailed clinical care records.

Site monitoring may require access to medical records by those outside the direct healthcare team.

A37. Please describe the physical security arrangements for storage of personal data during the study?

Patient identifiable data will be held on NHSBT secure servers requiring a security login, in restricted folders and only accessible by designated statisticians and data management staff. The trial statistician(s) will ensure that onward data transfer (to TARN/ICNARC) is performed securely and in agreement with the terms of the relevant Data Transfer Agreement.

A38. How will you ensure the confidentiality of personal data? Please provide a general statement of the policy and procedures for ensuring confidentiality, e.g. anonymisation or pseudonymisation of data.

All staff working with personally identifiable information will have Good Clinical Practice training and be aware of the requirements for handling sensitive information. All study data captured on the study database will be pseudo-anonymised using a unique trial number.

Each participating site will maintain their own enrolment log that matches the unique trial number to the participant, but this will remain at the site in a locked filing cabinet or equivalent and be archived with the site file at the end of the study.

Patient identifiable data will be provided by treating hospitals to NHSBT CTU. This data is sent from and to secure email addresses. Data is held on NHSBT secure servers requiring security login, in restricted folders and only accessible by designated statisticians and data management staff.

Patient identifiable data will be securely destroyed once it is no longer required - it will not be retained for the analysis.

A39. Please specify whether identifiers will be held in the same database as the clinical data, or in a separate database and linked through a unique study or case number. If held separately, please specify how and at what point the separation will occur. If held in the same database, will the identifiers be encrypted? If so, specify what will be encrypted and who will continue to have access.

Patient identifiable information will not be held in the same database as clinical data. They will be linked via a unique study ID.

A40. Who will have access to participants' personal data during the study? Where access is by individuals outside the direct care team, please justify and say whether consent will be sought.

The research team at the treating hospital, designated NHSBT statisticians and data management staff will have access to participants personal data during the study.
Site monitoring may require access to participants personal data.

Storage and use of data after the end of the study

A41. Where will the data generated by the study be analysed and by whom?

The data generated by the study will be analysed by the trial statistician(s) at NHSBT CTU.

A42. Who will have control of and act as the custodian for the data generated by the study?

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A43. How long will personal data be stored or accessed after the study has ended?

- ☐ Less than 3 months
☐ 3 – 6 months
☐ 6 – 12 months
☒ 12 months – 3 years
☐ Over 3 years

If longer than 12 months, please justify:

Personal identifiable data will be deleted as soon as possible following the end of the study. The destruction process

will be evidenced in the trial master file.

A44. For how long will you store research data generated by the study?

Years: 15

Months: 0

A45. Please give details of the long term arrangements for storage of research data after the study has ended. Say where data will be stored, who will have access and the arrangements to ensure security.

Research data will be stored securely within NHSBT when the trial ends. Paper records (e.g. the trial master files) will be stored in locked cabinets behind security accessed doors. Electronic data will be kept on password protected databases held on NHSBT servers, accessible only by the research team.

All personal identifiable data will be deleted 12 months after the end of the study by the trial statisticians and the process evidenced in the trial master file.

Participating sites will archive site files via their usual arrangements.

NHSBT has archiving arrangements in place with Iron Mountain.

The archiving period is 15 years.

INCENTIVES AND PAYMENTS**A46. Will research participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in this research?**

☒ Yes ☐ No

If Yes, please give details. For monetary payments, indicate how much and on what basis this has been determined.
Health Care Professionals that take part in an interview for the Implementation Study (qualitative research) will receive a £10 voucher as a token of thanks.

Patient representatives and blood donors who take part in a focus group or an interview for the Implementation Study will receive £75 (in line with NIHR Involve Guidelines).

A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?

☐ Yes ☒ No

A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

☐ Yes ☒ No

NOTIFICATION OF OTHER PROFESSIONALS**A49-1. Will you inform the participants' General Practitioners (and/or any other health or care professional responsible for their care) that they are taking part in the study?**

☒ Yes ☐ No

If Yes, please enclose a copy of the information sheet/letter for the GP/health professional with a version number and date.

A49-2. Will you seek permission from the research participants to inform their GP or other health/ care professional?

☒ Yes ☐ No

It should be made clear in the participant's information sheet if the GP/health professional will be informed.

PUBLICATION AND DISSEMINATION

A50. Will the research be registered on a public database?

The UK Policy Framework for Health and Social Care Research sets out the principle of making information about research publicly available. Furthermore: Article 19 of the World Medical Association Declaration of Helsinki adopted in 2008 states that "every clinical trial must be registered on a publicly accessible database before recruitment of the first subject"; and the International Committee of Medical Journal Editors (ICMJE) will consider a clinical trial for publication only if it has been registered in an appropriate registry. Please see guidance for more information.

☒ Yes ☐ No

Please give details, or justify if not registering the research.

The study will be registered with ISRCTN and will also be registered on the NIHR Clinical Research Network Portfolio.

Please ensure that you have entered registry reference number(s) in question A5-1.

A51. How do you intend to report and disseminate the results of the study? Tick as appropriate:

- ☒ Peer reviewed scientific journals
- ☒ Internal report
- ☒ Conference presentation
- ☒ Publication on website
- ☐ Other publication
- ☒ Submission to regulatory authorities
- ☐ Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
- ☐ No plans to report or disseminate the results
- ☐ Other (please specify)

A52. If you will be using identifiable personal data, how will you ensure that anonymity will be maintained when publishing the results?

Data will be pseudo-anonymised using a unique study number, ensuring that personally identifiable data cannot be published.

A53. How and when will you inform participants of the study results?

If there will be no arrangements in place to inform participants please justify this.

Participants will not be directly informed of the study results, but the information will be available via the study website. This will happen once the trial results have been published.

We will also seek advice from our Trial Steering Committee and the NHSBT Patient and Public Advisory Group on how best to communicate the study results and disseminate them to the public.

5. Scientific and Statistical Review

A54. How has the scientific quality of the research been assessed? Tick as appropriate:

- ☒ Independent external review
☐ Review within a company
☐ Review within a multi-centre research group
☒ Review within the Chief Investigator's institution or host organisation
☒ Review within the research team
☐ Review by educational supervisor
☐ Other

Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:

Independent external peer review was conducted in March 2021. The study was sent to three independent experts in the fields of pre-hospital emergency medicine and transfusion medicine. These were reviewed extensively by the Sponsor (NHS Blood and Transplant) before funding was awarded. The peer reviews have been attached to this application.

The study has also been through the Ministry of Defence's scientific review process: the Defence Medical Services Research Steering Group (the DMSRSG).

For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports, together with any related correspondence.

For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/ institution.

A56. How have the statistical aspects of the research been reviewed? Tick as appropriate:

- ☐ Review by independent statistician commissioned by funder or sponsor
☐ Other review by independent statistician
☐ Review by company statistician
☒ Review by a statistician within the Chief Investigator's institution
☐ Review by a statistician within the research team or multi-centre group
☐ Review by educational supervisor
☐ Other review by individual with relevant statistical expertise
☐ No review necessary as only frequencies and associations will be assessed – details of statistical input not required

In all cases please give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.

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Please enclose a copy of any available comments or reports from a statistician.

A57. What is the primary outcome measure for the study?

Proportion of participants who have died (all-cause mortality) or received a total of 10 or more units of any blood components in the first 24 hours from randomisation.

A58. What are the secondary outcome measures?(if any)

- Individual components of the primary outcome: Proportion of participants who:
 - o Experienced all-cause mortality at 24 hours from randomisation.
 - o Received a total of 10 or more units of any blood components in the first 24 hours of randomisation IV.
- All-cause mortality within 6 hours and separately 30 and 90 days of randomisation.
- Number of organ failure free days up to 30 days after randomisation, defined as the number of days free of advanced cardiovascular, advanced respiratory and advanced renal support. Each component of organ failure free days will also be reported separately:
 - o Number of days free of advanced respiratory support
 - o Number of days free of advanced cardiovascular support
 - o Number of days free of advanced renal support
- Days in ICU and separately in an acute care hospital (up to 90 days).
- Units of each blood component received in the 24 hours after randomisation IV (including prehospital transfusions): WB, RBC, plasma, platelets and cryoprecipitate.
- Amount of cell salvage received at 24 hours (in mLs) after randomisation IV.
- Number of participants receiving additional haemostatic agents received at 24 hours after randomisation IV: recombinant Factor VIIa, fibrinogen concentrate, prothrombin complex concentrate (PCC), tranexamic acid (TXA).
- Presence of coagulopathy (defined as prothrombin time above the limits of a normal range) in the first sample taken on arrival at an acute care hospital.
- Acid-base disturbance measured by lactate, base excess and pH level in first sample taken on arrival at acute care hospital.
- Incremental cost of the whole blood intervention.
- Hospital resource use to discharge or death.
- Health, social and wider care resource use to 90 days after randomisation.
- Health-related quality of life as measured by EQ-5D-5L at 90 days after randomisation.
- Thrombosis (arterial and venous thrombosis) up to 30 days after randomisation.
- All transfusion reactions/events relating to pre-hospital blood components which have been reported to SHOT (Serious Hazards of Transfusion) occurring in the first 14 days after randomisation.

A59. What is the sample size for the research? How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.

Total UK sample size: 848

Total international sample size (including UK): 848

Total in European Economic Area: 0

Further details:

Recruitment of operational staff, and patient/donor representatives into the qualitative research study (the Implementation Study) has not been counted in the total above.

A60. How was the sample size decided upon? If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.

A formal sample size calculation was undertaken, using data from the Red Cells & Plasma pilot study. The observed event rate (24 hour mortality and massive transfusion (defined as the total blood products given ≥ 10 units) in the first 24 hours) was 68%. We have powered the study to detect a 12% absolute (38% relative) difference in the composite endpoint between the two treatment arms (68% vs 56%).

A two-sided test with 85% power, 5% type I error, 1-1 allocation and one interim analysis would require 602 patients. After allowing for 5% drop out and an additional 25% for excluding traumatic cardiac arrest* patients (identified from

Red Cells & Plasma study), the total number of participants required for this trial is 848.

*The survival rate is much lower for patients who are found to be in traumatic cardiac arrest on arrival of the Air Ambulance team (26% in the Red Cell and Plasma study). These participants will therefore be excluded from the main analysis of the primary outcome and will be analysed separately. This is in line with recent trials in the pre-hospital setting (REPHILL, COMBAT).

A61. Will participants be allocated to groups at random?

☒ Yes ☐ No

If yes, please give details of the intended method of randomisation:

Yes - a restricted randomisation method will be used in this trial. It will consist of randomly permuted blocks of varying undisclosed sizes, and stratified by Air Ambulance Service, to account for variation in trauma care and type of trauma between delivery sites.

Participants will be allocated on a 1:1 ratio to the intervention or control arm. The allocation sequence will be produced from a specification provided by the trial statistician to a centralised web-based randomisation service (www.sealedenvelope.com) and quality checked by the trial statistician.

A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

The primary outcome will be determined as the proportion of participants who have either died (from all causes) or received more than 10 units of blood components, within the 24 hours from randomisation. The following will be included in the blood component count: RBC, platelets, whole blood, thawed plasma (or LyoPlas) and cryoprecipitate. In this trial, for the purposes of analysis, two units of whole blood will be counted as equivalent to four total units due to the volume difference between the intervention and control arm, the fact that two units of whole blood contain the equivalent of two units of plasma plus two units of packed RBCs, and for the massive transfusion part of the primary analysis, both arms will start with an equal baseline (section 10.3). The composite outcome will be analysed using a mixed logistic regression model with adjustment for AAS, fitted as a random effect. A superiority hypothesis will be tested and the results from the adjusted analysis will be considered the primary analysis.

The secondary outcomes will be analysed as follows:

All-cause mortality at 6 hours, 24 hours, 30 days and 90 days, the proportion of participants who receive 10 or more units of any blood components and presence of coagulopathy will each be analysed separately using the same model that is described for the primary outcome.

Organ failure free days, days in critical care and an acute care hospital will be reported as a median and IQR, by treatment arm and overall.

Units of each blood component received in the 24 hours after randomisation will be summarised with a median and interquartile range and analysed using a negative binomial model, with adjustment for AAS.

Amount in millilitres (mls) of cell salvage at 24 hours after randomisation and lactate, base excess and pH level in first sample taken on arrival at acute care hospital will be analysed separately using a mixed linear regression model, with adjustment for AAS.

For each of the additional haemostatic agents, the number of participants who received each agent will be presented by trial arm and overall.

Thrombosis (arterial or venous thrombosis) up to 30 days after randomisation and transfusion reactions/events relating to pre-hospital blood components which have been reported to SHOT (Serious Hazards of Transfusion) occurring in the first 14 days after randomisation, will be summarised.

An economic evaluation will establish the resources required to provide the whole blood intervention, estimate intervention and standard care costs, and conduct a full incremental cost-effectiveness analysis. This will be undertaken against a primary perspective of the NHS/Social Care and will include:

- Incremental cost-effectiveness ratios for: i) the primary outcome, to give cost per death averted/participant received a total of 10 or more units of any blood components in the first 24 hours following randomisation and; ii) the policy relevant economic endpoint - cost per quality-adjusted life-year (QALY) at 3 months post-randomisation.
- Intervention resource use will be identified, measured (e.g. whole blood production resources such as specific filters/bags, blood product wastage, clinical time), and costed to estimate the cost-per-participant of the intervention.

This process will also be undertaken for standard care.

- Participant hospital resource use will be captured up to discharge from hospital by research nurses, and subsequent health, social and wider care service use will be captured from participants at 3 month follow-up.

- The EQ-5D-5L will be used with the UK health state value set recommended by the National Institute for Health and Care Excellence at the time of data analysis to estimate QALYs. Incremental costs and incremental QALYs over 3 months will be used to estimate the cost-per-QALY of whole blood versus standard care.

The internationally-recognised CHEERS guidelines for reporting cost-effectiveness studies will be followed. Descriptive statistics will be used to summarise the costs (by type of service) and QALYs. Regression analyses will be used to adjust for systematic differences between intervention and control arms that have not been accounted for by randomisation, and bootstrapping will be employed. Cost-effectiveness acceptability curves will be presented and multiple imputation will be used as appropriate to correct for bias that may result from data that is missing at random. Analyses will also explore uncertainty, and provide a clear, policy-relevant presentation of findings.

Alongside the main trial, a qualitative sub-study will be conducted to assess the acceptability and implementation of the intervention (whole blood), and will involve interviews and focus groups with operational staff, patient representatives and blood donors. The objectives of the sub-study are to:

- Gain a deeper understanding of the contexts within which the intervention will be delivered and its impact on local (hospitals) and central (central blood service) processes and systems.
- Identify implementation mechanisms and factors that might promote and inhibit the incorporation of the intervention into standard care.
- Identify factors that influence the acceptability of the intervention from the perspective of healthcare professionals involved in the whole WB pathway (from donor to recipients).
- Inform future adoption and implementation of the WB pathway in other settings by identifying potential strategies for sustainable implementation.

6. MANAGEMENT OF THE RESEARCH

A63. Other key investigators/collaborators. *Please include all grant co-applicants, protocol co-authors and other key members of the Chief Investigator's team, including non-doctoral student researchers.*

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Work Email laura.smith2@nhsbt.nhs.uk

Title Forename/Initials Surname
Professor Simon Stanworth

Post Consultant Haematologist

Qualifications MA, MRCP, FRCPath, DPhil

Employer NHS Blood and Transplant

Work Address John Radcliffe Hospital (Oxford University Hospitals Foundation Trust)
Headley Way
Headington, Oxford

Post Code OX3 9BQ

Telephone 01865447917

Fax

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Title Forename/Initials Surname
Mrs Helen Thomas

Post Head of Clinical Trial Statistics

Qualifications

Employer NHS Blood and Transplant

Work Address NHS Blood and Transplant
Fox Den Road
Stoke Gifford

Post Code BS34 8RR

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Title Forename/Initials Surname
Dr Anne Weaver

Post Consultant in Emergency Medicine & Pre-Hospital Care, Clinical Director for Trauma

Qualifications

Employer	Barts Health NHS Trust
Work Address	Royal London Hospital London
Post Code	E1 1FR
Telephone	
Fax	
Mobile	
Work Email	anne.weaver@nhs.net
	Title Forename/Initials Surname
	Prof Tom Woolley
Post	Consultant Anaesthetist and Defence Professor
Qualifications	
Employer	
Work Address	Royal Centre for Defence Medicine Queen Elizabeth Hospital Birmingham Mindelsohn Way, Edgbaston, Birmingham
Post Code	B15 2GW
Telephone	
Fax	
Mobile	
Work Email	t.woolley@nhs.net

A64. Details of research sponsor(s)

A64-1. Sponsor

SP1

Status: ☐ NHS or HSC care organisation

Commercial status: Non-Commercial

☐ Academic

☐ Pharmaceutical industry

☐ Medical device industry

☐ Local Authority

☐ Other social care provider (including voluntary sector or private organisation)

☒ Other

If Other, please specify: Special Health Authority

Contact person

Name of organisation NHS Blood and Transplant

Given name Yomi

Family name Adegbaju

Address 500, North Bristol Park

Town/city Filton, Bristol

Post code BS34 7QH

Country United Kingdom
Telephone 07590352169
Fax
E-mail research.office@nhsbt.nhs.uk

Legal Representative for the purpose of this CTIMP.

A legal representative must be appointed for a clinical trial of an investigational medicinal product (CTIMP) if the sponsor is not established in the UK or on the MHRA approved country list (please refer to question specific guidance).

Legal representative**Contact person**

Name of organisation
Given name
Family name
Address
Town/city
Post code
Country
Telephone
Fax
E-mail

Legal representative for clinical investigation of medical device (studies involving Northern Ireland only)

Clinical Investigations of Medical Devices that take place in Northern Ireland must have a legal representative of the sponsor that is based in Northern Ireland or the EU

Contact person

Name of organisation
Given name
Family name
Address
Town/city
Post code
Country
Telephone
Fax
E-mail

A65. Has external funding for the research been secured?

Please tick at least one check box.

☒ Funding secured from one or more funders

☐ External funding application to one or more funders in progress☐ No application for external funding will be made

What type of research project is this?

☒ Standalone project☐ Project that is part of a programme grant☐ Project that is part of a Centre grant☐ Project that is part of a fellowship/ personal award/ research training award☐ Other

Other – please state:

Please give details of funding applications.

Organisation NHS Blood and Transplant

Address Oak House
Reeds Crescent
Watford

Post Code WD24 4QN

Telephone

Fax

Mobile

Email research.office@nhsbt.nhs.uk

Funding Application Status: ☒ Secured ☐ In progress

Amount: 322,294

Duration

Years: 3

Months: 0

If applicable, please specify the programme/ funding stream:

What is the funding stream/ programme for this research project?

Organisation Air Ambulance Charities x 10

Address (various)

Post Code

Telephone

Fax

Mobile

Email

Funding Application Status: ☒ Secured ☐ In progress

Amount: 322,294

Duration

Years: 3

Months: 0

If applicable, please specify the programme/ funding stream:

What is the funding stream/ programme for this research project?

The following Charities have provided funding for this trial (£35,810 per Charity):

- Air Ambulance Kent Surrey Sussex (AAKSS)
- Essex and Herts Air Ambulance (EHAAT)
- Hampshire and Isle of Wight Air Ambulance (HIOWAA)
- Great North Air Ambulance (GNAAS)
- Great Western Air Ambulance (GWAAC)
- London's Air Ambulance (LAA)
- Magpas Air Ambulance (Magpas)
- North West Air Ambulance (NWAA)
- Thames Valley Air Ambulance (TVAA)

Organisation Ministry of Defence

Address Royal Centre for Defence Medicine

Vincent Drive

Birmingham

Post Code B15 2SQ

Telephone

Fax

Mobile

Email Samantha.Brown275@mod.gov.uk

Funding Application Status: ☒ Secured ☐ In progress

Amount: 190,000

Duration

Years: 3

Months: 0

If applicable, please specify the programme/ funding stream:

What is the funding stream/ programme for this research project?

A66. Has responsibility for any specific research activities or procedures been delegated to a subcontractor (other than a co-sponsor listed in A64-1) ? Please give details of subcontractors if applicable.

☐ Yes ☒ No

A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another country?

☐ Yes ☒ No

Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the reasons for the unfavourable opinion have been addressed in this application.

A68-1. Give details of the lead NHS R&D contact for this research:

	Title Forename/Initials Surname
	Ms Yomi Adegaju
Organisation	NHS Blood and Transplant
Address	500, North Bristol Park
	Filton
	Bristol
Post Code	BS34 7QH
Work Email	research.office@nhsbt.nhs.uk
Telephone	07590352169
Fax	
Mobile	07590352169

Details can be obtained from the NHS R&D Forum website: <http://www.rdforum.nhs.uk>

A68-2. Select Local Clinical Research Network for NHS Organisation identified in A68-1:

North Thames

For more information, please refer to the question specific guidance.

A69-1. How long do you expect the study to last in the UK?

Planned start date: 01/05/2022
Planned end date: 01/05/2025
Total duration:
Years: 3 Months: 0 Days: 1

A69-2. How long do you expect the study to last in all countries?

Planned start date: 01/05/2022
Planned end date: 01/05/2025
Total duration:
Years: 3 Months: 0 Days: 1

A70. Definition of the end of trial, and justification in the case where it is not the last visit of the last subject undergoing the trial ⁽¹⁾

The End of Trial is defined as the date when follow-up data is completed for all participants.

A71-1. Is this study?

- ☐ Single centre
☒ Multicentre

A71-2. Where will the research take place? (Tick as appropriate)

A74. What arrangements are in place for monitoring and auditing the conduct of the research? A detailed study-specific monitoring plan will be finalised prior to the trial commencing, which will be based upon the Risk Assessment. Remote and/or on-site monitoring visits will be conducted by the Trial Manager to verify the data received against the source data.
--

A75-1. What arrangements will be made to review interim safety and efficacy data from the trial? Will a formal data monitoring committee or equivalent body be convened?

A formal Data Monitoring Committee has been convened and will review safety and efficacy data from the trial on a six-monthly basis.

If a formal DMC is to be convened, please forward details of the membership and standard operating procedures to the Research Ethics Committee when available. The REC should also be notified of DMC recommendations and receive summary reports of interim analyses.

A75-2. What are the criteria for electively stopping the trial or other research prematurely?

The trial has an embedded internal pilot to assess recruitment rate and primary outcome data completion. This will be conducted nine months after the first participant has been recruited, assessing data from the first 6 months. The target figures are listed in the protocol. If the target figures have not been met, strategies will be developed and implemented to improve the rates. This may include opening additional trial sites or providing additional site support and training. The Trial Steering Committee (TSC) will be actively involved in this review.

There will be one interim analysis which will look for harm or benefit (not futility), using the O'Brien Fleming method. This will be conducted by the trial statistician once 400 participants have been recruited (it will exclude participants who were found to be in traumatic cardiac arrest (TCA) upon arrival of the Air Ambulance Service clinical team). In addition, the dropout and TCA rate will be examined to ensure that they are in line with the expected 5% and 25% respectively, which was initially anticipated. This analysis will be presented to and reviewed by the Data Monitoring Committee (DMC) only and will help inform early stopping of the trial in the case of strong evidence of harm or benefit. The stopping rules will be used as a guideline, alongside the other safety data available to the DMC, and used as part of their overall assessment of the trial. They will have overall oversight and can recommend terminating the trial early for these or any other safety concerns. The TSC will have the ultimate authority to stop or modify the trial.

In addition, a blinded sample size reassessment may lead to premature termination of the trial. This could occur if for example, the estimates observed are significantly different from those anticipated in the original sample size calculations and hence this significantly increases the total sample size. The outcome of this assessment will be reviewed by the DMC and trial statisticians only and a recommendation will be sent to the TSC and TMG.

A76. Insurance/ indemnity to meet potential legal liabilities

Note: in this question to NHS indemnity schemes include equivalent schemes provided by Health and Social Care (HSC) in Northern Ireland

A76-1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research? Please tick box(es) as applicable.

Note: Where a NHS organisation has agreed to act as sponsor or co-sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, please describe the arrangements and provide evidence.

- ☒ NHS indemnity scheme will apply (NHS sponsors only)
- ☐ Other insurance or indemnity arrangements will apply (give details below)

Please enclose a copy of relevant documents.

A76-2. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research? Please tick box(es) as applicable.

Note: Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), please describe the arrangements and provide evidence.

- ☒ NHS indemnity scheme will apply (protocol authors with NHS contracts only)

☐ Other insurance or indemnity arrangements will apply (give details below)

Please enclose a copy of relevant documents.

A76-3. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the conduct of the research?

Note: Where the participants are NHS patients, indemnity is provided through the NHS schemes or through professional indemnity. Indicate if this applies to the whole study (there is no need to provide documentary evidence). Where non-NHS sites are to be included in the research, including private practices, please describe the arrangements which will be made at these sites and provide evidence.

☒ NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)

☒ Research includes non-NHS sites (give details of insurance/ indemnity arrangements for these sites below)

This study will involve 10 non-NHS sites (Air Ambulance Services). Evidence of insurance/indemnity is being obtained from each service.

Please enclose a copy of relevant documents.

A77. Has the sponsor(s) made arrangements for payment of compensation in the event of harm to the research participants where no legal liability arises?

☒ Yes ☐ No

If Yes, please give details of the compensation policy:

The Sponsor (NHSBT) is covered under The Department of Health Contingent Liability Minute for non-negligent harm including trial design and no-fault compensation. This is an arrangement to pay compensation for harm where no legal liability arises.

Please enclose a copy of relevant documents.

A78. Could the research lead to the development of a new product/process or the generation of intellectual property?

☐ Yes ☒ No ☐ Not sure

Part B Section 1: Investigational Medicinal Products**Information on each IMP.**

Information on each 'bulk product' before trial-specific operations (blinding, trial specific packaging and labelling) should be provided in this section for each investigational medicinal product (IMP) being tested including each comparator, if applicable.

If the trial is performed with several products please create a separate set of the following questions for each product. If the product is a combination product please give separate information for each active substance. Click on the first row and enter details of the product in the following screens. When you have completed the details, click on the navigate button or the "See All" link and return to this section to enter details of the next product. When you have completed details of all products please move to question 13 using the navigation screen.

Investigational medicinal products

PR1 LyoPlas N-w

13. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR1**

Investigational medicinal product category:

Comparator

14. STATUS OF THE IMP

If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to question 14-.2

14-1. Does the IMP to be used in the trial have a marketing authorisation?

☒ Yes ☐ No ☐ Not Answered

Trade name:

LyoPlas N-w

EV Product Code

Name of the MA holder:

DRK-Blutspendedienst West

MA number (if MA granted by a Member State):

PEI.H.03075.01.1

Is the IMP modified in relation to its MA?

☐ Yes ☒ No ☐ Not Answered

Which country granted the MA?

Germany

Is this the Member State concerned with this application?

☐ Yes ☒ No ☐ Not Answered

14-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

☐ Yes ☒ No ☐ Not Answered

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

☐ Yes ☒ No ☐ Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group

☐ Yes ☒ No ☐ Not Answered

Other :

☐ Yes ☒ No ☐ Not Answered

14-3. IMPD submitted:

Full IMPD

☐ Yes ☒ No ☐ Not Answered

Simplified IMPD

☐ Yes ☒ No ☐ Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

☒ Yes ☐ No ☐ Not Answered

14-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

☐ Yes ☒ No ☐ Not Answered

14-5. Has the IMP been designated in this indication as an orphan drug in the Community?

☐ Yes ☒ No ☐ Not Answered

14-6. Has the IMP been the subject of scientific advice related to this clinical trial?

☐ Yes ☒ No ☐ Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

☐ Yes ☒ No ☐ Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

☐ Yes ☒ No ☐ Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

Description of IMP**15-1. Description of IMP**

Product name where applicable LyoPlas N-w

Product code where applicable

ATC codes, if officially registered

Pharmaceutical form (use
standard terms)

Powder for solution for infusion

Is this a specific paediatric
formulation?☐ Yes ☒ No ☐ Not AnsweredMaximum duration of treatment
of a subject according to the
protocol

D1 only

Dose allowed

First dose for first-in-human clinical trial

Not applicable

Specify per day or total:

☐ per day ☐ total ☒ Not Answered

Specify total dose (number and unit)

Route of administration (relevant to the first dose):

Maximum dose allowed

Not applicable

Specify per day or total

☐ per day ☐ total ☒ Not Answered

Specify total dose (number and unit)

Route of administration (relevant to the maximum dose):

Routes of administration for this IMP

Intravenous use

Intraosseous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

15-2. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1Name of active substance (INN or
proposed INN if available):

Coagulable human plasma

CAS number:

Current sponsor code:

Other descriptive name:

Freeze-dried plasma

Full Molecular formula

N/A

Chemical/biological description
of the Active Substance

Freeze-dried human plasma.

Strength

Concentration unit:	Other
Concentration type:	range
Concentration number (only use both fields for range):	0.70 0.85

15-3. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? ☐ Yes ☒ No ☐ Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) ☐ Yes ☒ No ☐ Not Answered*Is this a:*Advanced Therapy IMP (ATIMP) ⁽¹⁾ ☐ Yes ☒ No ☐ Not AnsweredCombination product that includes a device, but does not involve an Advanced Therapy ☐ Yes ☒ No ☐ Not AnsweredRadiopharmaceutical medicinal product? ☐ Yes ☒ No ☐ Not AnsweredImmunological medicinal product (e.g. vaccine, allergen, immune serum)? ☐ Yes ☒ No ☐ Not AnsweredPlasma derived medicinal product? ☒ Yes ☐ No ☐ Not AnsweredExtractive medicinal product? ☐ Yes ☒ No ☐ Not AnsweredRecombinant medicinal product? ☐ Yes ☒ No ☐ Not AnsweredMedicinal product containing genetically modified organisms? ☐ Yes ☒ No ☐ Not AnsweredHerbal medicinal product? ☐ Yes ☒ No ☐ Not AnsweredHomeopathic medicinal product? ☐ Yes ☒ No ☐ Not AnsweredAnother type of medicinal product? ☐ Yes ☒ No ☐ Not Answered

Specify the mode of action for the active substance in this medicinal product

*The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Emergency substitution of plasma for patients with life-threatening haemorrhage.*Is it an IMP to be used in a first-in-human clinical trial? ☐ Yes ☒ No ☐ Not Answered*(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable**(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended**(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC**(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007*

Information on Placebo

13. Is there a placebo:

Yes



No

Index of Sites where the qualified person certifies batch release

14. IMPs and placebos for which no responsible site needs to be identified:

This section is used to identify IMPs and placebos which:

- Have an MA in the EU **and**
- Are sourced from the EU market **and**
- Are used in the trial without modification (eg not overencapsulated) **and**
- The packaging and labeling is carried out for local use only as per article 9.2 of the Directive 2005/28/EC (GCP Directive).

If all the conditions above are met, then select below the IMPs and placebos to which this applies.

Finished IMP
PR1

This section is dedicated to finished IMPs, i.e. medicinal products randomised, packaged, labelled and certified for use in the clinical trial. In the case of multiple sites indicate the product certified by each site.

15. Identify who is responsible in the Community for the certification of the finished IMPs.

Where the product does not have a MA in the EU, but is supplied in bulk and final packaging and labelling for local use is carried out in accordance with article 9.2. of Directive 2005/28/EC (GCP Directive) then enter the site where the product was finally certified for release by the Qualified Person for use in the clinical trial.

RS1

Organisation

Address

Town/city

Post code

Country

Give the manufacturing authorisation number

If no authorisation, give the reasons:

Select the relevant IMP(s) and Placebo(s) from the drop down lists.

Part B: Section 6 - Adults unable to consent for themselves**A. Clinical trials of investigational medicinal products**

In this sub-section, an adult means a person aged 16 or over.

A1. What clinical condition(s) will the participants have? The trial must relate directly to this condition.

Major traumatic haemorrhage.

A2. Could the trial be carried out equally effectively if confined to adults capable of giving consent?

☐ Yes ☒ No

A3. Who in the research team will decide whether or not the participants have the capacity to give consent? What training/experience will they have to enable them to reach this decision?

Patients will be enrolled into the trial by the attending Air Ambulance clinicians (doctors and or paramedics) under the Emergency Waiver of Consent. Once the patient is admitted to the receiving hospital, the PI and Research Team there will become responsible for the trial consent and follow-up procedures. Mental capacity will be determined by either the consultant in charge of the patient or an experienced medically qualified member of the research team. These individuals will all be familiar with assessing critically ill patients for capacity.

A4. What benefit is the administration of the investigational medicinal product expected to produce for these participants? You may refer back to your answer to Question A24.

For information: there is one IMP in this trial (LyoPlas - freeze-dried plasma), which is part of the comparator arm. The other interventions (whole blood, red blood cells, and fresh-frozen plasma) are blood components and are outside of the scope of the Medicines for Human Use (Clinical Trials) Regulations 2004 (together with its amendments).

The trial aims to show that transfusion of whole blood may arrest bleeding sooner, thereby limiting further transfusion exposure and improving the survival rate at 24 hours (in comparison to the current standard of care, which is a combination of red blood cell and plasma transfusion).

A5. Will the trial involve any foreseeable risk or burden for these participants, or interfere in any way with their freedom of action or privacy?

☒ Yes ☐ No

If Yes, please give an assessment below. You may refer back to your answers to Questions A22 and A23. Highlight any risk, burden or discomfort specific to these participants. Justify in relation to the potential benefits.

All participants in this trial will have been determined (by the attending Air Ambulance Service team) to require pre-hospital blood transfusion. We do not expect any anticipated risk associated to whole blood, in comparison to the current standard of care products (red blood cells, fresh frozen plasma, LyoPlas). However, safety events will be monitored.

Participation in this trial will not affect the medical care or legal rights of participants in any way, and this has been made clear in the Participant / Legal Representative Information Sheet and consent forms. It will also be made clear to potential participants (or their representatives) that they can withdraw from the trial at any time, without having to give a reason. Their privacy will be protected throughout their participation in the trial – all information collected will be kept strictly confidential and stored anonymously.

A6. What arrangements will be made to identify and seek informed consent from a legal representative?

For patients who lack capacity, who are anticipated to be the majority of participants in the trial, informed consent will be sought from the Personal Legal Representative (a relative or friend who is suitable to act in this capacity by virtue of their relationship with the patient, and is available and willing to do so).

Every effort will be made to contact an appropriate Personal Legal Representative of the patient. However, a Professional Legal Representative (a Clinician who is independent of the trial and responsible for the medical care of the patient) may be approached if no Personal Legal Representative can be identified.

In the cases where informed consent is obtained from a Legal Representative, and the participant regains capacity, they will be approached to ask for their consent to continue in the study. The Participant Information Sheet should be provided to them, as this will explain to the participant what has happened to them so far and what the options available to them are (consent to continued study participation, or withdraw from the study).

A7. Is it possible that a participant requiring urgent treatment might need to be recruited into the trial before it is possible to identify and seek consent from a legal representative?

☒ Yes ☐ No

If Yes, outline how decisions will be made on the inclusion of participants and what arrangements will be made to seek consent from the participant (if capacity has been recovered) or a legal representative as soon as practicable thereafter.

Due to the emergency nature of major trauma time will not allow for written informed consent to be obtained before randomisation into the trial. Attempting to gain informed consent at this time could delay life-saving treatment. It would be clinically unjustifiable to delay treatment until full informed consent can be obtained from a personal legal representative or parent/guardian. For this reason, we believe that using the Emergency Waiver of Consent process is justified.

However, in all cases, consent to continue in the trial must be sought from the participant or a Legal Representative as soon as practicable following the incident (once the participant has been admitted to hospital).

A8. What arrangements will be made to continue to consult legal representatives during the course of the research where necessary?

- When obtaining informed consent from a Legal Representative, it should be made clear to them that the participant will be approached to discuss continuation if they regain capacity (at the earliest opportunity).
- If new information becomes available during the course of the study (about the trial treatment), the Legal Representative who provided informed consent will be consulted to check whether they are still in agreement for the participant to remain in the study.
- Information will also be made available via the study website.

A9. Will steps be taken to provide information about the trial to participants, according to their capacity of understanding, and to consider the wishes of participants capable of forming an opinion?

☒ Yes ☐ No

If Yes, give details.

Capacity will be assessed by trained members of staff within the Emergency Department at each site. Information about the study will be provided to the patient according to their level of understanding, and the ways in which they are able to communicate. Staff in the Emergency Department are highly trained in this area. The patient must be able to retain information about the study, and evaluate it's risks and benefits, as well as being able to indicate whether or not they agree to participate. If a patient is unable to read or write, the study information may be read to him/her and he/she may mark the consent form with either a cross or a thumbprint. The consent form must also be witnessed.

A10-1. What will be the criteria for withdrawal of participants?

There are no set criteria for withdrawal:

- Participants will be withdrawn at their request, or at the request of their Legal Representative (if applicable).
- Participants can also be withdrawn at the request of their treating clinician - for example, if a change in their condition occurred and the clinician felt it was no longer appropriate for them to remain in the study.

A10-2. Where a participant is recruited prior to consent being obtained, and consent is later withheld or the participant dies before consent can be given, what provisions will apply to the study data collected up to this point?

If the participant or their Legal Representative does not give consent for continuation in the trial, they will be asked whether they agree for the data that has already been collected up to that point to be retained. If they agree to the data being used, this decision will be documented on the appropriate Case Report Form and in the patient's medical records. If they do not agree, the data will not be used for the study.

It is expected that in some cases, participants will die before informed consent has been obtained. We do not think it would be appropriate to actively seek consent via a personal legal representative of the participant in these cases, as it may cause additional distress. Instead, we will ask each of the participating hospitals to display a poster about the study in relevant locations (i.e. where it is likely to be seen by relatives of the deceased).

We are seeking approval from the Confidentiality Advisory Group to perform data linkage for patients who die after admission to hospital (before consent can be obtained), or are discharged prior to any form of consent being obtained, under the provisions of Section 251 of the National Health Service Act 2006.

PART B: Section 7 - Children**1. Please specify the potential age range of children under 16 who will be included and give reasons for carrying out the research in this age group.**

Blood transfusion is a life-saving treatment for all patients who are bleeding due to trauma and thus is a standard of care for all these patients (including children). Since this is a pragmatic trial, excluding patients aged under 16 years would be unethical. Furthermore, if we exclude children from this trial and the results of the study showed that whole blood is beneficial and thus it becomes the standard of care, we will not be able to transfuse it to children, which again will discriminate this age group further.

2. Indicate whether any children under 16 will be recruited as controls and give further details.

Not applicable.

3-1. Please describe the arrangements for seeking informed consent from a person with parental responsibility or another legal representative.

An appropriate adult will be identified by the PI/Research Team for each participant aged <16 years. This will be a parent or someone with parental responsibility (agreement of only one parent is required), or a personal legal representative i.e. a person not connected with the conduct of the trial who is suitable to act as the legal representative by virtue of their relationship with the child.

A legal representative will only ever be approached if someone with parental responsibility cannot be contacted. If a personal legal representative is not available, a professional legal representative i.e. a doctor responsible for the medical treatment of the child if they are independent of the study, or a person nominated by the healthcare provider can be approached instead.

Parents or legal representatives must understand that they are being asked to give consent on behalf of the child, they must be informed of the objectives and risks of the trial and informed that they can withdraw the child from the trial at any time. They must also be given a contact point where further information about the trial can be obtained.

Children who have capacity should be involved in the decision-making process whenever possible. Age appropriate information will be provided to them to facilitate this.

4. If you intend to provide children under 16 with information about the research and seek their consent or agreement, please outline how this process will vary according to their age and level of understanding.

Information sheets have been produced which are specifically aimed at children aged 6-10 years and 11-15 years.

There are no information sheets aimed at children aged under 6. We believe this is appropriate due to the nature of the study, which would be very difficult for children of this age to understand.

Copies of written information sheet(s) for parents and children, consent/assent form(s) and any other explanatory material should be enclosed with the application.

5. Is it possible that a child might need to be treated urgently as part of the trial before it is possible to identify and seek consent from a person with parental responsibility or another legal representative?

☒ Yes ☐ No

If Yes, outline how decisions will be made on the inclusion of children and what arrangements will be made to seek consent as soon as practicable thereafter.

This will be the case for all participants enrolled into the SWiFT trial, as their condition will be life-threatening and treatment must be initiated immediately. A Parent/Guardian will be approached for consent as soon as practically possible after the child's admission to hospital. If no Parent/Guardian can be contacted, a personal legal representative may be approached instead. If no personal legal representative is available, a professional legal representative may be approached instead.

Children with capacity should be involved in the consent process and asked to provide assent (this is only appropriate for older children, i.e. those aged 6+).

PART C: Overview of research sites

Please enter details of the host organisations (Local Authority, NHS or other) in the UK that will be responsible for the research sites. For further information please refer to guidance.

Investigator identifier	Research site	Investigator Name
IN1	☒ NHS/HSC Site ☐ Non-NHS/HSC Site Organisation name CAMBRIDGE UNIVERSITY HOSPITALS NHS FOUNDATION TRUST Address CAMBRIDGE BIOMEDICAL CAMPUS HILLS ROAD CAMBRIDGE Post Code CB2 0QQ Country ENGLAND	Forename Eoin Middle name Family name Macdonald-Nethercott Email eoin.macdonaldnethercott@addenbrookes.nhs.uk Qualification (MD...) Consultant in Emergency Medicine Country United Kingdom
IN3	☒ NHS/HSC Site ☐ Non-NHS/HSC Site Organisation name SOUTH TEES HOSPITALS NHS FOUNDATION TRUST Address JAMES COOK UNIVERSITY HOSPITAL MARTON ROAD MIDDLESBROUGH Post Code TS4 3BW Country ENGLAND	Forename Richard Middle name Family name Procter Email richard.procter@nhs.net Qualification (MD...) Consultant in Emergency Medicine Country United Kingdom
IN4	☒ NHS/HSC Site ☐ Non-NHS/HSC Site	Forename Oliver Middle name Family name Hawksley

Organisation name	OXFORD UNIVERSITY HOSPITALS NHS FOUNDATION TRUST	Email	oliver.hawksley@ouh.nhs.uk
Address	JOHN RADCLIFFE HOSPITAL HEADLEY WAY HEADINGTON OXFORD	Qualification (MD...)	Consultant in Emergency and Pre-hospital Medicine
Post Code	OX3 9DU	Country	United Kingdom
Country	ENGLAND		

IN5

- ☒ NHS/HSC Site
☐ Non-NHS/HSC Site

Forename	Dan
Middle name	
Family name	Frith
Email	dan.frith@nhs.net
Qualification (MD...)	Consultant in Trauma and Emergency Surgery
Country	United Kingdom

Organisation name	IMPERIAL COLLEGE HEALTHCARE NHS TRUST
Address	THE BAYS ST MARYS HOSPITAL SOUTH WHARF ROAD LONDON
Post Code	W2 1BL
Country	ENGLAND

IN6

- ☒ NHS/HSC Site
☐ Non-NHS/HSC Site

Forename	Phil
Middle name	
Family name	Moss
Email	phil.moss@stgeorges.nhs.uk
Qualification (MD...)	Consultant in Emergency Medicine
Country	

Organisation name	ST GEORGE'S UNIVERSITY HOSPITALS NHS FOUNDATION TRUST
Address	ST GEORGE'S HOSPITAL BLACKSHAW ROAD TOOTING LONDON
Post Code	SW17 0QT
Country	ENGLAND

IN7

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Anne

Middle name

Family name Weaver

Email anne.weaver@nhs.net

Organisation name BARTS HEALTH
NHS TRUSTQualification (MD...) Consultant in Emergency and Pre-Hospital
MedicineAddress THE ROYAL
LONDON
HOSPITAL

Country United Kingdom

80 NEWARK
STREET
LONDON

Post Code E1 2ES

Country ENGLAND

IN8

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Matthew

Middle name

Family name Edwards

Email medwards9@nhs.net

Organisation name KING'S COLLEGE
HOSPITAL NHS
FOUNDATION
TRUST

Qualification (MD...) Consultant in Emergency Medicine

Address DENMARK HILL

Country United Kingdom

LONDON

Post Code SE5 9RS

Country ENGLAND

IN9

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Rachel

Middle name

Family name Hawes

Email rachel.hawes@nhs.net

Organisation name THE NEWCASTLE
UPON TYNE
HOSPITALS NHS
FOUNDATION
TRUSTQualification (MD...) Consultant in Anaesthesia and Pre-Hospital
Emergency MedicineAddress FREEMAN
HOSPITAL

Country United Kingdom

IN10

FREEMAN ROAD
HIGH HEATON
NEWCASTLE
UPON TYNE
Post Code NE7 7DN
Country ENGLAND

- ☒ NHS/HSC Site
☐ Non-NHS/HSC Site

Forename Bentley
Middle name
Family name Waller
Email bentley.waller@uhs.nhs.uk
Qualification (MD...) Consultant in Emergency Medicine
Country United Kingdom

Organisation name UNIVERSITY
HOSPITAL
SOUTHAMPTON
NHS
FOUNDATION
TRUST
Address SOUTHAMPTON
GENERAL
HOSPITAL
TREMONA ROAD
SOUTHAMPTON
Post Code SO16 6YD
Country ENGLAND

IN12

- ☒ NHS/HSC Site
☐ Non-NHS/HSC Site

Forename Prasad
Middle name
Family name Siddalingeswara
Email prasad.siddalingeswara@nhs.net
Qualification (MD...) Consultant in Emergency Medicine
Country United Kingdom

Organisation name NORTH WEST
ANGLIA NHS
FOUNDATION
TRUST
Address PETERBOROUGH
CITY HOSPITAL
BRETTON GATE
BRETTON
PETERBOROUGH
Post Code PE3 9GZ
Country ENGLAND

IN13

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Edd

Middle name

Family name Carlton

Email ed.carlton@nbt.nhs.uk

Organisation name NORTH BRISTOL
NHS TRUSTQualification Professor and Consultant in Emergency
(MD...) MedicineAddress SOUTHMEAD
HOSPITAL
SOUTHMEAD
ROAD
WESTBURY-ON-
TRYM BRISTOL

Country United Kingdom

Post Code BS10 5NB

Country ENGLAND

IN14

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Abdo

Middle name

Family name Sattout

Email abdo.sattout@liverpoolft.nhs.uk

Organisation name LIVERPOOL
UNIVERSITY
HOSPITALS NHS
FOUNDATION
TRUSTQualification Consultant in Emergency Medicine
(MD...)

Country United Kingdom

Address ROYAL
LIVERPOOL
UNIVERSITY
HOSPITAL
PRESCOT
STREET
LIVERPOOL

Post Code L7 8XP

Country ENGLAND

IN15

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Ansar

Middle name

Family name Mahmood

Email ansar.mahmood@uhb.nhs.uk

Organisation name UNIVERSITY
HOSPITALS
BIRMINGHAM
NHS
FOUNDATION
TRUSTQualification Consultant Orthopaedic Surgeon and Lead
(MD...) for Trauma Research

Country United Kingdom

Address QUEEN
ELIZABETH

IN16

HOSPITAL
MINDELSON
WAY
EDGBASTON
BIRMINGHAM
WEST MIDLANDS
Post Code B15 2GW
Country ENGLAND

- ☒ NHS/HSC Site
☐ Non-NHS/HSC Site

Organisation name UNIVERSITY
HOSPITALS
COVENTRY AND
WARWICKSHIRE
NHS TRUST
Address WALSGRAVE
GENERAL
HOSPITAL
CLIFFORD
BRIDGE ROAD
COVENTRY
Post Code CV2 2DX
Country ENGLAND

Forename Caroline
Middle name
Family name Leech
Email caroline.leech@uhcw.nhs.uk
Qualification (MD...) Consultant in Emergency and Pre-Hospital
Medicine
Country United Kingdom

IN17

- ☒ NHS/HSC Site
☐ Non-NHS/HSC Site

Organisation name LANCASHIRE
TEACHING
HOSPITALS NHS
FOUNDATION
TRUST
Address ROYAL PRESTON
HOSPITAL
SHAROE GREEN
LANE
FULWOOD
PRESTON
Post Code PR2 9HT
Country ENGLAND

Forename Kirsty
Middle name
Family name Challen
Email kirsty.challen@lthtr.nhs.uk
Qualification (MD...) Consultant in Emergency and Pre-Hospital
Medicine
Country United Kingdom

IN18

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Robert

Middle name

Family name Kong

Email robert.kong@bsuh.nhs.uk

Qualification (MD...) Consultant in Anaesthesia & Intensive Care

Country United Kingdom

Organisation name UNIVERSITY
HOSPITALS
SUSSEX NHS
FOUNDATION
TRUST

Address WORTHING
HOSPITAL
LYNDHURST
ROAD

Post Code WORTHING

Country BN11 2DH

ENGLAND

IN19

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Richard

Middle name

Family name Hall

Email richard.hall@uhnm.nhs.uk

Qualification (MD...) Consultant in Emergency Medicine

Country United Kingdom

Organisation name UNIVERSITY
HOSPITALS OF
NORTH
MIDLANDS NHS
TRUST

Address NEWCASTLE
ROAD

Post Code ST4 6QG

Country ENGLAND

STOKE-ON-
TRENT

IN20

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Daniel

Middle name

Family name Horner

Email daniel.horner@nca.nhs.uk

Qualification (MD...) Consultant in Emergency and Critical Care Medicine

Country United Kingdom

Organisation name SALFORD ROYAL
NHS
FOUNDATION
TRUST

Address SALFORD ROYAL
STOTT LANE

IN21

SALFORD
GREATER
MANCHESTER

Post Code M6 8HD
Country ENGLAND

☒ NHS/HSC Site
☐ Non-NHS/HSC Site

Organisation name MANCHESTER
UNIVERSITY NHS
FOUNDATION
TRUST

Address COBBETT HOUSE
OXFORD ROAD
MANCHESTER

Post Code M13 9WL
Country ENGLAND

Forename Simon
Middle name
Family name Carley
Email simon.carley@mft.nhs.uk
Qualification Consultant in Emergency Medicine and
(MD...) Major Trauma
Country United Kingdom

IN22

☒ NHS/HSC Site
☐ Non-NHS/HSC Site

Organisation name UNIVERSITY
HOSPITALS
BRISTOL AND
WESTON NHS
FOUNDATION
TRUST

Address TRUST
HEADQUARTERS
MARLBOROUGH
STREET
BRISTOL

Post Code BS1 3NU
Country ENGLAND

Forename Paul
Middle name
Family name Reavley
Email paul.reavley@uhbw.nhs.uk
Qualification Consultant in Adult and Paediatric
(MD...) Emergency Medicine
Country United Kingdom

IN23

☒ NHS/HSC Site
☐ Non-NHS/HSC Site

Forename Shrouk
Middle name
Family name Messahel

Organisation name
ALDER HEY
CHILDREN'S NHS
FOUNDATION
TRUST

Address
ALDER HEY
HOSPITAL
EATON ROAD
WEST DERBY
LIVERPOOL

Post Code
L12 2AP
Country
ENGLAND

Email
shrouk.messahel@alderhey.nhs.uk
Qualification
(MD...)
Consultant in Paediatric Emergency
Medicine
Country
United Kingdom

IN24

- ☐ NHS/HSC Site
☒ Non-NHS/HSC Site

Institution name
Magpas Air
Ambulance
Department name
Centenary House
Street address
St. Marys Street
Town/city
Huntingdon,
Cambridgeshire
Post Code
PE29 3PE
Country
United Kingdom

Forename
Simon
Middle name
Family name
Lewis
Email
simon@magpas.org.uk
Qualification
(MD...)
Medical Director
Country
United Kingdom

IN25

- ☐ NHS/HSC Site
☒ Non-NHS/HSC Site

Institution name
Thames Valley Air
Ambulance
Department name
Stokenchurch
House
Street address
Oxford Road,
Stokenchurch
Town/city
High Wycombe,
Buckinghamshire
Post Code
HP14 3SX
Country
United Kingdom

Forename
James
Middle name
Family name
Raitt
Email
james.raitt@tvairambulance.org.uk
Qualification
(MD...)
Consultant in Emergency Medicine and Pre-
Hospital Emergency Medicine
Country
United Kingdom

IN26

- ☐ NHS/HSC Site
☒ Non-NHS/HSC Site

Institution name
Air Ambulance
Charity Kent

Forename
Richard
Middle name
Family name
Lyons
Email
richardlyon@aakss.org.uk
Qualification
(MD...)
Medical Director

IN27

Surrey Sussex
Department name Air Ambulance
Building
Street address Rochester City
Airport, Maidstone
Road
Town/city Chatham
Post Code ME5 9SD
Country United Kingdom

Country United Kingdom

- ☐ NHS/HSC Site
☒ Non-NHS/HSC Site

Forename Matthew
Middle name
Family name Sawyer
Email matthew.sawyer@swast.nhs.uk
Qualification (MD...) Paramedic Advanced Practitioner
Country United Kingdom

Dorset and
Institution name Somerset Air
Ambulance
Department name Landacre House,
Castle Road
Street address Chelston
Business Park
Town/city Wellington,
Somerset
Post Code TA21 9JQ
Country United Kingdom

IN28

- ☐ NHS/HSC Site
☒ Non-NHS/HSC Site

Forename Laurie
Middle name
Family name Phillipson
Email laurie.phillipson@ehaat.org
Qualification (MD...) Head of Clinical Development and Critical
Care Paramedic
Country United Kingdom

Essex & Herts Air
Institution name Ambulance
Department name The Business
Centre
Street address Business Park
Earls Colne
Town/city Colchester, Essex
Post Code CO6 2NS
Country United Kingdom

IN29

- ☐ NHS/HSC Site
☒ Non-NHS/HSC Site

Forename Ed
Middle name
Family name Valentine
Email ed.valentine@gwaac.com
Qualification (MD...) Critical Care Doctor
Country United Kingdom

Great Western Air
Institution name Ambulance Charity
Department name County Gates
Street address Ashton Road
Town/city Bristol
Post Code BS3 2JH

	Country	United Kingdom		
IN30	☐ NHS/HSC Site ☒ Non-NHS/HSC Site		Forename	Elizabeth
			Middle name	
			Family name	Shewry
			Email	elizabeth.shewry@uhs.nhs.uk
	Institution name	Hampshire & Isle of Wight Air Ambulance	Qualification (MD...)	Helicopter Emergency Medical Service (HEMS) Doctor
	Department name	F4 Adanac Park	Country	United Kingdom
	Street address	Adanac Drive, Nursling,		
	Town/city	Southampton, Hampshire		
	Post Code	SO16 0BT		
	Country	United Kingdom		
IN31	☐ NHS/HSC Site ☒ Non-NHS/HSC Site		Forename	Anne
			Middle name	
			Family name	Weaver
			Email	anne.weaver@nhs.net
	Institution name	London's Air Ambulance	Qualification (MD...)	Consultant in Emergency and Pre-Hospital Medicine
	Department name	5th Floor	Country	United Kingdom
	Street address	77 Mansell Street		
	Town/city	London		
	Post Code	E1 8AN		
	Country	United Kingdom		
IN32	☐ NHS/HSC Site ☒ Non-NHS/HSC Site		Forename	Andy
			Middle name	
			Family name	Curran
			Email	andy.curran1@nhs.net
	Institution name	North West Air Ambulance	Qualification (MD...)	Medical Director
	Department name	North Mersey Business Centre	Country	United Kingdom
	Street address	Woodward Road, Knowsley		
	Town/city	Liverpool, Merseyside		
	Post Code	L33 7UY		
	Country	United Kingdom		
IN34	☒ NHS/HSC Site ☐ Non-NHS/HSC Site		Forename	Ian
			Middle name	
			Family name	Mew

Organisation name	DORSET COUNTY HOSPITAL NHS FOUNDATION TRUST	Email	ian.mew@dchft.nhs.uk
Address	DORSET COUNTY HOSPITAL WILLIAMS AVENUE DORCHESTER	Qualification (MD...)	Intensive Care Consultant
Post Code	DT1 2JY	Country	United Kingdom
Country	ENGLAND		

IN35

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename	Emma
Middle name	
Family name	O'Donovan
Email	emma.odonovan@nhs.net
Qualification (MD...)	Consultant Haematologist (Lead for Transfusion)
Country	United Kingdom

Organisation name	SURREY AND SUSSEX HEALTHCARE NHS TRUST
Address	TRUST HEADQUARTERS EAST SURREY HOSPITAL CANADA AVENUE REDHILL SURREY
Post Code	RH1 5RH
Country	ENGLAND

IN36

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename	Catherine
Middle name	
Family name	Roughley
Email	catherine.roughley@nhs.net
Qualification (MD...)	Consultant Haematologist (Lead for Transfusion)
Country	United Kingdom

Organisation name	EAST KENT HOSPITALS UNIVERSITY NHS FOUNDATION TRUST
Address	KENT & CANTERBURY HOSPITAL ETHELBERT ROAD CANTERBURY
Post Code	CT1 3NG

Country ENGLAND

IN37

☐ NHS/HSC Site☒ Non-NHS/HSC Site

Forename Rachel

Middle name

Family name Hawes

Email rachel.hawes@nhs.net

Institution name The Great North
Air Ambulance
ServiceQualification Consultant in Anaesthesia and Pre-Hospital
(MD...) Emergency Medicine

Country United Kingdom

Department name Progress House

Street address Urray Nook Road

Town/city Eaglescliffe,
Stockton-On-Tees

Post Code TS16 0QB

Country United Kingdom

IN38

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Paul

Middle name

Family name Reavley

Email paul.reavley@uhbw.nhs.uk

Organisation name UNIVERSITY
HOSPITALS
BRISTOL AND
WESTON NHS
FOUNDATION
TRUSTQualification Consultant in Adult and Paediatric
(MD...) Emergency Medicine

Country United Kingdom

Address TRUST
HEADQUARTERS
MARLBOROUGH
STREET
BRISTOL

Post Code BS1 3NU

Country ENGLAND

IN39

☒ NHS/HSC Site☐ Non-NHS/HSC Site

Forename Andy

Middle name

Family name Curran

Email andy.curran1@nhs.net

Organisation name NORTH WEST
AMBULANCE
SERVICE NHS
TRUSTQualification Medical Director
(MD...)

Country United Kingdom

Address LADYBRIDGE
HALL

	399 CHORLEY
	NEW ROAD
	BOLTON
Post Code	BL1 5DD
Country	ENGLAND

PART D: Declarations**D1. Declaration by Chief Investigator**

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.
2. I undertake to fulfil the responsibilities of the chief investigator for this study as set out in the UK Policy Framework for Health and Social Care Research.
3. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.
4. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.
5. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.
6. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.
7. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.
8. I understand that research records/data may be subject to inspection by review bodies for audit purposes if required.
9. I understand that any personal data in this application will be held by review bodies and their operational managers and that this will be managed according to the principles established in the Data Protection Act 2018.
10. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:
 - ◊ Will be held by the REC (where applicable) until at least 3 years after the end of the study; and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
 - ◊ May be disclosed to the operational managers of review bodies, or the appointing authority for the REC (where applicable), in order to check that the application has been processed correctly or to investigate any complaint.
 - ◊ May be seen by auditors appointed to undertake accreditation of RECs (where applicable).
 - ◊ Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.
 - ◊ May be sent by email to REC members.
11. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 2018.
12. I understand that the main REC or its operational managers may share information in this application or supporting documentation with the Medicines and Healthcare products Regulatory Agency (MHRA) where it is relevant to the Agency's statutory responsibilities.
13. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the Health Research Authority (HRA) together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after the issue of the ethics committee's final opinion or the withdrawal of the application.

Contact point for publication*(Not applicable for R&D Forms)*

HRA would like to include a contact point with the published summary of the study for those wishing to seek further information. We would be grateful if you would indicate one of the contact points below.

- ☐ Chief Investigator
- ☐ Sponsor
- ☐ Study co-ordinator
- ☐ Student
- ☐ Other – please give details
- ☐ None

Access to application for training purposes *(Not applicable for R&D Forms)*

Optional – please tick as appropriate:

☐ I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

This section was signed electronically by Dr Laura Green on 28/02/2022 11:55.

Job Title/Post: Consultant Haematologists

Organisation: NHSBT and Barts Health Trust

Email: laura.green@nhsbt.nhs.uk

D2. Declaration by the sponsor's representative

If there is more than one sponsor, this declaration should be signed on behalf of the co-sponsors by a representative of the lead sponsor named at A64-1.

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.
2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.
3. Any necessary indemnity or insurance arrangements, as described in question A76, will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.
4. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.
5. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.
6. The responsibilities of sponsors set out in the UK Policy Framework for Health and Social Care Research will be fulfilled in relation to this research.
7. The statutory responsibilities of sponsors set out in the Medicines for Human Use (Clinical Trials) Regulations 2004 will be undertaken in relation to this trial.

Please note: The declarations below do not form part of the application for approval above. They will not be considered by the Research Ethics Committee.

8. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.
9. Specifically, for submissions to the Research Ethics Committees (RECs) I declare that any and all clinical trials approved by the HRA since 30th September 2013 (as defined on IRAS categories as clinical trials of medicines, devices, combination of medicines and devices or other clinical trials) have been registered on a publically accessible register in compliance with the HRA registration requirements for the UK, or that any deferral granted by the HRA still applies.

This section was signed electronically by Mrs Yomi Adegbaaju on 28/02/2022 12:21.

Job Title/Post:

Organisation:

Email: