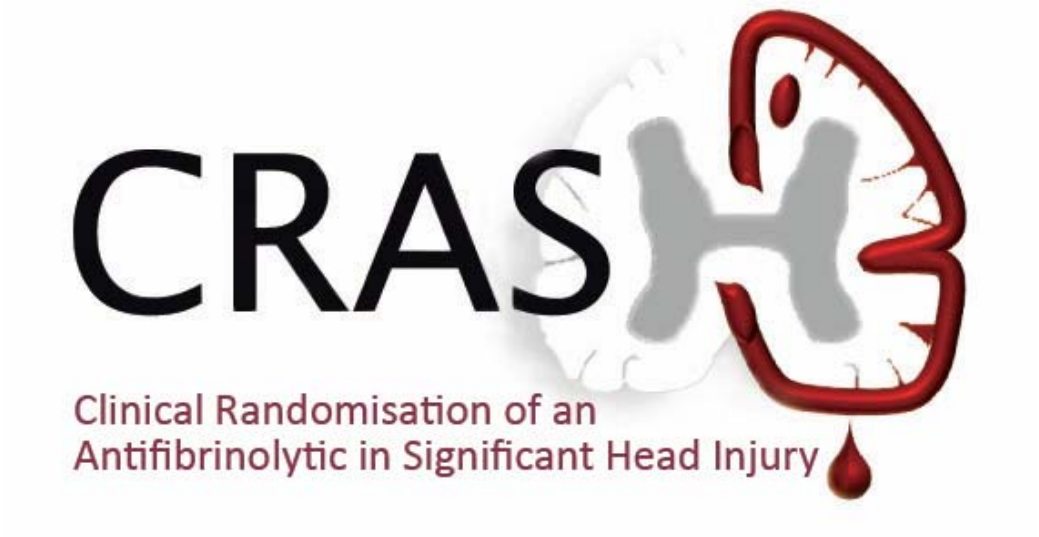
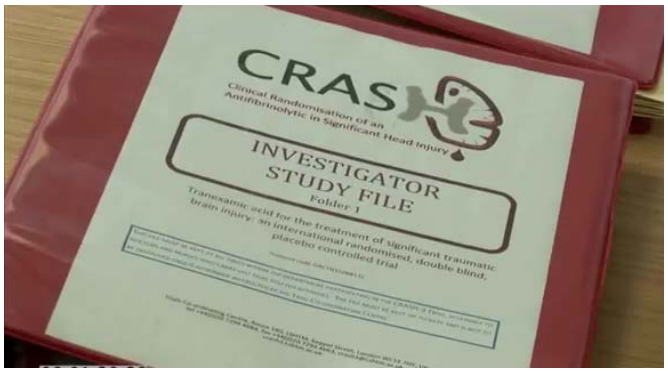


Maintaining the Investigator's Study File

Protocol Code: ISRCTN15088122
V1.1 15 Nov 2016

Investigator Study File

- Sent when all the necessary approvals / agreements are in place at your hospital
- Please return the receipt inside the front cover
- Familiarise yourself with the contents of all sections, so you know where to find the information when needed
- Contains all the information you need to conduct the trial, including training materials
- Keeps all study related documents together
- Documents will demonstrate your compliance with the protocol, GCP, regulatory requirements



Investigator Study File

- To be held in a secure location but accessible to the trial team
- It is a legal requirement to keep the study file up to date
- Must be available for monitoring visits by the TCC / National Coordinator / any relevant regulatory authorities

Maintaining the Study File

- Ensure all logs are up to date:
  - Site responsibility delegation log
  - Screening log
  - Randomisation log
  - Drug accountability log
  - Site visit log

- Documents eg data forms, reports, communication with the TCC, to be filed regularly

- Arrangements for archiving for at least five years after the end of the trial

Site responsibility delegation log

This log is contained in section 19 Site responsibilities

SITE RESPONSIBILITY DELEGATION LOG

SITE ID NUMBER	0	0	0	SITE NAME	Royal London Hospital

THE PERSONS NAMED BELOW ARE AUTHORISED BY THE PRINCIPAL INVESTIGATOR TO CARRY OUT THE SPECIFIED DUTIES FOR THE CRASH-3 TRIAL.

NAME	JOB TITLE	SPECIFIED DUTIES (please insert number codes as listed below)	TRAINING COMPLETED? (Y/N)	SIGNATURE	PI SIGNATURE & START DATE	END DATE
TIM HARRIS	A&E CONSULTANT	1,2,3	Y	T. HARRIS	SIGN: T.HARRIS DATE: 01/05/2013	01/05/2012
BEN ENGLISH	REGISTRAR	1,2,3,5,6	Y	BEN ENGLISH	SIGN: T.HARRIS DATE:05/06/2013	
					SIGN:	

- List all members of staff involved in the conduct of the trial eg doctors, nurses, research coordinators and administrators
- Add new staff members when they join the trial team; note the end date for those who leave
- When a team member leaves the trial, ensure they are replaced with a new team member trained for their allocated tasks
- A brief CV (signed and dated) for each person listed on the log, to be filed in section 19

Screening log

This log is contained in section 15 Patient Entry

PATIENT SCREENING LOG

Hospital ID: 0 0 0 Hospital name: Royal London Hospital

PLEASE RECORD DETAILS OF ALL PATIENTS SCREENED BUT NOT RANDOMISED TO THE CRASH-3 TRIAL

Please keep the original Entry Form for these patients in the Study File Folder 2 Section 15

Date	Patient's Initials (first & last)	Date of Birth	Adults with traumatic brain injury with any intracranial bleeding on CT scan or GCS of 12 or less, and no significant extra cranial bleeding		The patient was not randomised to the trial because:			Signature
			YES	NO	Patient did not meet eligibility criteria (tick if applies)	Patient/relative refused to take part (tick if applies)	Other reason (please document reason below)	
14/05/12	AB	15/02/89		✓	✓			Tim Harris

- Identify a potentially eligible patient and complete the relevant sections of the ENTRY FORM to determine if they can be randomised.
- Screening log keeps a record of patients considered but not randomised. Reasons for not randomising may include ineligibility eg not adult, or having extra cranial bleeding that requires an immediate blood transfusion.
- Entry forms completed for patients considered but not randomised to be filed in Section 15 together with the Screening log.

Randomisation log

This log is contained in section 15 Patient Entry

RANDOMISATION LOG

Hospital ID | 0 | 0 | 0 | Hospital name | Royal London Hospital |

PLEASE RECORD DETAILS OF ALL PATIENTS RANDOMISED TO THE CRASH-3 TRIAL

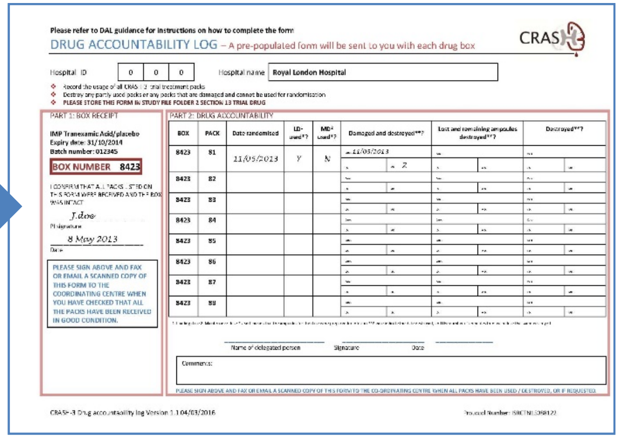
Patient's name	Patient's Hospital ID number	Date of birth	Date randomised	Treatment Box number	Pack number	Name of person who obtained consent
Sean Smith	X123	23/01/87	15/05/12	9251	91	Tim Harris

- Keeps a record of patients randomised into the CRASH-3 trial
- To be updated after every randomisation
- A patient is considered to be randomised at the point when the next treatment pack is removed from the box and found to be intact
- Number of treatment pack (box-pack number) is the 'randomisation number'
- Once a randomisation number has been allocated to a patient, the pack cannot be used again, even if the treatment is not given

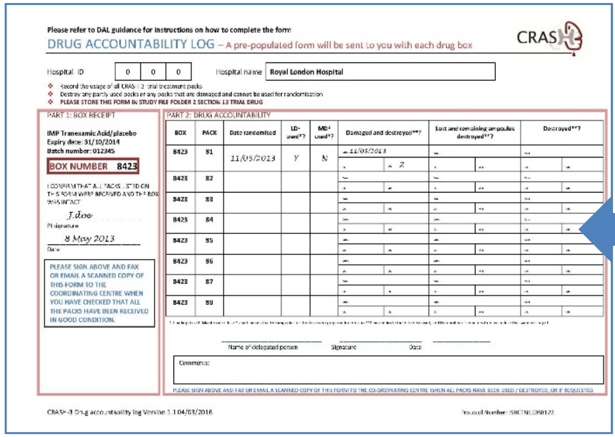
Drug accountability log (DAL)

This log to be kept in section 13 Trial Drugs Documentation

- Pre-printed form sent with every box
- Complete **PART 1** to acknowledge receipt as soon as the box arrives and send a copy to TCC by fax or email
- File in Section 13 Trial Drugs Documentation



Please refer to DAL guidance for instructions on how to complete the form
DRUG ACCOUNTABILITY LOG – A pre-populated form will be sent to you with each drug box
CRASH
Hospital ID
Hospital name
Royal London Hospital
PART 1: BOX RECEIPT
PART 2: DRUG ACCOUNTABILITY
IMP Tranexamic Acid/placebo
Expiry date: 31/10/2014
Batch number: 012345
BOX NUMBER 8423
BOX
PACK
Date randomised
Damaged and destroyed**?
Lost and remaining ampoules destroyed**?
Destroyed**?
PLEASE SIGN ABOVE AND FAX OR EMAIL A SCANNED COPY OF THIS FORM TO THE COORDINATING CENTRE WHEN YOU HAVE CHECKED THAT ALL THE PACKS HAVE BEEN RECEIVED IN GOOD CONDITION.
Comments:

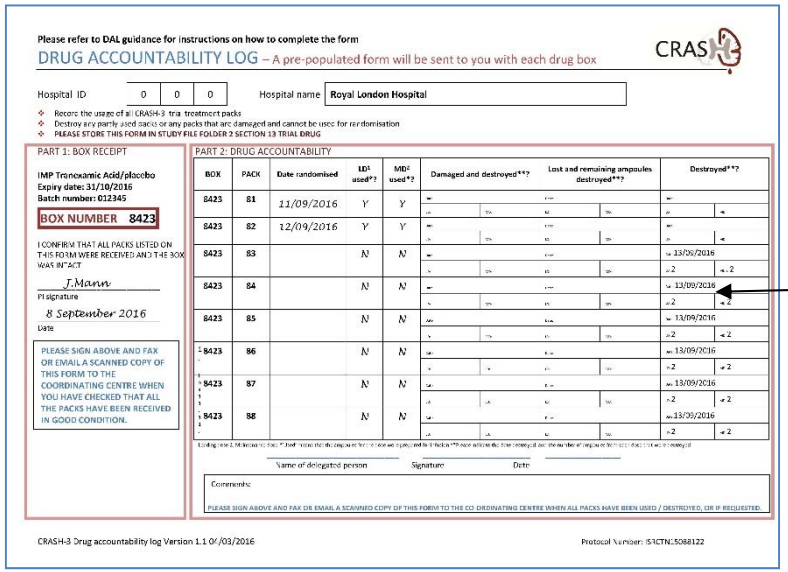


Please refer to DAL guidance for instructions on how to complete the form
DRUG ACCOUNTABILITY LOG – A pre-populated form will be sent to you with each drug box
CRASH
Royal London Hospital
PART 1: BOX RECEIPT
PART 2: DRUG ACCOUNTABILITY
BOX NUMBER 8423
Comments:

- Complete **PART 2** after each randomisation to account for when each treatment pack is used
- When form is complete (all packs accounted for) send signed copy to TCC by fax or email
- PI or delegate is responsible for accounting for every treatment pack sent to your hospital
- Usage of each pack and vials to be recorded (randomisation, damaged, lost destroyed due to withdrawal or expiry)

Trial treatment can only be used for patients randomised to the CRASH-3 trial

Examples of how to fill out the DAL



Please refer to DAL guidance for instructions on how to complete the form

DRUG ACCOUNTABILITY LOG – A pre-populated form will be sent to you with each drug box

Hospital ID 0 0 0 Hospital name Royal London Hospital

- Record the usage of all CRASH-3 trial treatment packs
- Destroy any partly used packs or any packs that are damaged and cannot be used for randomisation
- PLEASE STORE THIS FORM IN STUDY FILE FOLDER 2 SECTION 13 TRIAL DRUG

PART 1: BOX RECEIPT

IMP Tranexamic Acid/placebo
Expiry date: 31/10/2016
Batch number: 012345

BOX NUMBER 8423

I CONFIRM THAT ALL PACKS LISTED ON THIS FORM WERE RECEIVED AND THE BOX WAS INTACT

J.Mann
PI signature

8 September 2016
Date

PLEASE SIGN ABOVE AND FAX OR EMAIL A SCANNED COPY OF THIS FORM TO THE COORDINATING CENTRE WHEN YOU HAVE CHECKED THAT ALL THE PACKS HAVE BEEN RECEIVED IN GOOD CONDITION.

PART 2: DRUG ACCOUNTABILITY

BOX	PACK	Date randomised	LD[1] used*?	MD[2] used*?	Damaged and destroyed**?	Lost and remaining ampoules destroyed**?	Destroyed**?
8423	81	11/09/2016	Y	Y			
8423	82	12/09/2016	Y	Y			
8423	83		N	N			13/09/2016
8423	84		N	N			13/09/2016
8423	85		N	N			13/09/2016
8423	86		N	N			13/09/2016
8423	87		N	N			13/09/2016
8423	88		N	N			13/09/2016

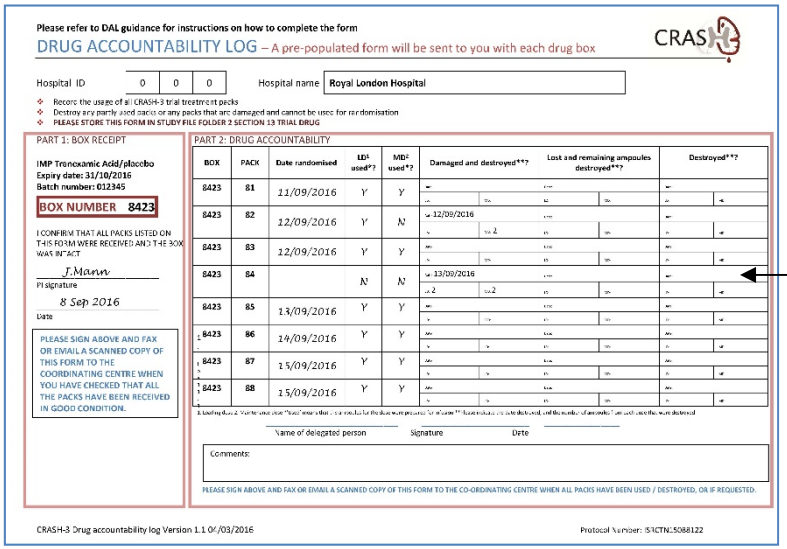
Name of delegated person Signature Date

Comments:

PLEASE SIGN ABOVE AND FAX OR EMAIL A SCANNED COPY OF THIS FORM TO THE CO-ORDINATING CENTRE WHEN ALL PACKS HAVE BEEN USED / DESTROYED, OR IF REQUESTED.

CRASH-3 Drug accountability log Version 1.1 04/03/2016 Protocol Number: ISRCTN15088122

When a pack is destroyed due to e.g. expiry or if it is the end of the trial, in the 'destroyed' column please indicate the number of vials destroyed from each dose and the date that they were destroyed



Please refer to DAL guidance for instructions on how to complete the form

DRUG ACCOUNTABILITY LOG – A pre-populated form will be sent to you with each drug box

Hospital ID 0 0 0 Hospital name Royal London Hospital

- Record the usage of all CRASH-3 trial treatment packs
- Destroy any partly used packs or any packs that are damaged and cannot be used for randomisation
- PLEASE STORE THIS FORM IN STUDY FILE FOLDER 2 SECTION 13 TRIAL DRUG

PART 1: BOX RECEIPT

IMP Tranexamic Acid/placebo
Expiry date: 31/10/2016
Batch number: 012345

BOX NUMBER 8423

I CONFIRM THAT ALL PACKS LISTED ON THIS FORM WERE RECEIVED AND THE BOX WAS INTACT

J.Mann
PI signature

8 Sep 2016
Date

PLEASE SIGN ABOVE AND FAX OR EMAIL A SCANNED COPY OF THIS FORM TO THE COORDINATING CENTRE WHEN YOU HAVE CHECKED THAT ALL THE PACKS HAVE BEEN RECEIVED IN GOOD CONDITION.

PART 2: DRUG ACCOUNTABILITY

BOX	PACK	Date randomised	LD[1] used*?	MD[2] used*?	Damaged and destroyed**?	Lost and remaining ampoules destroyed**?	Destroyed**?
8423	81	11/09/2016	Y	Y			
8423	82	12/09/2016	Y	N		12/09/2016	
8423	83	12/09/2016	Y	Y			
8423	84		N	N		13/09/2016	
8423	85	13/09/2016	Y	Y			
8423	86	14/09/2016	Y	Y			
8423	87	15/09/2016	Y	Y			
8423	88	15/09/2016	Y	Y			

Name of delegated person Signature Date

Comments:

PLEASE SIGN ABOVE AND FAX OR EMAIL A SCANNED COPY OF THIS FORM TO THE CO-ORDINATING CENTRE WHEN ALL PACKS HAVE BEEN USED / DESTROYED, OR IF REQUESTED.

CRASH-3 Drug accountability log Version 1.1 04/03/2016 Protocol Number: ISRCTN15088122

Where a pack is damaged in the 'damaged and destroyed' column, please indicate the number of vials destroyed from each dose and the date that they were destroyed

Site visit log

This log is contained in section 12 Trial Monitoring

SITE VISIT LOG

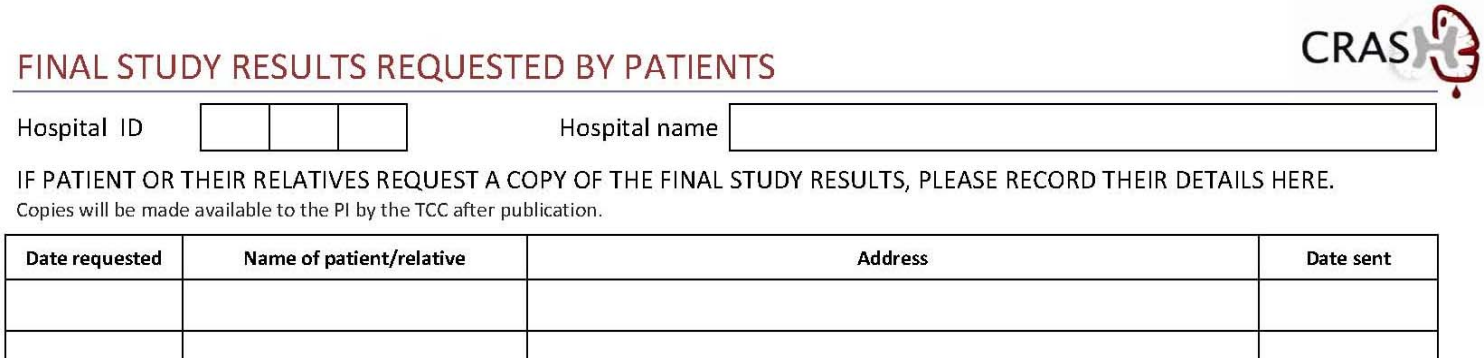
TO BE COMPLETED BY ALL PERSONNEL CONDUCTING SITE VISITS
INCLUDING NATIONAL COORDINATORS, TRIAL MONITORS AND TCC STAFF

DATE	SITE VISIT DONE BY	REPORT RECEIVED AND FILED IN THE STUDY FILE – DATE

- Should be updated every time there is a trial related visit to your site eg TCC representative, national coordinator, regulatory body

Final study results log

This log is contained in section 20 Reports



FINAL STUDY RESULTS REQUESTED BY PATIENTS

CRASH

Hospital ID | | | | Hospital name | |

IF PATIENT OR THEIR RELATIVES REQUEST A COPY OF THE FINAL STUDY RESULTS, PLEASE RECORD THEIR DETAILS HERE.

Copies will be made available to the PI by the TCC after publication.

Date requested	Name of patient/relative	Address	Date sent

- Ask the patients you have considered for participation, or relatives, if they wish to receive a copy of the final trial results
- If so, record the contact details
- At the end of the trial TCC will send you copies of the final report
- PI to send to individuals listed on this log

Documents to be routinely filed

These documents must be systematically filed when they become available

Type of Document	Section number where this document to be filed
Adverse Event reporting forms	17 – Completed forms
Correspondence with ethics committees	8 – Ethics
Correspondence with regulatory agencies	9 – Regulatory
Visit and monitoring reports (including consent monitoring)	12 – Trial Monitoring
Shipping Documents for the trial drugs	13 – Trial Drugs Documentation
Original Signed CONSENT FORMS (for patient/ representative)	14 – Patient information sheets and consent forms
Original ENTRY FORMS	17 – Completed forms
Original OUTCOME FORMS	17 – Completed forms
Data queries	18 – Correspondence
Correspondence with TCC (emails, letters etc)	18 – Correspondence
CVs of trial team	19 – Site Responsibilities
GCP training certificates of trial team	19 – Site Responsibilities

Training materials

Additional training materials may be requested at any time

THE PROTOCOL

- The copy for you and your team to use is inside the front cover
- The copy in Section 2 is the version submitted for your ethics and regulatory approvals and must not be removed from the Study File

MANUAL OF OPERATING PROCEDURES (MOP)

in section 3 Training Materials

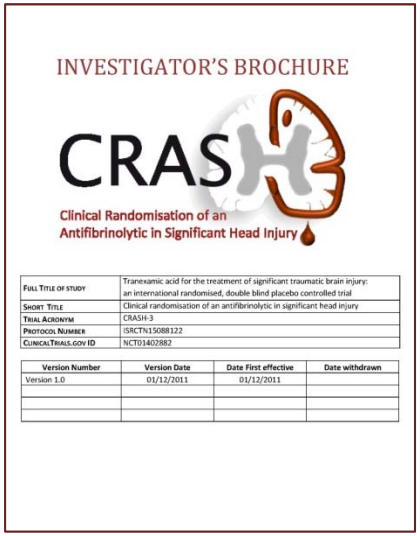
- Detailed guidance on all aspects of the practical conduct of the trial

PRESENTATIONS

- PowerPoint presentations on various aspects of the trial on CD in the front cover of the Study File
- Film on Trial Procedures and the Scientific Rationale on DVD in section 3 Training Materials

Training materials

INVESTIGATOR'S BROCHURE (IB) is contained in section 4 Trial drug guidance


INVESTIGATOR'S BROCHURE

CRASH

Clinical Randomisation of an Antifibrinolytic in Significant Head Injury

Full Title of study	Tranexamic acid for the treatment of significant traumatic brain injury: an international randomised, double blind placebo controlled trial
Short Title	Clinical randomisation of an antifibrinolytic in significant head injury
Trial Acronym	CRASH-3
Protocol Number	ISRCTN15088122
ClinicalTrials.gov ID	NCT01402882

Version Number	Version Date	Date First effective	Date withdrawn
Version 1.0	01/12/2011	01/12/2011	

- Compilation of the clinical/nonclinical data on an Investigational Medicinal Product (IMP)
- Provides information to help understand the rationale for, and compliance with, the protocol eg the dose, dose frequency/interval, methods of administration, safety monitoring procedures
- Important that the PI has read and understood the IB before the trial starts. Familiarity with the IB particularly important for assessing eligibility of a patient under the uncertainty principle.
- Contains the Summary of Product Characteristics (SPC) for IMP – guidelines for the use of the trial treatment provided by the manufacturer (Pharmacia) and approved by the UK regulatory agency
- May be updated as information accumulates during the trial. Updated numbered versions will be sent to you. Familiarise yourself with the updates and file in the Investigator Study File. When a new version is sent, clearly mark the previous version *'NOT IN USE'* and file in the Investigator Study File.

Training materials

PowerPoint presentations on CD

- Scientific background and CRASH-3 introduction
- Conducting the trial at your hospital
- Maintaining your Investigator Study File
- GCP test guidance
- TBI management
- How to assess eligibility
- How to complete the entry form
- How to obtain consent
- How to randomise an eligible patient
- How to manage and administer the trial treatment
- How to complete the outcome form
- How to send data electronically
- How to submit data online
- What to do if a patient develops an unexpected problem
- Reporting Adverse Events
- Why reducing time to treatment is critical

Training materials

- **GCP training** available on the trial website
- Email crash@Lshtm.ac.uk for a username and password
- Email crash@Lshtm.ac.uk for additional training materials

CRASH

Clinical Randomisation of an Antifibrinolytic in Significant Head Injury

Trial Coordinating Centre
London School of Hygiene & Tropical Medicine
Room 180, Keppel Street, London WC1E 7HT
Tel +44(0)20 7299 4684 | Fax +44(0)20 7299 4663
crash@Lshtm.ac.uk

crash3.Lshtm.ac.uk

UKCRC Registered Clinical Trials Units