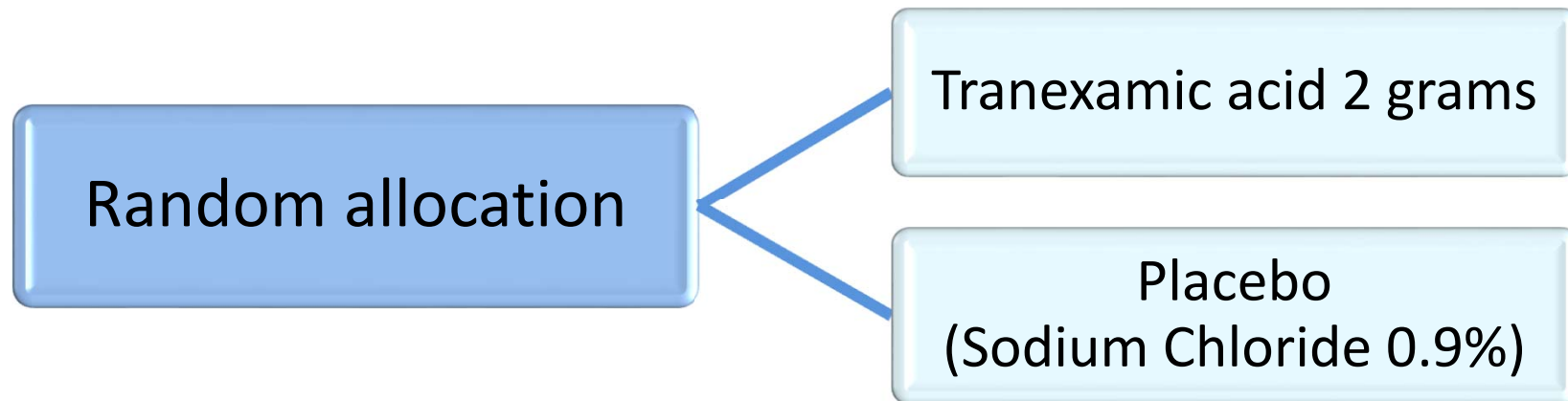


Managing and administering The trial treatment

Protocol Code: ISRCTN15088122
V 1.1 date 15 Nov 2016

What is the trial treatment



Managing stock

- Initial supply: one drug box containing eight individual patient treatment packs
- Thereafter, minimum stock level based on your average monthly recruitment
- When TCC receives entry form the pack is removed from your stock in the trial database
- At minimum level we will automatically send a new box/boxes – no need to remind us
- We can monitor your drug stock level **ONLY** if you send the entry form (within 24 hours of randomisation)
- PI or his/her delegate is responsible for accounting for every pack of trial treatment sent to your hospital

Packs		
Number	Status	Date
21	used in trial	6 Jun 2012
22	used in trial	10 Jun 2012
23	unused	
24	unused	
25	unused	
26	unused	
27	unused	
28	unused	

Receiving new supplies

- Box should be received intact
- Inspect for damage
- Sign PART 1 of **Drug Accountability Log** sent with each box, send to TCC by fax or email
- Store securely, but accessible to the trial team for randomisation at all times
Please discuss with your pharmacist responsible for clinical trials if required
- Store in a cool dry place protected from excessive heat and freezing



Do not open individual packs to inspect the contents until used for randomisation!

What is in the box



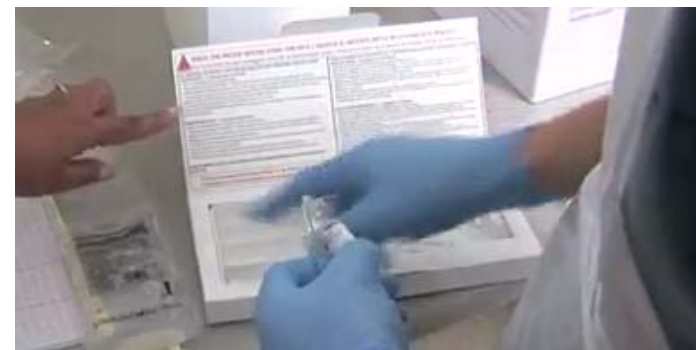
- **Site box** contains:
 - Treatment box
 - 8 x 100mL bags of normal saline for loading dose
- **Treatment box** contains:
 - 8 individual patient treatment packs
- **Treatment pack** contains:
 - 4 x 500mg ampoules of TXA or placebo
 - 2 x sterile 10mL syringe and 21FG needle

- With each drug box you will also receive **envelopes** of:
 - Entry forms
 - Outcome forms
 - Label sheets for recording the treatment
 - Brief information leaflets for family and friends
 - Hospital specific information sheets and consent forms
 - Patient alert cards



Before treatment is given

- Trial treatment to be used only for patients randomised to the CRASH-3 trial – **NOT for any other purpose**
- To assess eligibility, **screening and consent details** on the entry form must be captured before randomising a patient
- **Always use the treatment packs in sequential number order**
- Check **expiry date** before giving the treatment
- Before allocating box/pack number to the patient, check that **all four ampoules are intact** – if any are broken:
 - discard the complete treatment pack
 - take next available number
 - report broken pack on the Drug Accountability Log and **inform TCC**
- The intact pack chosen will be the randomisation number



Trial treatment

TREATMENT	AMPOULES	DOSE TXA / PLACEBO	ADMINISTRATION INSTRUCTION
Loading Dose	2	1 gram	Added to 100mL sodium chloride 0.9% (provided in site box) and infused over 10 minutes
Maintenance Dose	2	1 gram	Added to 500mL of any isotonic intravenous solution and infused at 120mg/hr [60 mL/hr] for about 8 hours

Trial treatment injections should not be mixed with blood for transfusion or infusion solutions containing penicillin or mannitol.



Infusion – Loading dose

Loading dose to be given to all randomised patients

Using syringe provided draw up 10mL (2 ampoules) of TXA/placebo and add to 100mL normal saline 0.9% (provided) and give as an intravenous infusion over 10 minutes

- Peel off pre-printed yellow randomisation stickers and attach one on each blue form
- Using the pre-printed blue label provided PRESCRIBE: “CRASH-3 trial loading dose (1g of tranexamic acid/ placebo)”
- Place prescription label in the patient’s medical records
- Give immediately after randomisation



**Instructions printed inside the lid of the treatment pack.
Can be provided in local language if required.**

Infusion – Maintenance dose

Maintenance dose to be given to all randomised patients immediately following the loading dose

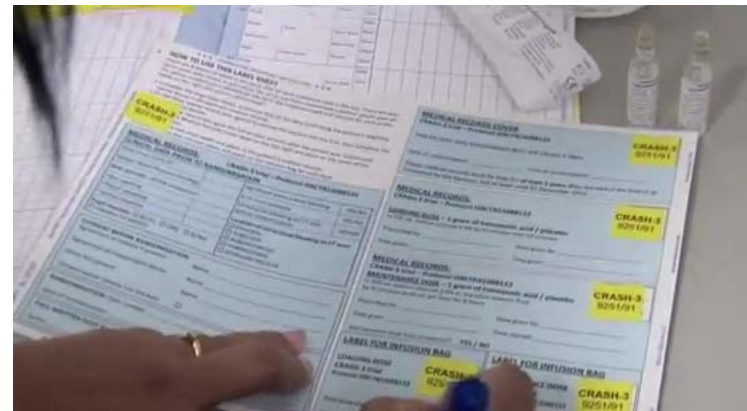
Using syringe provided draw up 10mL (2 ampoules) of TXA/placebo and add to 500mL of any isotonic intravenous solution and infuse over 8 hours

- Using the pre-printed blue label provided PRESCRIBE:
“CRASH-3 trial maintenance dose (1g of tranexamic acid/ placebo)”
- Place prescription label in the patient’s medical records



Labelling

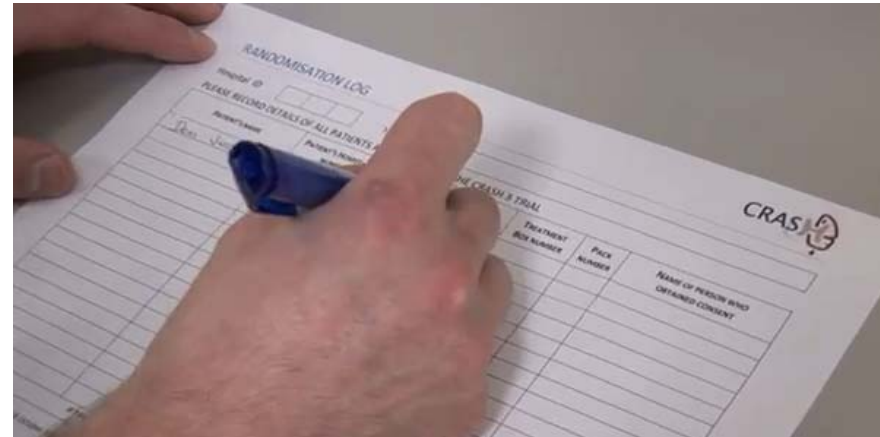
- Peelable stickers with the randomisation number on the lid of each treatment pack
- Presentation titled “Randomising an eligible patient” will give you more details about how to use the labels



**TRANSMIT ENTRY DATA TO TCC
WITHIN 24 HOURS**

Recording the use of packs

- Remember to update the relevant logs in the Study File
 - Randomisation log
 - Drug Accountability log Part 2



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	11/05/2013	Y	N	Date: 11/05/2013	Date:	Date:
					ID: MD: 2	ID: MD:	ID: MD:
8423	82				Date:	Date:	Date:
					ID: MD:	ID: MD:	ID: MD:

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 Triclosomic Acid/placebo
 Expiry date: 31/10/2016
 Batch number: 022345
BOX NUMBER 8423

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

J. Martin
 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	LDI used?*	MDI 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 COORDINATING CENTRE WHEN ALL PACKS HAVE BEEN USED / DESTROYED, OR IF REQUESTED.

CRASH-3 Drug accountability log Version 1.1 01/03/2016 Protocol Number: S1CTN:5088122

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
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8423	82	12/09/2016	Y	N			
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	25/09/2016	Y	Y			

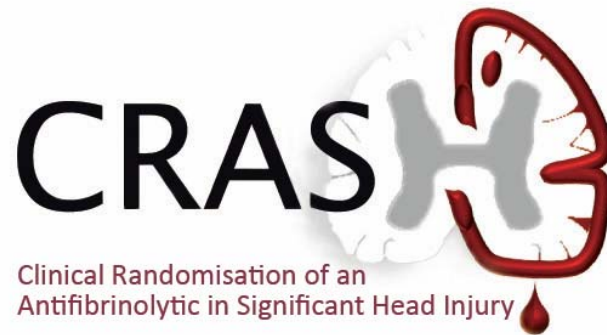
Name of delegated person: _____ Signature: _____ Date: _____

Comments: _____

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

CRASH-3 Drug accountability log Version 1.1 01/03/2016 Protocol Number: S1CTN:5088122

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



Clinical Randomisation of an
Antifibrinolytic in Significant Head Injury

Trial Coordinating Centre

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