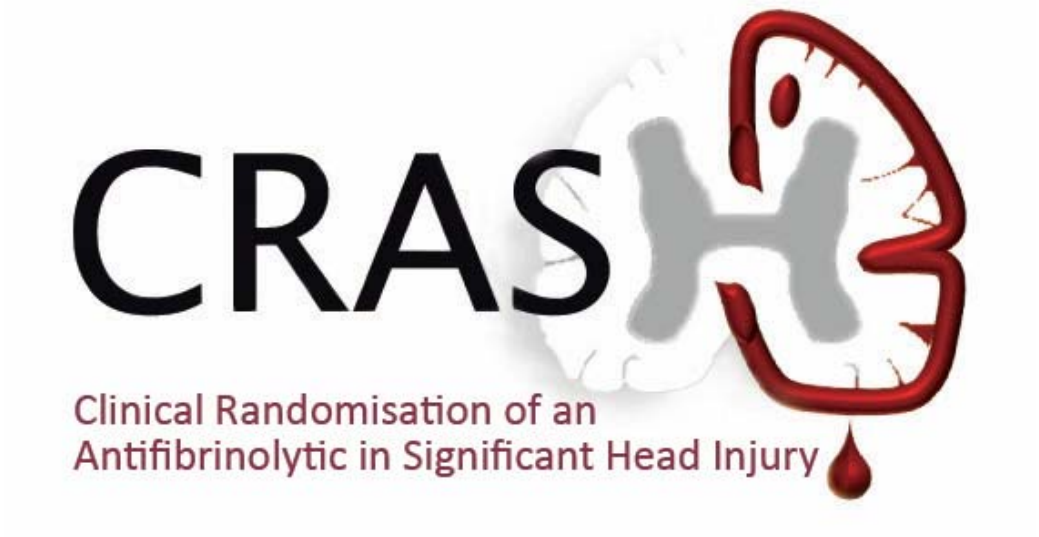


Giving information and obtaining informed consent

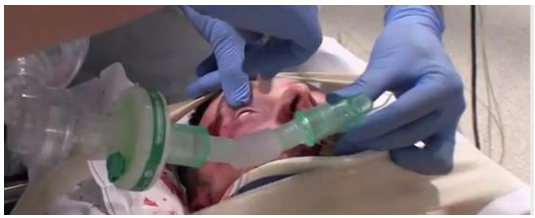
Protocol Code: ISRCTN15088122
V 1.0 date 30 Jan 2012

Overview

- What is valid Informed Consent
- Consent in an emergency situation
- Consent process prior to randomisation
  - Waiver of informed consent
  - Representative agreement
  - Informed consent
- Consent process after randomisation
- When is a *witness* required
- Completing the consent form
- Common consent form errors

What is valid informed consent?

- Informed consent is based on respect for the individual and in particular the individual's autonomy/capacity and right to define his or her own goals and make choices designed to achieve those goals for his/her own life.
- This right is well established in many national laws.
- Informed consent in research means **more than simply obtaining the signature** of the potential research participant.
- It is a process that involves:
  - conveying accurate and relevant information about the study and its purpose;
  - disclosing known risks, benefits, alternatives and procedures;
  - answering questions;
  - enabling the potential participant to make an informed decision about whether to participate.



What is valid informed consent?

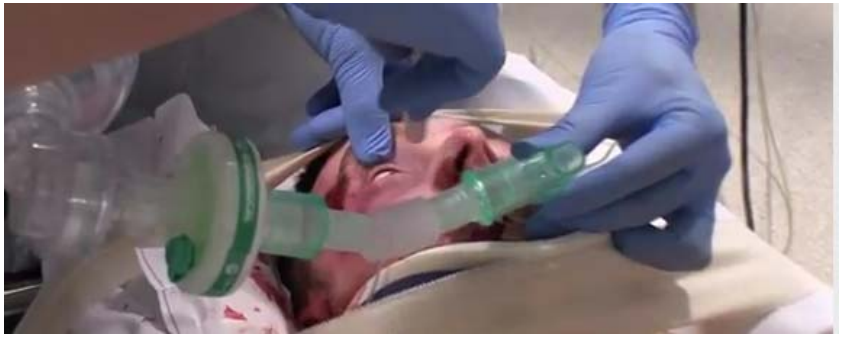
In order for consent to be valid it should be based on the following critical elements:

- **Competence:** The participant/representative must be competent to begin the informed consent process.
- **Fully informed:** The research team must disclose all relevant information to the potential participant. The information in this study must comply with ICH-GCP requirements. The minimum information for a valid informed consent is the approved version of the Information Sheet and Consent forms.
- **Understanding:** The participant or their representative must comprehend the information. The research team must evaluate the potential participant‘s or representative’s ability to understand the proposed intervention in the study.

What is valid informed consent?

- **Agree:** The participant/representative must agree to the proposed intervention in the research study.
- **Voluntary:** The participant's/representative's agreement must be voluntary and free from coercion.
- **Freedom to withdraw:** Participants/representatives must be informed that even after they have made a voluntary agreement to participate in the study, they may withdraw such agreement at any time without penalty.

Consider if this can be achieved in a critical emergency when the patient has suffered a head injury



What is valid informed consent?

If a person is asked to sign a written consent form, then it is assumed that;

- the person has the **capacity** to do so;
- the doctor has **disclosed** all information needed for the person to understand the trial and its procedures;
- the person is able to **understand** the information given and appreciates its relevance to their individual situation;
- the person then gives their **authorisation** allowing the trial team to carry out the trial procedures;
- the authorisation is **voluntary**.

To achieve all of the above requires adequate time to be available for the person to read and absorb the information, ask questions, reflect on their decision, and complete the relevant sections of the consent form themselves (if able to read and write).

If a doctor has to complete sections of the form to speed up the process, then there is not adequate time for a valid, written, informed consent to be obtained.

Please remember that the consent process must not be viewed as only having a written consent form completed.

Capacity to consent?

- **Capable adult:** Adults have the capacity to consent when they:
  - possess sufficient mental capability to understand the information provided
  - appreciate how it is relevant to their circumstances, and
  - are able to make a reasoned decision about whether or not to participate in a particular study (bearing in mind the need for urgent treatment in the critical situation)

- **Representative:** A person who can give permission for participation in research for another person eg relative or professional representative

Capacity can be affected by several things including age, cognitive impairment, illness and treatments.

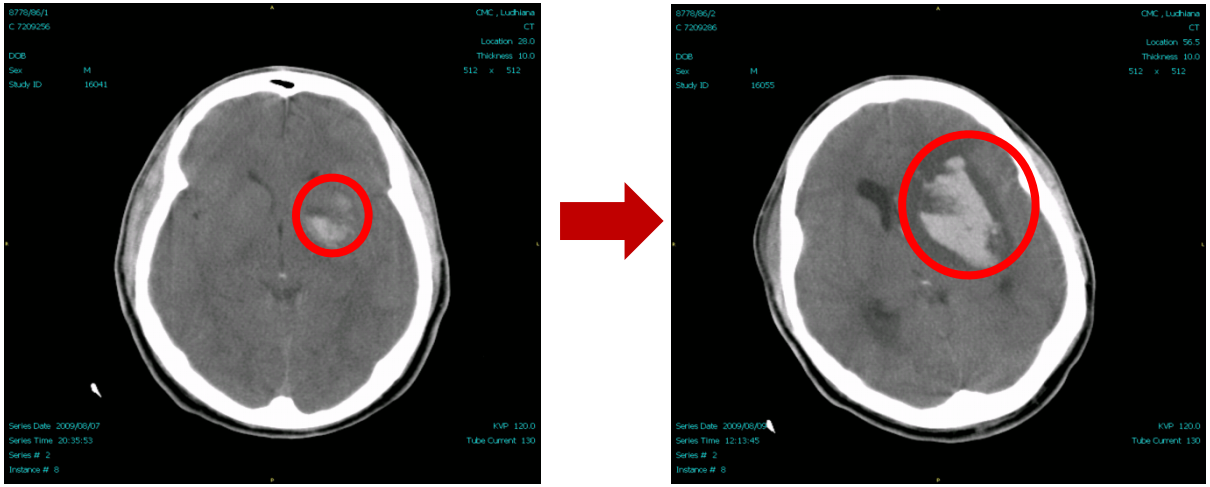
Consent in an emergency situation

- If the patient has a GCS of 12 or less – are they mentally capable of giving informed consent?
  - Patients with a GCS of 12 or less are generally not fully conscious and therefore would not be physically or mentally capable of providing consent prior to randomisation.
- If a representative is present will they be capable of providing informed consent?
  - Bear in mind the distressing nature of the clinical situation. It may be best to provide brief information about the trial and obtain an **agreement** to proceed; however this is not regarded as full, valid informed consent. The representative has the option to refuse participation on the patient's behalf, and their wishes must be respected.

Once the clinical emergency is over consent should be sought for the patient to remain in the trial

Consent in an emergency situation

- If no representative is present or able to give consent, should trial treatment be delayed until one can be found?
- What is happening while you wait?

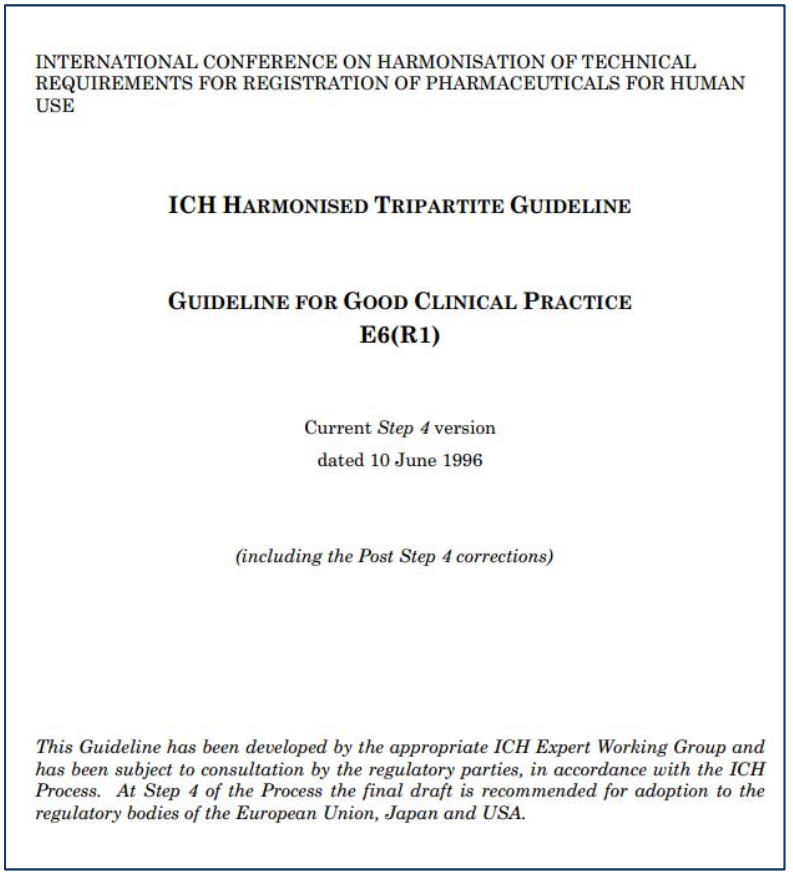


  - Traumatic brain injury is an emergency situation where treatment should be given as soon as possible.
  - Evidence shows that Tranexamic Acid is more effective when given early.
  - Most deaths from TBI occur soon after injury

Consent in an emergency situation

- Declaration of Helsinki and ICH-GCP guidelines provide guidance on consenting in emergency situations

When prior consent of the patient is not possible, and the subject's representative is not available, the study may proceed without informed consent as long as the reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the trial should be obtained as soon as possible from the subject or a legally authorised representative (WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI. Ethical Principles for Medical Research Involving Human Subjects)



INTERNATIONAL CONFERENCE ON HARMONISATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED TRIPARTITE GUIDELINE

GUIDELINE FOR GOOD CLINICAL PRACTICE
E6(R1)

Current *Step 4* version
dated 10 June 1996

(including the Post Step 4 corrections)

This Guideline has been developed by the appropriate ICH Expert Working Group and has been subject to consultation by the regulatory parties, in accordance with the ICH Process. At Step 4 of the Process the final draft is recommended for adoption to the regulatory bodies of the European Union, Japan and USA.

Consent process prior to randomisation

There are three possible options prior to Randomisation:

1) **WAIVER of prior informed consent** – If no representative is able/present, then two clinicians (one ***independent*** of the trial) should review eligibility criteria and any known views of the patient, and decide whether to enrol patient in the trial. This should be clearly documented in the patient's medical records. **OR**

2) **Written Informed Consent** – Representative is available and able to provide valid, fully informed consent which is documented on the Consent Form. **OR**

3) **Agreement** – Representative is available but not capable of providing full informed consent due to the distressing nature of the clinical situation or due to time constraints. If they disagree their wishes must be respected.

It is extremely important that you and all members of your trial team have a good knowledge of the approved consent procedure.

- The processes which can be used at your hospital are as per the approved protocol
- If in any doubt, please contact the TCC

Consent from a representative

- If a Personal Representative (eg relative) is not available or is unable to give consent, an **independent** doctor or other site staff member allowed to fulfil this role may be asked to consent as a Professional Representative – bearing in mind that, in the emergency situation, they will need to be immediately available and have prior information about the trial.
- Informed consent given by a representative shall represent the patient's presumed will.

Please remember that the Professional Representative cannot be the randomising doctor or anyone who is involved in any trial related activities.

Consent process after randomisation

Once the emergency situation is over and as soon as practicably possible, obtain valid written informed consent for the patient to remain in the trial,

- from patient (if capacity has returned)
- or representative

Consent process after randomisation

- The patient or representative should be given sufficient time to read through the Information Sheet and the opportunity to ask questions.
- The *original* signed consent form should be filed in the Study file section 14.
  - The Information Sheet, and a *copy* of the consent form should be given to the patient.
  - A *copy* of the consent form should also be placed in the patient's medical records.

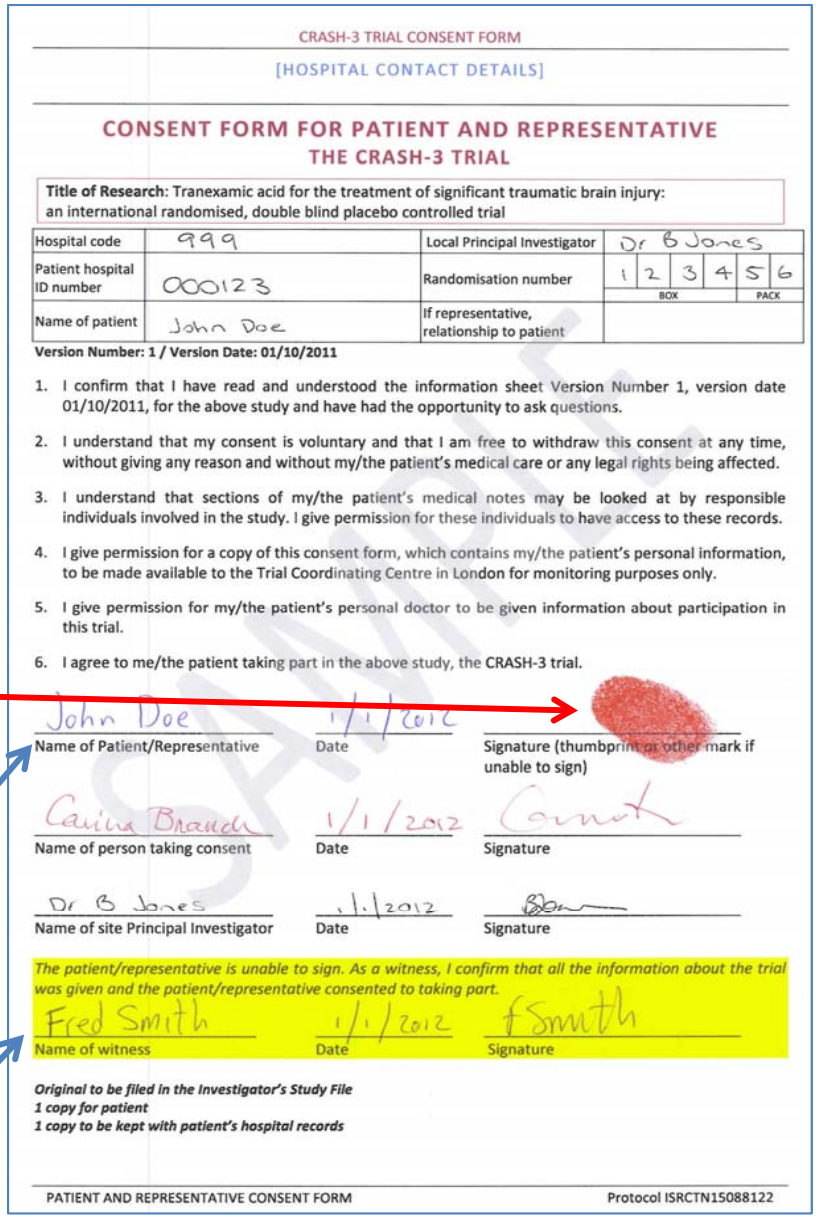
When is a witness needed?

- A witness is required if the person giving consent (patient or representative) is unable to read or write.
- The witness needs to verify that the information sheet and consent form have been read and explained to the patient or representative. The witness is not giving consent on behalf of the patient/representative.
- The witness must be INDEPENDENT of the trial team (must not be involved in the conduct of the trial).

The patient/representative will sign or provide a mark (eg thumbprint).

If the patient/representative is unable to write, the **witness** should write the name and date on his/her behalf.

The **witness** will also sign and date the consent form.



CRASH-3 TRIAL CONSENT FORM

[HOSPITAL CONTACT DETAILS]

CONSENT FORM FOR PATIENT AND REPRESENTATIVE
THE CRASH-3 TRIAL

Title of Research: Tranexamic acid for the treatment of significant traumatic brain injury: an international randomised, double blind placebo controlled trial

Hospital code	999	Local Principal Investigator	Dr B Jones
Patient hospital ID number	000123	Randomisation number	1 2 3 4 5 6 (BOX / PACK)
Name of patient	John Doe	If representative, relationship to patient	

Version Number: 1 / Version Date: 01/10/2011

1. I confirm that I have read and understood the information sheet Version Number 1, version date 01/10/2011, for the above study and have had the opportunity to ask questions.
2. I understand that my consent is voluntary and that I am free to withdraw this consent at any time, without giving any reason and without my/the patient's medical care or any legal rights being affected.
3. I understand that sections of my/the patient's medical notes may be looked at by responsible individuals involved in the study. I give permission for these individuals to have access to these records.
4. I give permission for a copy of this consent form, which contains my/the patient's personal information, to be made available to the Trial Coordinating Centre in London for monitoring purposes only.
5. I give permission for my/the patient's personal doctor to be given information about participation in this trial.
6. I agree to me/the patient taking part in the above study, the CRASH-3 trial.

John Doe	1/1/2012	
Name of Patient/Representative	Date	Signature (thumbprint or other mark if unable to sign)
Carina Brandt	1/1/2012	
Name of person taking consent	Date	Signature
Dr B Jones	1/1/2012	
Name of site Principal Investigator	Date	Signature

The patient/representative is unable to sign. As a witness, I confirm that all the information about the trial was given and the patient/representative consented to taking part.

Fred Smith	1/1/2012	
Name of witness	Date	Signature

Original to be filed in the Investigator's Study File
1 copy for patient
1 copy to be kept with patient's hospital records

PATIENT AND REPRESENTATIVE CONSENT FORM — Protocol ISRCTN15088122

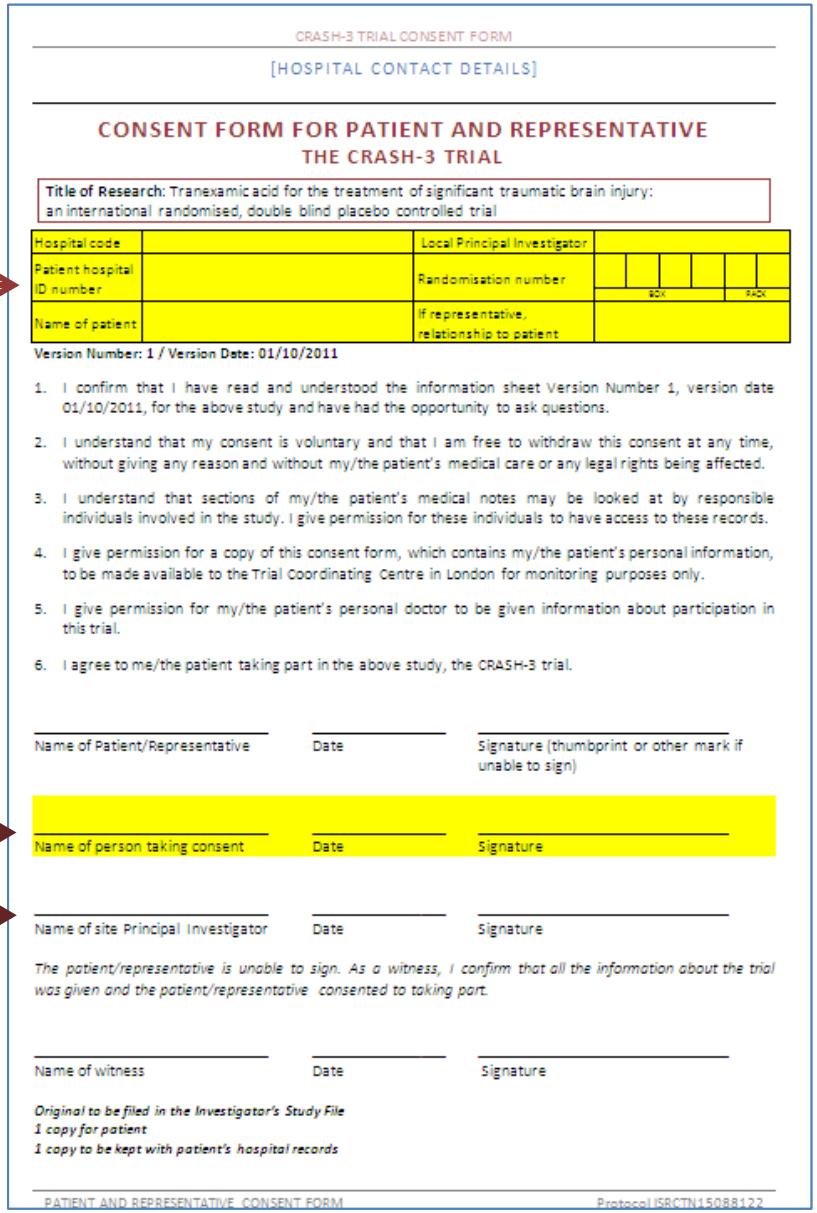
Completing the consent form

Person ***Taking*** Consent (eg Doctor)
to complete the following:

- Header information at the top of the form
  - name of patient and relationship of representative
  may also be completed by the patient/representative

Do not complete the sections (including dates) for other people listed on the form.

- Name, date and signature
- If the person taking consent is the Principal Investigator, this section must also be completed.



CRASH-3 TRIAL CONSENT FORM

[HOSPITAL CONTACT DETAILS]

CONSENT FORM FOR PATIENT AND REPRESENTATIVE
THE CRASH-3 TRIAL

Title of Research: Tranexamic acid for the treatment of significant traumatic brain injury: an international randomised, double blind placebo controlled trial

Hospital code		Local Principal Investigator	
Patient hospital ID number		Randomisation number	BOX PACK
Name of patient		If representative, relationship to patient	

Version Number: 1 / Version Date: 01/10/2011

1. I confirm that I have read and understood the information sheet Version Number 1, version date 01/10/2011, for the above study and have had the opportunity to ask questions.
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6. I agree to me/the patient taking part in the above study, the CRASH-3 trial.

Name of Patient/Representative | Date | Signature (thumbprint or other mark if unable to sign)

Name of person taking consent | Date | Signature

Name of site Principal Investigator | Date | Signature

The patient/representative is unable to sign. As a witness, I confirm that all the information about the trial was given and the patient/representative consented to taking part.

Name of witness | Date | Signature

Original to be filed in the Investigator's Study File
1 copy for patient
1 copy to be kept with patient's hospital records

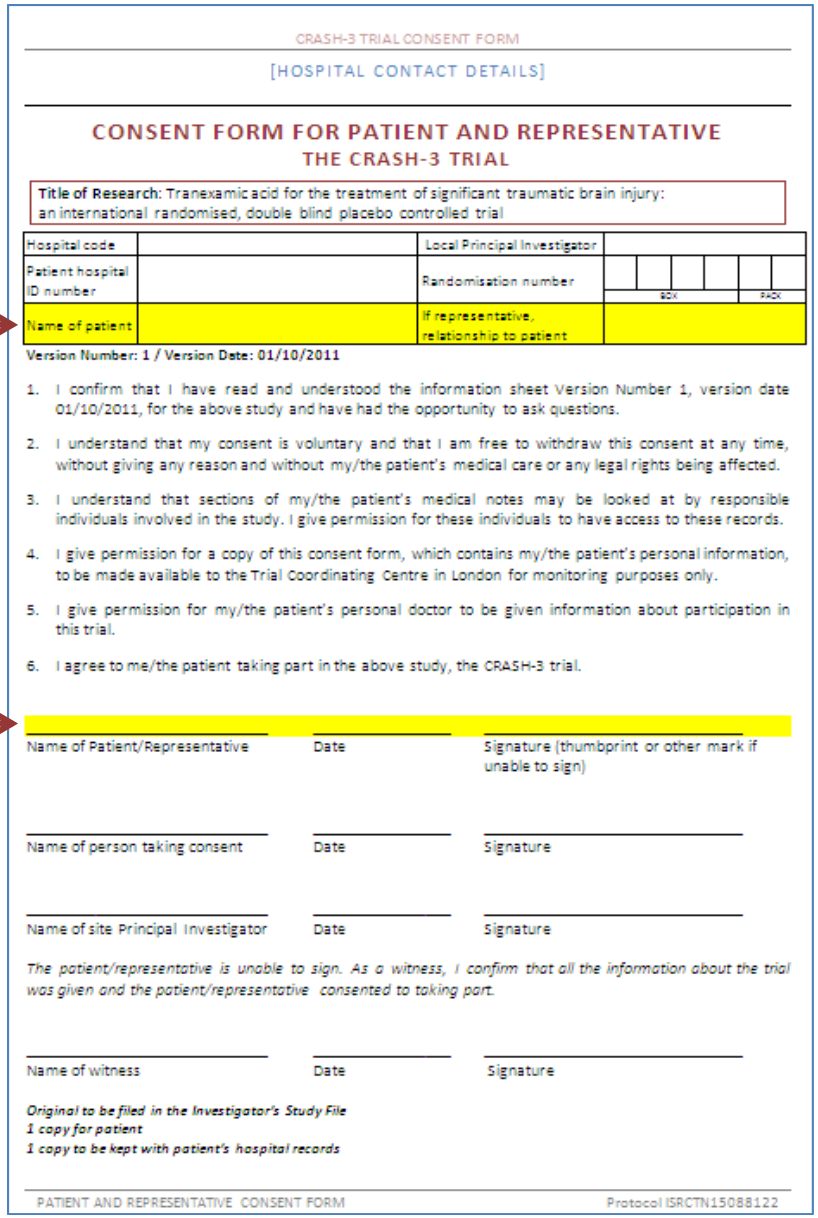
PATIENT AND REPRESENTATIVE CONSENT FORM Protocol ISRCTN15088122

Completing the consent form

Person ***Giving*** Consent (Patient or Representative) to complete the following:

- Name of patient/relationship of representative
- Name, date and signature

Please refer to the slide 'When is a witness needed' if the patient or representative is unable to read/write.



CRASH-3 TRIAL CONSENT FORM

[HOSPITAL CONTACT DETAILS]

CONSENT FORM FOR PATIENT AND REPRESENTATIVE
THE CRASH-3 TRIAL

Title of Research: Tranexamic acid for the treatment of significant traumatic brain injury: an international randomised, double blind placebo controlled trial

Hospital code		Local Principal Investigator	
Patient hospital ID number		Randomisation number	BOX PACK
Name of patient		If representative, relationship to patient	

Version Number: 1 / Version Date: 01/10/2011

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3. I understand that sections of my/the patient's medical notes may be looked at by responsible individuals involved in the study. I give permission for these individuals to have access to these records.
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5. I give permission for my/the patient's personal doctor to be given information about participation in this trial.
6. I agree to me/the patient taking part in the above study, the CRASH-3 trial.

Name of Patient/Representative	Date	Signature (thumbprint or other mark if unable to sign)
Name of person taking consent	Date	Signature
Name of site Principal Investigator	Date	Signature

The patient/representative is unable to sign. As a witness, I confirm that all the information about the trial was given and the patient/representative consented to taking part.

Name of witness	Date	Signature

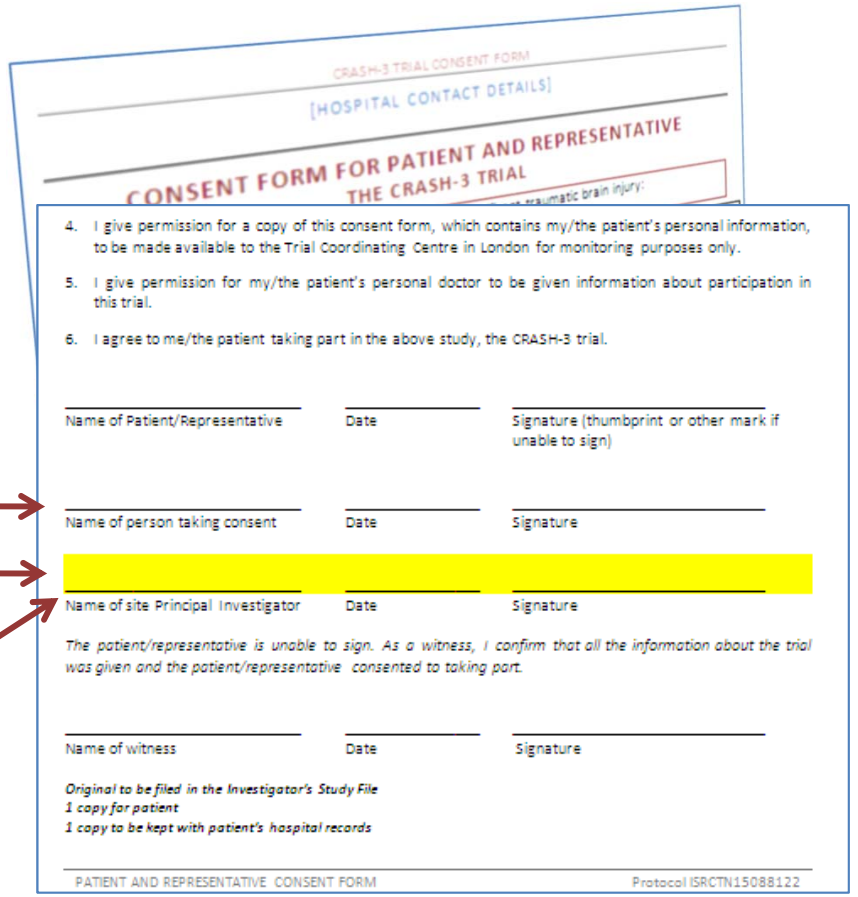
Original to be filed in the Investigator's Study File
1 copy for patient
1 copy to be kept with patient's hospital records

Completing the consent form

Principal Investigator
to complete the following:

If consent taken by the PI;
- Name of person taking consent, date and signature, and
- Name of Principal Investigator, date and signature

If consent NOT taken by the PI;
- PI to review all sections for completeness, print name and date and sign the form



CRASH-3 TRIAL CONSENT FORM

[HOSPITAL CONTACT DETAILS]

CONSENT FORM FOR PATIENT AND REPRESENTATIVE
THE CRASH-3 TRIAL

traumatic brain injury:

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5. I give permission for my/the patient's personal doctor to be given information about participation in this trial.

6. I agree to me/the patient taking part in the above study, the CRASH-3 trial.

Name of Patient/Representative | Date | Signature (thumbprint or other mark if unable to sign)

Name of person taking consent | Date | Signature

Name of site Principal Investigator | Date | Signature

The patient/representative is unable to sign. As a witness, I confirm that all the information about the trial was given and the patient/representative consented to taking part.

Name of witness | Date | Signature

Original to be filed in the Investigator's Study File
1 copy for patient
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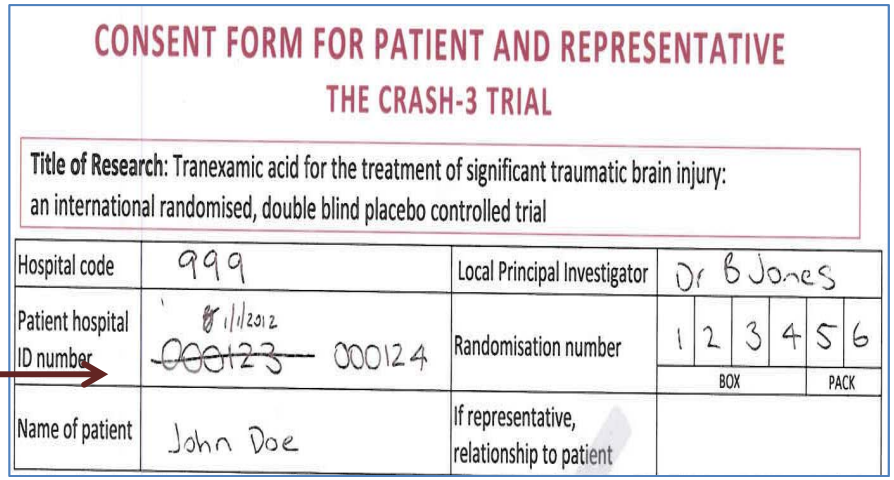
Common consent form errors

- The name and/or date for Doctor, Principal Investigator and Patient have all been written by the same person:
  - *Each person must complete their own sections themselves.*

- The date of patient giving consent and doctor taking consent are different:
  - *The consent form should be signed by both parties at the same time. The only person who may sign the form at a later date is the Principal Investigator if they were not the doctor taking consent in the first place.*

- Header information incomplete or some data missing, or does not match information provided on the data forms;
- Mistakes have not been corrected properly:
  - *To make a correction, draw a line through the error, write the correct information nearby, initial and date the correction .*



CONSENT FORM FOR PATIENT AND REPRESENTATIVE

THE CRASH-3 TRIAL

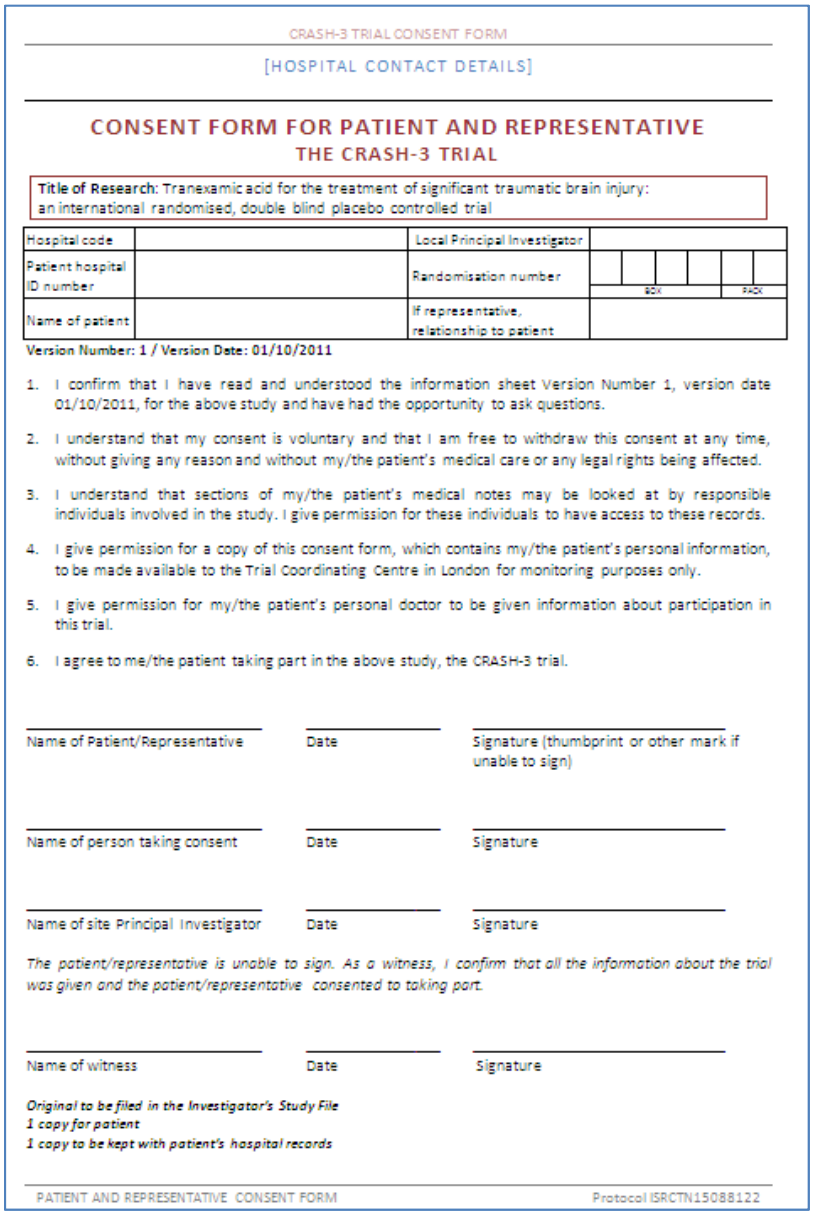
Title of Research: Tranexamic acid for the treatment of significant traumatic brain injury: an international randomised, double blind placebo controlled trial

Hospital code	999	Local Principal Investigator	Dr B Jones
Patient hospital ID number	~~000123~~ 000124 1/1/2012	Randomisation number	1 2 3 4 5 6 (BOX / PACK)
Name of patient	John Doe	If representative, relationship to patient	

Summary

- Although waiver of prior consent is allowed by most ethics committees, written consent MUST be provided for each patient, either by the patient or representative.

- Until there is a written, signed consent form, the **Informed Consent** process has not been completed.



CRASH-3 TRIAL CONSENT FORM

[HOSPITAL CONTACT DETAILS]

CONSENT FORM FOR PATIENT AND REPRESENTATIVE
THE CRASH-3 TRIAL

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Patient hospital ID number		Randomisation number	BOX / PACK
Name of patient		If representative, relationship to patient	

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5. I give permission for my/the patient's personal doctor to be given information about participation in this trial.
6. I agree to me/the patient taking part in the above study, the CRASH-3 trial.

Name of Patient/Representative — Date — Signature (thumbprint or other mark if unable to sign)

Name of person taking consent — Date — Signature

Name of site Principal Investigator — Date — Signature

The patient/representative is unable to sign. As a witness, I confirm that all the information about the trial was given and the patient/representative consented to taking part.

Name of witness — Date — Signature

Original to be filed in the Investigator's Study File
1 copy for patient
1 copy to be kept with patient's hospital records

PATIENT AND REPRESENTATIVE CONSENT FORM — Protocol ISRCTN15088122

CRASH

Clinical Randomisation of an Antifibrinolytic in Significant Head Injury

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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