Haemorrhage alleviation with tranexamic acid - Intestinal system

GIVING INFORMATION AND OBTAINING INFORMED CONSENT

Overview

- What is valid Informed Consent?
- Consent in an emergency situation
- Consent process prior to randomisation
  - Informed consent from *patient*
  - Informed consent from *representative*
  - Waiver of 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 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, alterna
  - 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:

- **Full Capacity:** The participant/representative must have the capacity to begin the informed consent process.
- **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 form.
- **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 a significant GI bleeding.

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, talk with relatives or friends, 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 i.e. relative or professional representative

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

Who can give valid informed consent?

1. The patient if he/she is capable of doing it

If the patient is unable to provide consent;

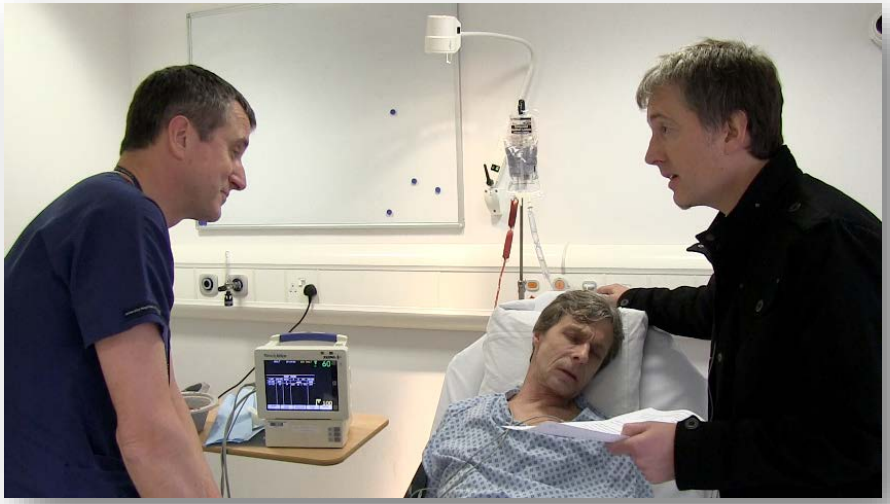
2. The patient's **personal representative** (a relative or friend), if capable
3. An **independent professional representative** (an independent doctor) allowed to fulfil this role

Consent in an emergency situation

- Significant acute GI bleeding is an emergency and the priority is to provide appropriate emergency care.
- Both clinical and trial interventions must be given rapidly and as soon as possible after a significant GI bleeding is suspected or diagnosed.
- Eligible patients have a life threatening condition. Their physical, mental and emotional state may be impaired by their blood loss or co-morbidities (i.e. liver failure). They might not be capable of providing consent prior to randomisation.

Consent in an emergency situation

- The availability of a personal representative (a relative or friend) and his/her ability and willingness to make a decision on the patient's behalf will have to be taken into consideration.
- Relatives and friends' emotional state may be affected by the stressful situation. They might not be willing and capable of providing informed consent.



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

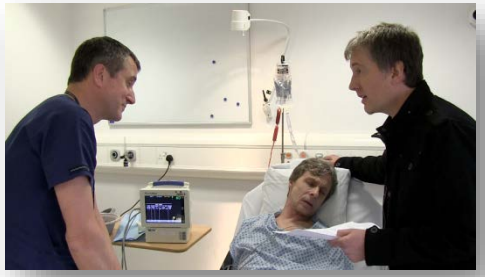
(including the Post Step 4 corrections)

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.

Prior Information giving

- Bearing in mind the clinical situation and their level of distress, the patient and the patient's relative (if present) will be provided with brief information about the trial:

1. All the usual treatments for the bleeding will be given.
2. In addition to these, the patient can be included in study to see if a drug called tranexamic acid (TXA) can help patients with GI bleeding.
3. TXA helps people with other types of bleeding but we don't know yet if it works in GI bleeding.
4. In this study, half the patients will get the study treatment (TXA) and half a dummy treatment (a placebo) through a drip over 24 hours.
5. Some information about the patient will be collected and sent to a central office in London.



Consent process prior to randomisation

There are three possible options:

1) Written Informed Consent from the patient
2) Written Informed Consent from a representative (Personal or Professional)
3) WAIVER of prior informed consent (= NO PRIOR INFORMED CONSENT)

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

Obtaining prior consent from the Patient

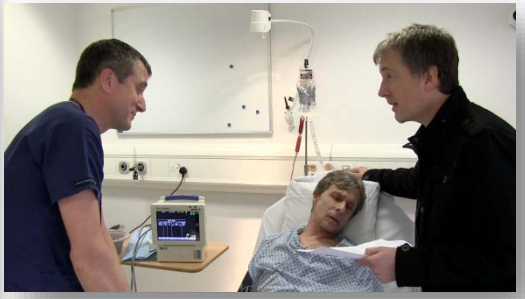
***Scenario 1**: Joanne, a 37-year-old woman, presented to the emergency department after an episode of hematemesis. She is haemodynamically stable. She is calm and capable to understand the information provided.*

- The patient should be approached with the agreement of the primary carer.
- An Information Sheet should be provided and the study discussed; if relatives are present the patient may wish to discuss with them first.
- The time allowed for discussion will depend on the criticality of the patient's condition. However, it should not be less than 20 minutes.
- If patient agrees, written consent must be obtained.

Prior consent from a Personal Representative

***Scenario 2**: John, a 60-year-old man, presented to the emergency department after an episode of hematemesis, accompanied by his brother. He is haemodynamically stable but also very anxious. He tells you he thinks he is going to die soon...*

John is not capable of providing full informed consent due to the distressing nature of his condition, but you feel that his brother may be willing and capable to consent. The situation is not urgent and there is time to fully inform John's brother and obtain a written consent.



- If possible, give information to the patient to his level of capacity. Oral refusal by the patient should be respected and he should not be enrolled.
- In this case his brother will be considered as the **Personal Representative (PeR).** It is assumed that he is knowledgeable about the patient's values and beliefs.
- A full Information Sheet should be provided and written consent obtained.

Please remember, a relative may not be capable of providing informed consent due to the stress of the emergency situation. They might not want to take on the responsibility of making a decision.

Prior consent from a Professional Representative

- If a Personal Representative (i.e. relative) is not available or is unable to give consent because of the distressing nature of the situation, an **independent** doctor or other site staff member allowed to fulfil this role may be asked to consent as a **Professional Representative (PrR)**.
- Considering 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.

Waiver of prior written consent (1)

***Scenario 3**: John was taken to A&E by ambulance after several episodes of hematemesis. He is pale, sweating and has a rapid and weak pulse. His brother is with him.*

Treatment must be given urgently, but because of the distressing nature of the situation and time constraints, neither the patient nor his relative are capable to give properly informed consent.

- If possible, give information to the patient and relative/friend (if present). **Oral refusals should be respected and the patient should not be enrolled**.
- Use the **Brief information leaflet** to get agreement from either the patient or accompanying person.

Please remember, this agreement is NOT a valid informed consent. Once the clinical emergency is over consent should be sought for the patient to remain in the trial.

Waiver of prior written consent (2)

If no relative or friend is present and the patient is not able to sign the brief information leaflet;

- The investigator and **ONE independent person** (doctor or nurse) who is not participating in this trial may enrol the patient by certifying in writing in the patient's medical records that:
  - the patient has significant gastrointestinal bleeding
  - the patient is unable to give consent as a result of his/her medical condition
  - it is not feasible to contact the patient's PeR/PrR to obtain consent; and
  - the investigator is not aware of any objections to the patient being enrolled as a participant in this trial.

Please remember, waiving the prior informed consent = NO PRIOR INFORMED CONSENT. Once the clinical emergency is over consent should be sought for the patient to remain in the trial.

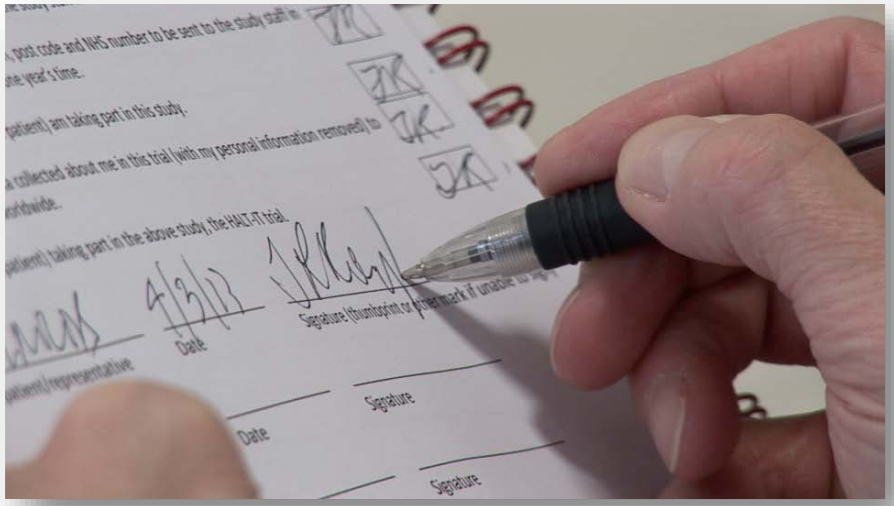
Consent process after randomisation

If the waiver of consent procedure has been used, 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

Obtaining a valid informed consent

- 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.



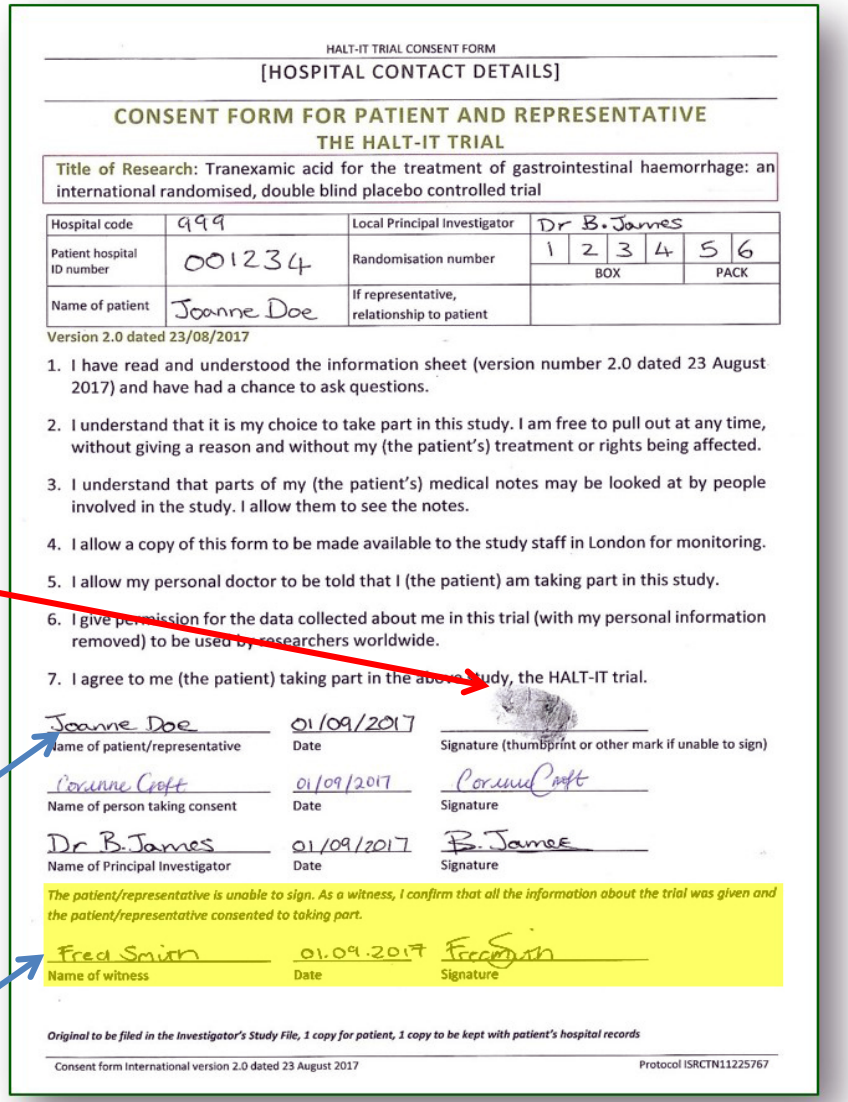
When is a witness needed?

- 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 (i.e. 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.



HALT-IT TRIAL CONSENT FORM

[HOSPITAL CONTACT DETAILS]

CONSENT FORM FOR PATIENT AND REPRESENTATIVE
THE HALT-IT TRIAL

Title of Research: Tranexamic acid for the treatment of gastrointestinal haemorrhage: an international randomised, double blind placebo controlled trial

Hospital code	999	Local Principal Investigator	Dr B. James
Patient hospital ID number	001234	Randomisation number	1 2 3 4 5 6 (BOX / PACK)
Name of patient	Joanne Doe	If representative, relationship to patient	

Version 2.0 dated 23/08/2017

1. I have read and understood the information sheet (version number 2.0 dated 23 August 2017) and have had a chance to ask questions.
2. I understand that it is my choice to take part in this study. I am free to pull out at any time, without giving a reason and without my (the patient's) treatment or rights being affected.
3. I understand that parts of my (the patient's) medical notes may be looked at by people involved in the study. I allow them to see the notes.
4. I allow a copy of this form to be made available to the study staff in London for monitoring.
5. I allow my personal doctor to be told that I (the patient) am taking part in this study.
6. I give permission for the data collected about me in this trial (with my personal information removed) to be used by researchers worldwide.
7. I agree to me (the patient) taking part in the above study, the HALT-IT trial.

Joanne Doe — Name of patient/representative	01/09/2017 — Date	Signature (thumbprint or other mark if unable to sign)
Corinne Croft — Name of person taking consent	01/09/2017 — Date	Corinne Croft — Signature
Dr B. James — Name of Principal Investigator	01/09/2017 — Date	B. James — 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 — Name of witness	01.09.2017 — Date	Fred Smith — 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

Consent form International version 2.0 dated 23 August 2017 — Protocol ISRCTN11225767

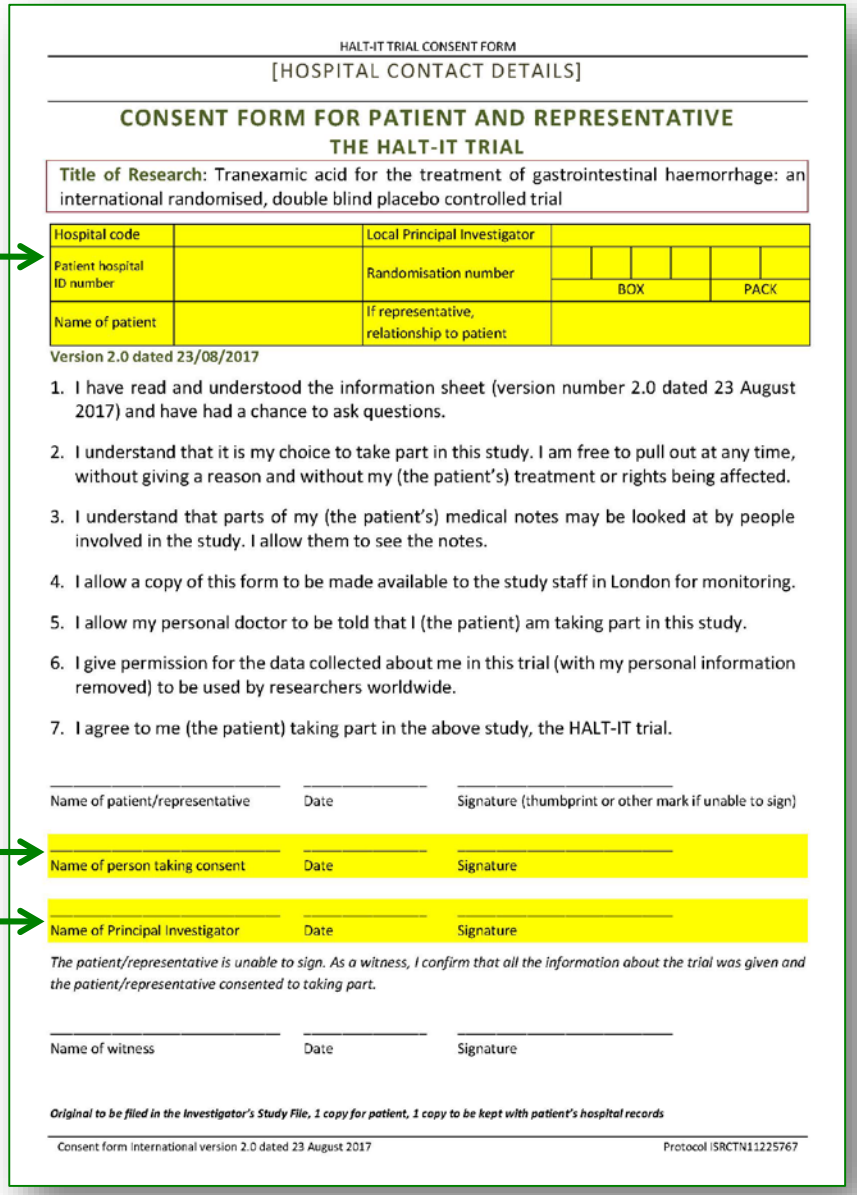
Completing the consent form

Person ***Taking*** Consent (i.e. Doctor/nurse) 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.



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Name of person taking consent	Date	Signature
Name of 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

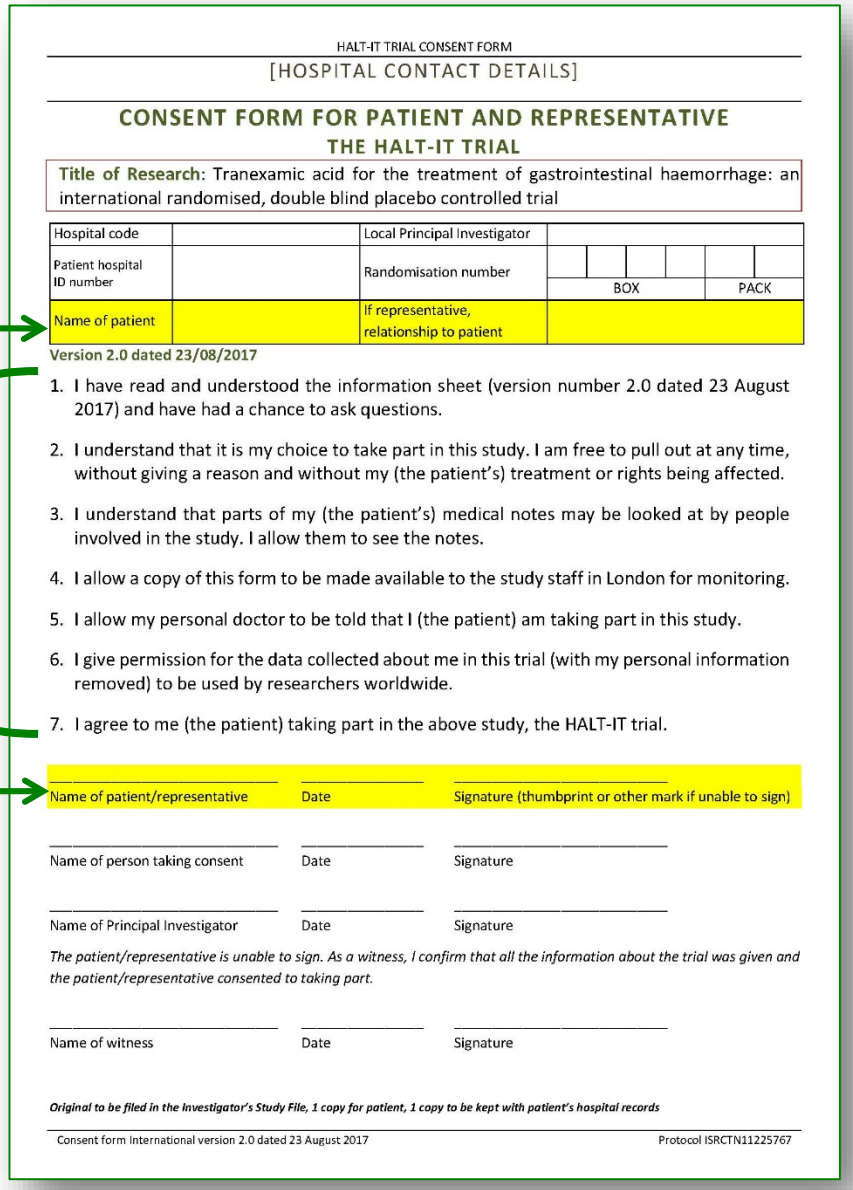
Original to be filed in the Investigator's Study File, 1 copy for patient, 1 copy to be kept with patient's hospital records

Completing the consent form

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

- Name of patient/relationship of representative
- In the consent forms for some countries the patient/representative will also be asked to initial a box for each statement.
- Name, date and signature

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



HALT-IT TRIAL CONSENT FORM

[HOSPITAL CONTACT DETAILS]

CONSENT FORM FOR PATIENT AND REPRESENTATIVE
THE HALT-IT TRIAL

Title of Research: Tranexamic acid for the treatment of gastrointestinal haemorrhage: an international randomised, double blind placebo controlled 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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Name of patient/representative	Date	Signature (thumbprint or other mark if unable to sign)
Name of person taking consent	Date	Signature
Name of 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

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Completing the consent form

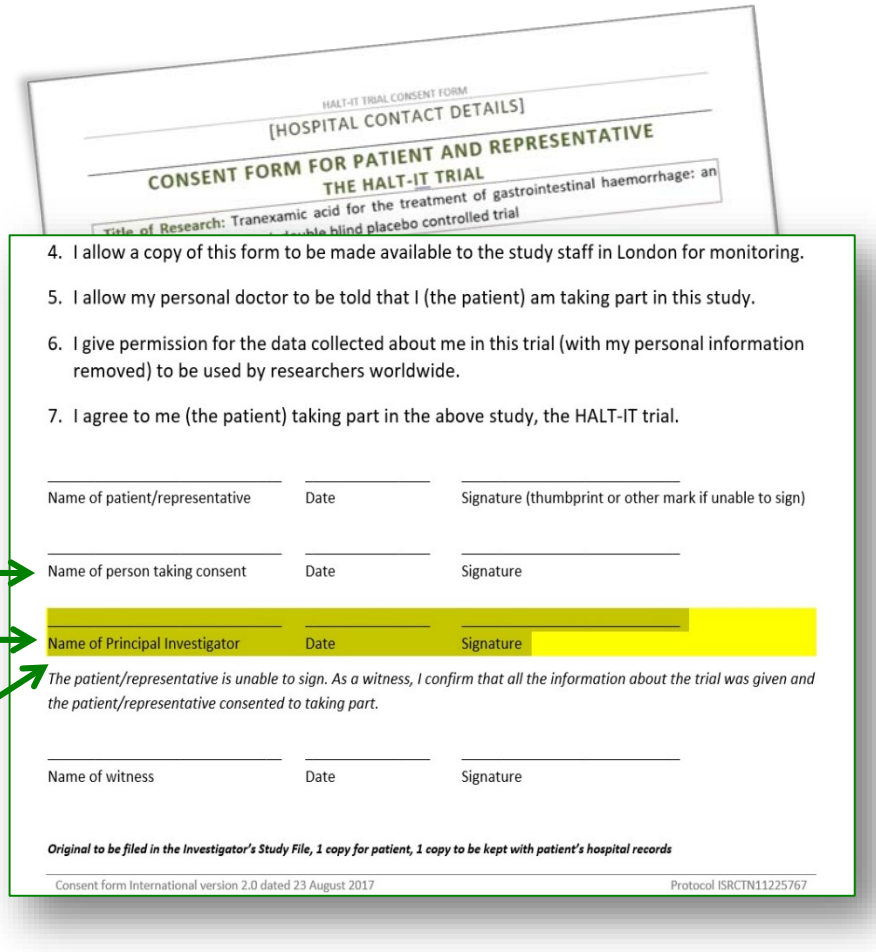
Principal Investigator
to complete the following:

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



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CONSENT FORM FOR PATIENT AND REPRESENTATIVE
THE HALT-IT TRIAL

Title of Research: Tranexamic acid for the treatment of gastrointestinal haemorrhage: an ... double blind placebo controlled trial

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

Name of person taking consent | Date | Signature

Name of Principal Investigator | Date | Signature

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Name of witness | Date | Signature

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Consent form International version 2.0 dated 23 August 2017 | Protocol ISRCTN11225767

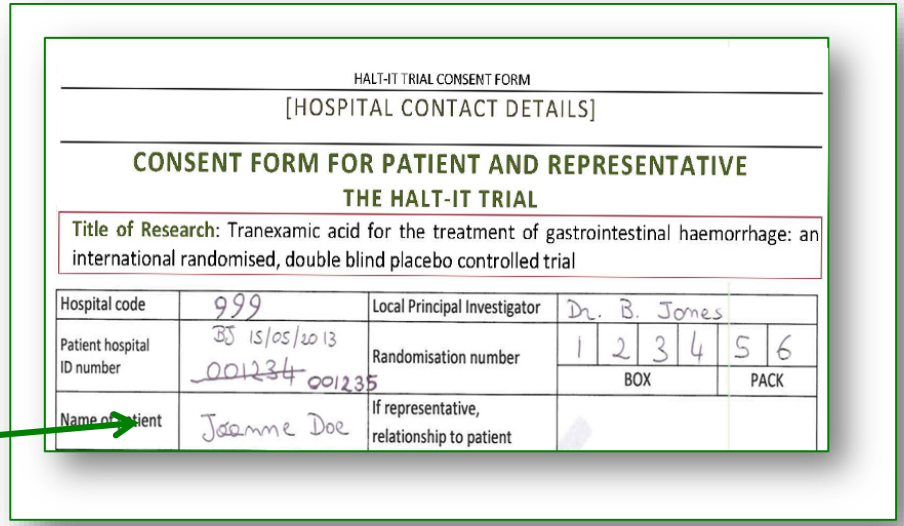
Common consent form errors

- 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.*



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CONSENT FORM FOR PATIENT AND REPRESENTATIVE

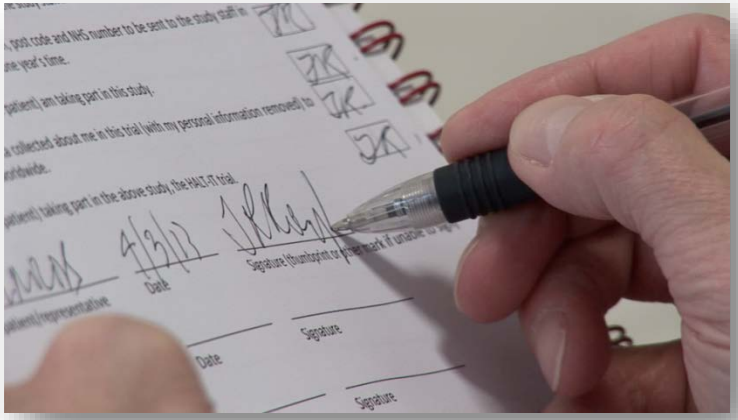
THE HALT-IT TRIAL

Title of Research: Tranexamic acid for the treatment of gastrointestinal haemorrhage: an international randomised, double blind placebo controlled trial

Hospital code	999	Local Principal Investigator	Dr. B. Jones
Patient hospital ID number	BJ 15/05/2013 ~~001234~~ 001235	Randomisation number	1 2 3 4 5 6 (BOX / PACK)
Name of patient	Joanne 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.



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Name of witness	Date	Signature

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JOIN THE GLOBAL COLLABORATION

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UKCRC Registered Clinical Trials Units

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Haemorrhage alleviation with tranexamic acid - Intestinal system