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ISRCTN97695350

TRANEXAMIC ACID FOR INTRACEREBRAL HAEMORRHAGE: TICH-3 TRIAL

INVESTIGATOR TRAINING:

Enrolling investigators & Emergency department

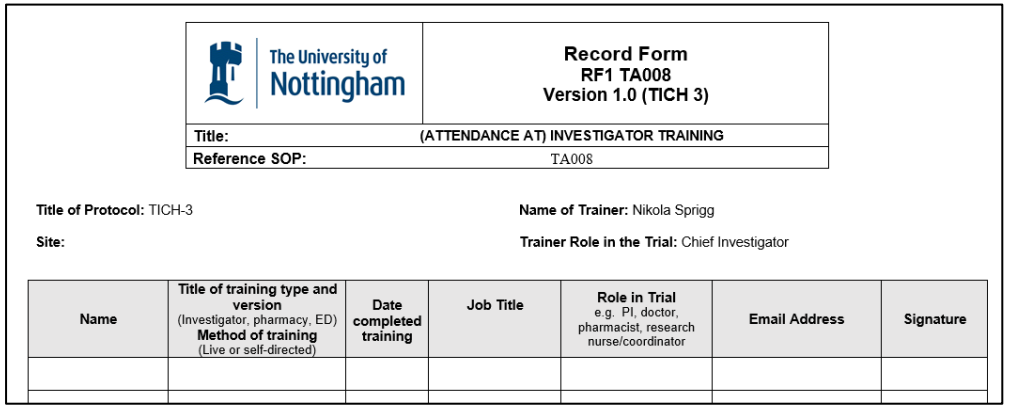
Professor Nikola Sprigg

On behalf TICH-3 Trial Team

Final v2.0 30/01/2023

Aims and Objectives

- Intracerebral haemorrhage and haematoma expansion
- Tranexamic acid
- Study design
- Inclusion and exclusion criteria
- Consent process
- Randomisation and randomisation alert
- Drug administration
- Safety monitoring



The University of Nottingham

Record Form
RF1 TA008
Version 1.0 (TICH 3)

Title:	**(ATTENDANCE AT) INVESTIGATOR TRAINING**
Reference SOP:	TA008

Title of Protocol: TICH-3

Name of Trainer: Nikola Sprigg

Site:

Trainer Role in the Trial: Chief Investigator

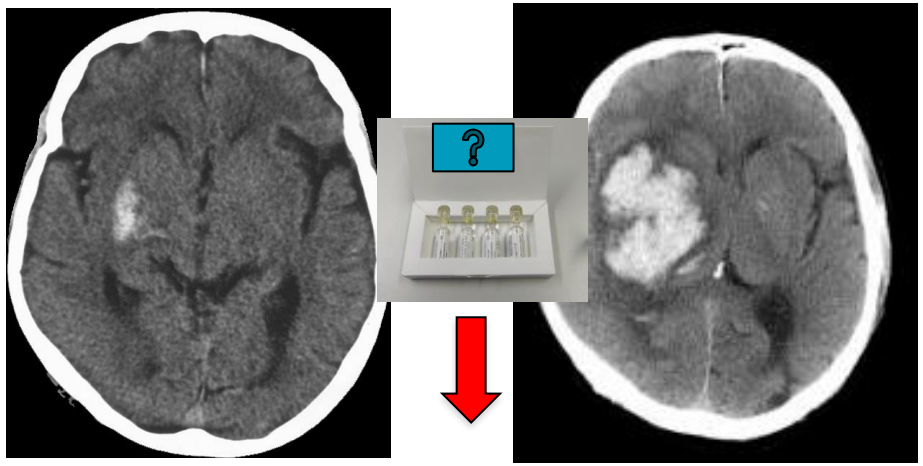
Name	Title of training type and version (Investigator, pharmacy, ED) **Method of training** (Live or self-directed)	Date completed training	Job Title	Role in Trial e.g. PI, doctor, pharmacist, research nurse/coordinator	Email Address	Signature

Please complete training log after completing to be added to the TICH-3 delegation log

Intracerebral Haemorrhage

Intracerebral haemorrhage can be devastating

- Haematoma expansion (HE) is common occurs early and is main cause of death
- Predictors – time, haematoma volume, anticoagulation and antiplatelets



- Drugs that stop bleeding (such as tranexamic acid), are effective in other bleeding conditions and could potentially reduce haematoma expansion

TICH-3: does giving tranexamic acid early after ICH prevent haematoma expansion and reduce death and disability

Tranexamic Acid

- TXA acts through antifibrinolytic mechanisms
- CRASH-2, in patients with traumatic haemorrhage (including from head injuries), TXA significantly reduces death due to bleeding and all-cause mortality, with no increase in vascular occlusive events.
- Analysis of the CRASH-2 trial showed that because death due to bleeding occurred early after trauma, hyperacute administration of TXA was necessary for patients to receive any benefit.
- A meta-analysis of TXA in traumatic intracranial haemorrhage showed that it was associated with a significant reduction in subsequent intracranial bleeding.
- CRASH-3, reduced head injury related deaths in patients with traumatic brain injury, with early treatment more effective than later treatment.
- Use of TXA after acute ICH was tested in TICH-1 which assessed the feasibility of a larger trial. The administration of TXA was feasible and well tolerated and led to TICH-2.
- In TICH-2 (in 2325 patients with ICH within 8 hours of onset) TXA was safe, reduced haematoma expansion and early death. It did not significantly change outcome at 3 months
- Tranexamic acid is inexpensive, easy to administer, seems to be safe, and is widely available, so even a modest treatment effect could have an important impact on the global scale.

CRASH-2 https://doi.org/10.1016/S0140-6736(10)60835-5, CRASH-3 https://doi.org/10.1016/S0140-6736(19)32233-0

TICH-3 Synopsis

ICH emergency condition - facilitate rapid enrolment

Design: Double blind randomised clinical trial, pragmatic streamlined design

Participants: Inclusion: Adults (≥ 18 years) within < 4.5 hours of stroke onset

Exclusion: Massive ICH (Glasgow Coma Scale < 5 or Haematoma Volume > 60ml)

Consent: Rapid emergency process – oral consent followed by written consent

Intervention: Tranexamic 1g IV bolus then 1g infusion 8hrs or saline by identical regime
Given alongside standard ICH care, including BP lowering as per clinical guidelines[1]

Randomisation: Simple - use the lowest available treatment pack number

Primary Outcome: Early death (day 7)

Secondary outcome: Function-Shift analysis modified Rankin Scale day at 6 months

Sample size: 5500 (3900 UK and 1900 Internationally)

Cost/funder: UK NIHR plus others internationally

Duration: 7.25 years - Aim 5 yrs UK recruitment note STOP GO DECISION OCT 23

1: https://www.nice.org.uk/guidance/ng128/chapter/Recommendations

TICH-3: Eligibility Criteria

Inclusion criteria

- Spontaneous ICH (confirmed on brain imaging) < 4.5 h of onset

CT (or MRI) is conducted pre-recruitment in line with standard care, the haematoma volume measurement will help assess whether the participant is eligible.

Note - ICH secondary to ruptured aneurysm or vascular malformation or brain tumor or ischaemic stroke (haemorrhagic transformation of infarct, HTI) or thrombolysis or venous infarct is NOT spontaneous ICH

Exclusion criteria

- Known indication for TXA treatment (e.g. traumatic brain injury) *in view of treating physician*
- Known contra-indication for TXA treatment (e.g. active seizures) *in view of treating physician*
- Patient known to be taking therapeutic anticoagulation with warfarin or low molecular weight heparin at time of enrolment. Patients taking direct oral anticoagulants can be included and are not excluded.
- Massive ICH (usually when haematoma volume > 60ml)
- Severe coma, Glasgow Coma Scale <5
- Decision for palliative (end of life) care

TICH-3: Patients taking DOACs

Which DOACs can the patients be on to be recruited for TICH 3?

- **Direct thrombin inhibitor** – Dabigatran
- **Factor 10a inhibitor** – Apixaban, rivaroxaban, edoxaban
- If they have only recently started taking a DOAC, for as long as they have regularly taken it for the last 48 hours, we would enrol them as patients taking regular DOAC

Types of anticoagulation (blood thinners) that cannot be included:

1. warfarin - exclude if INR shows levels high (>1.5). Cannot include unless the INR is sub therapeutic
2. LWHM - low molecular weight heparins at treatment dose eg for treating a DVT or PE. Note if LMWH is being used prophylactically at low dose to prevent DVT and PE these patients can be included in TICH-3

If patients on DOAC with ICH are enrolled to TICH-3 can they still have reversal agents?

- Yes, all patients should receive standard care, and be treated as per local DOAC ICH guidelines and given PCC or anticoagulation reversal agent (i.e Idarucizumab) in accordance with the treating physician. Please ensure you document which reversal agents were given in eCRF

Can they be co-enrolled to the Annexa-4 trial?

- No, if they have been recruited for the ANNEXA-4 trial they cannot be recruited for TICH 3

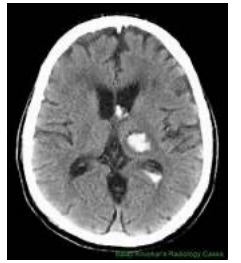
If the patient is on a DOAC is the haematoma volume estimation of 60ml still the cut off?

- Yes, the other exclusion criteria are the same – massive haematoma (usually > 60ml) is still excluded

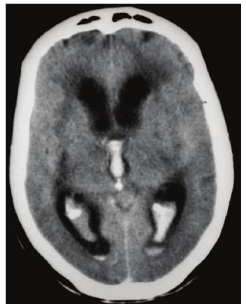
Eligibility: Frequently asked questions

- If time of stroke onset is unknown?
  Patient can be enrolled if presenting within 4.5 hours of discovery if HV < 60mls on CT scan
- If patient had a seizure in the past?
  Active seizures are a contraindication to tranexamic acid. Previous seizures e.g.
  recent likely to be a contraindication isolated proved seizure in past may not be decision rests with treating physician (see flowchart on next slide)
- Can patients with intraventricular haemorrhage (IVH) be enrolled?
  Yes so long as they have intracerebral haemorrhage, (fig 1) do not have other exclusion criteria.
  Isolated IVH (fig 2) should not be included.
- Can patient be enrolled if they are a candidate for neurosurgery?
  Yes – neurosurgery is not an exclusion
- Can patient be enrolled if they have a DNAR/from care home/already dependent ?
  Yes so long as they are still for active care and consent is obtained
- Can patients with recurrent bleeds be enrolled? Yes – it is likely that most patients will have an atereriopathy due to hypertension or cerebral amyloid angiopathy
- Can a nurse consultant assess eligibility? Confirming eligibility is defined as a medical decision, so must be undertake by a medically qualified doctor under the clinical trials regulations.

1. ICH and IVH



2. IVH only



Final decision on eligibility rests with treating physician

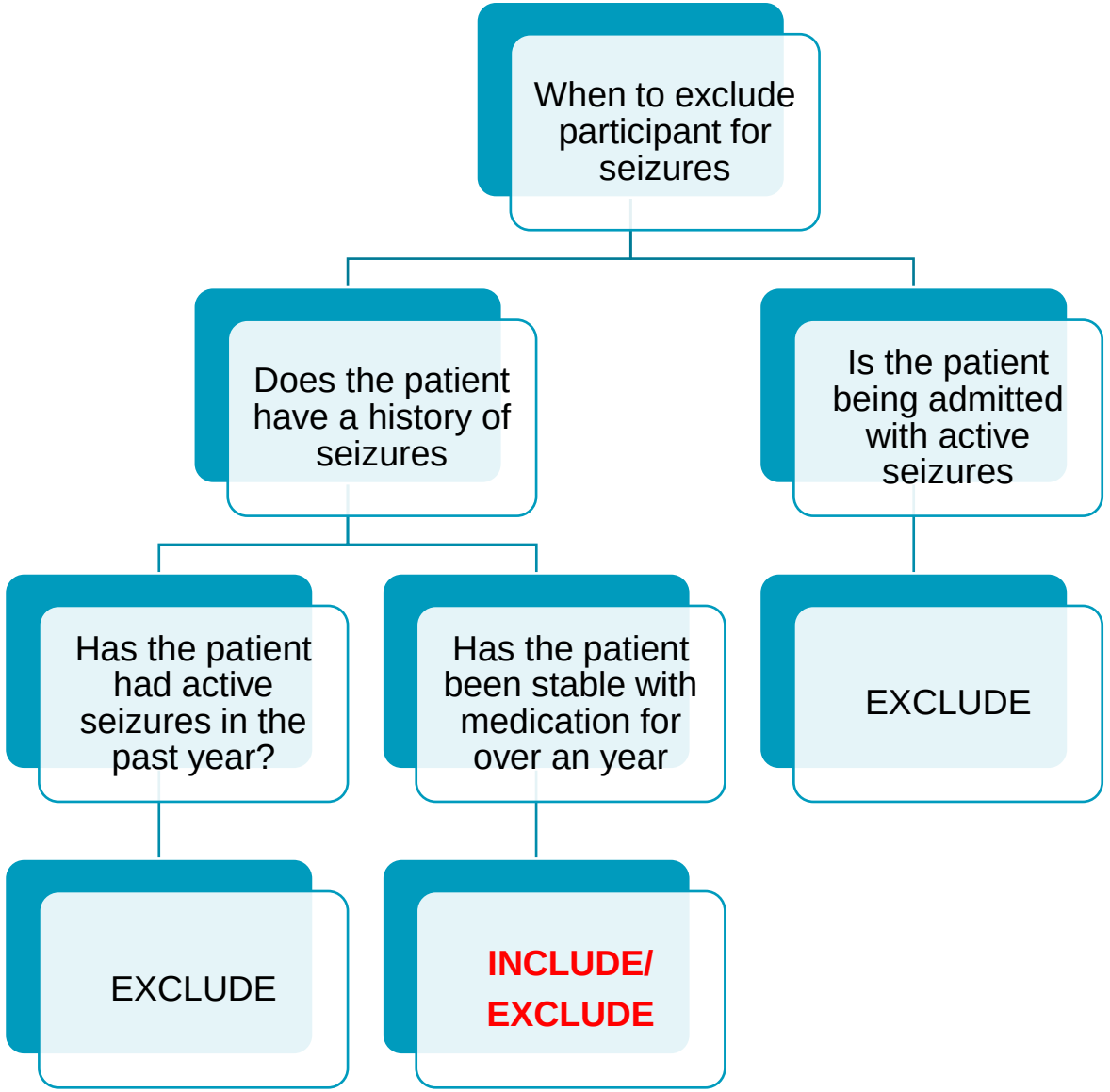
Eligibility: seizures

- Eligibility for TICH 3 in patients with a history of seizures is at the discretion of the treating physician

- If you have an eligibility query please call the emergency phone number

+44 (0)7725 580 092 +44 (0)7736 843 592

+44 (0)7798 670 726 +44 (0)7810 540 604

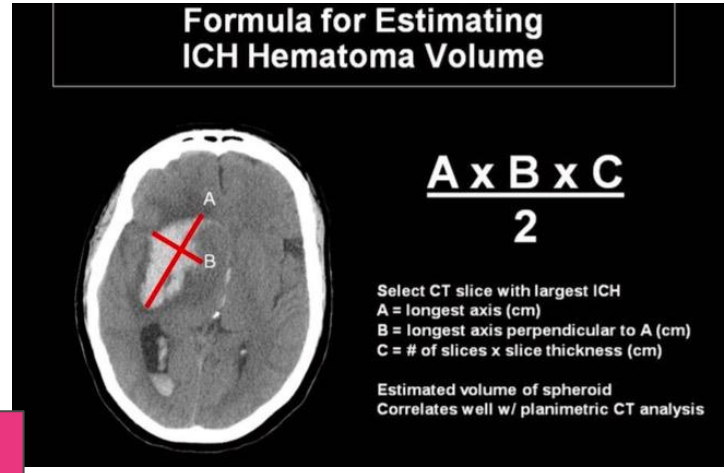


Haematoma volume measurement

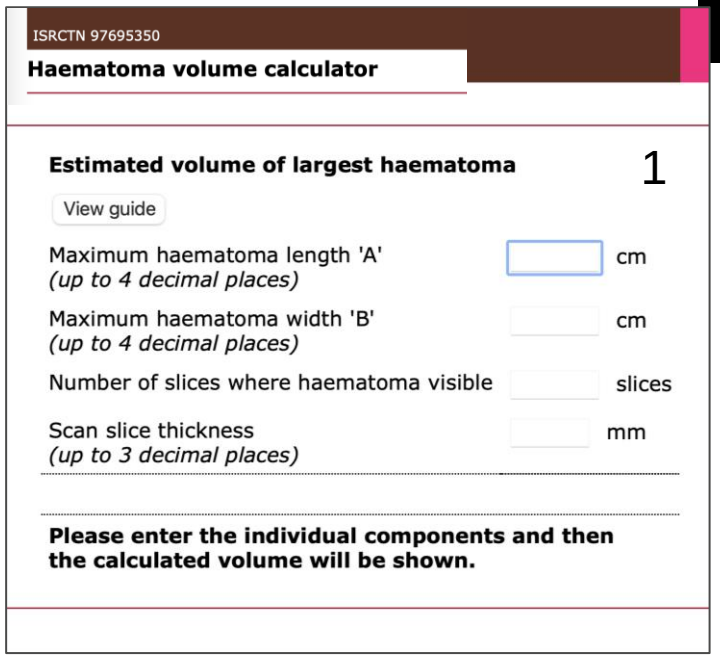
Exclude patients with massive haematoma (usually >60ml)

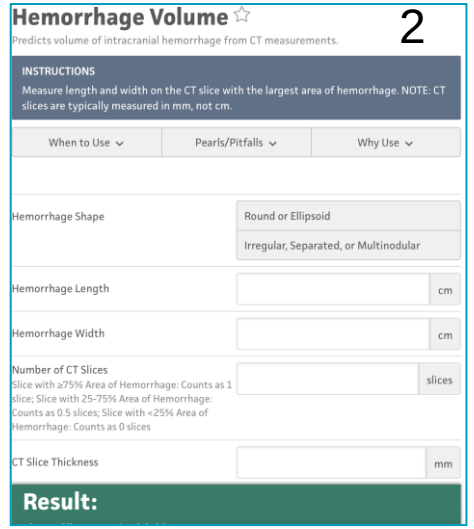
1. If CT scan uses automated haematoma volume software – patient can be enrolled if HV not greater than 60mls
2. Calculate HV manually using TICH-3 HV=ABC/2 calculator on the website[1] or alternatives e.g. mdcalc app[2] Dimensions can be obtained from neuroradiology or measured directly.
3. If ABC/2 not possible: measure the maximum length of the haematoma. Exclude - if max length A > 5cm

- HV can be estimated by anyone trained to do so



The ABC/2 calculator can be used to calculate haematoma volumes during eligibility checks, without needing to be logged in.





https://www.mdcalc.com/abc2-formula-intracerebral-hemorrhage-volume

Decision to confirm eligibility rests with treating physician

Emergency Consent Process

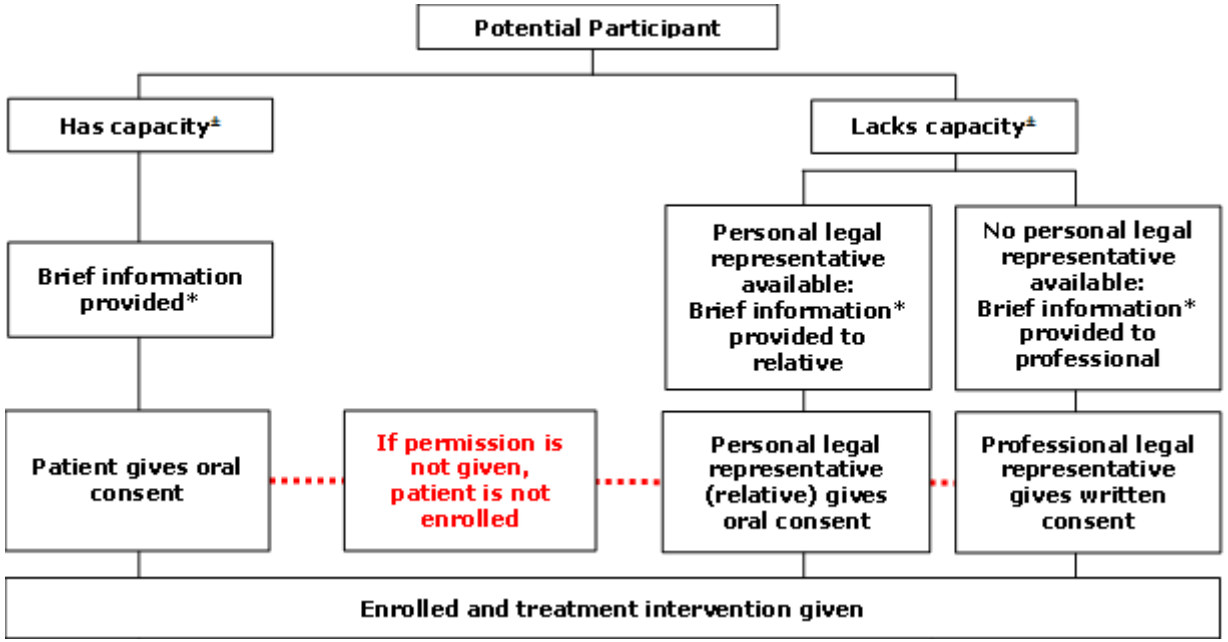
Rapid consent process, initially verbal consent

Full informed written consent to be obtained later after administration of IMP

<u>Hierarchy approach in UK</u>

1. Patient has capacity – gives oral consent
2. Patient does not have capacity – relative or close friend likely to know patient wishes provides oral consent
3. Patient does not have capacity and no relatives available – independent doctor provides written consent

- Oral consent can be given over the telephone.
- A delegated doctor may assesses the patient via telemedicine to obtain verbal consent.
- Medical record must document that the patient meets TICH-3 eligibility criteria and oral consent was given



The person taking consent must be appropriately trained and on the delegation log

± Assessment of capacity is the responsibility of the treating physician

Professional legal representative consent by an independent doctor (1)

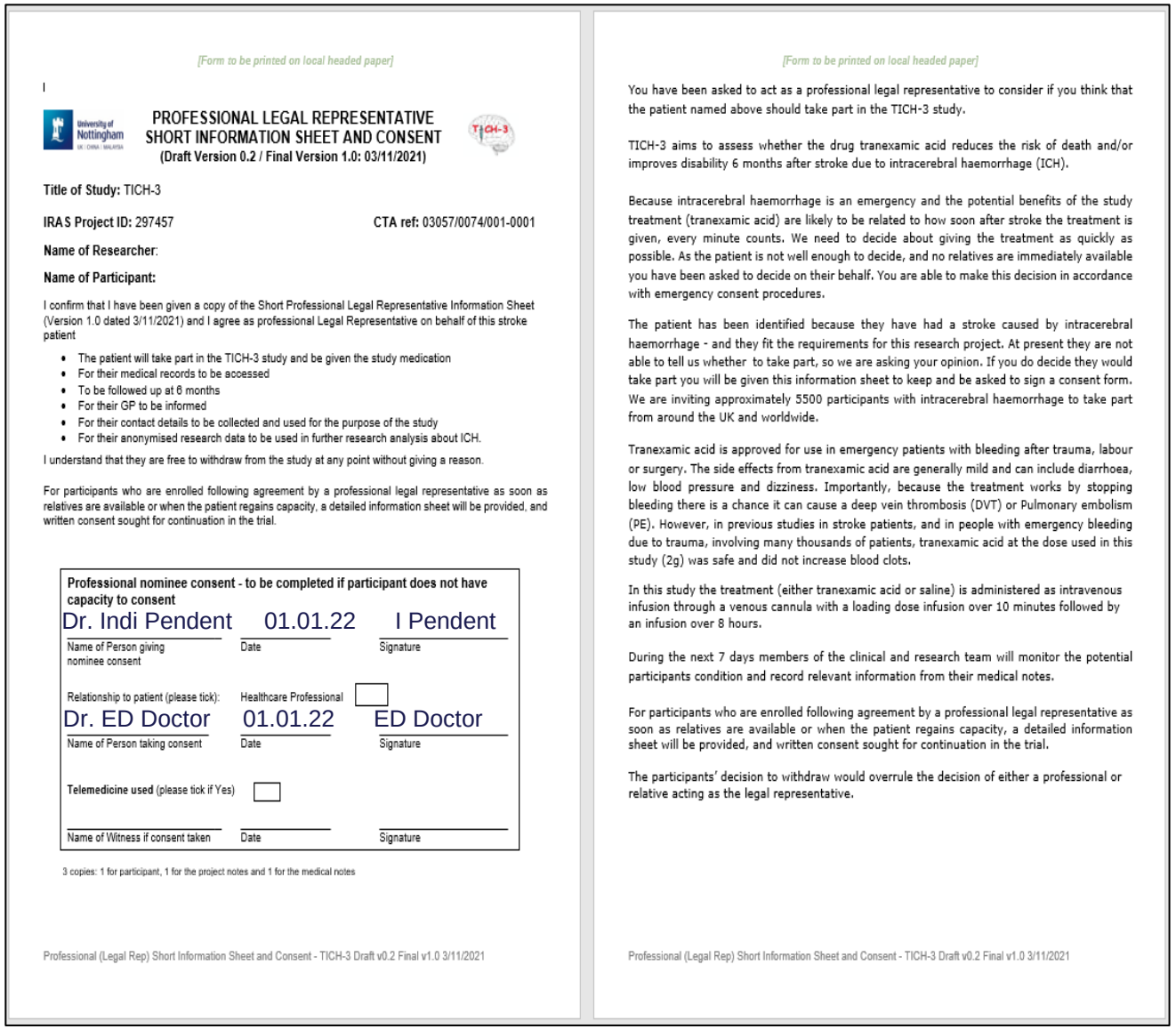
Enrolment consent

For enrolment consent that is given by an independent doctor/professional legal representative the Professional (Legal Rep) Short Information Sheet and Consent form should be used (pictured to the right). In this scenario this professional legal representative enrolment consent is handwritten and then a follow on written consent form is not required to be completed by the independent doctor. If the participant regains capacity or a relative becomes available they should complete the written follow on consent.

Independent doctor must not be an investigator in the TICH-3 trial (i.e. not on delegation log)

No specific grade of doctor is required (but usually registrar or above)

The independent doctor can give permission via telemedicine if not on site.



[Form to be printed on local headed paper]

I

PROFESSIONAL LEGAL REPRESENTATIVE
SHORT INFORMATION SHEET AND CONSENT
(Draft Version 0.2 / Final Version 1.0: 03/11/2021)

Title of Study: TICH-3

IRAS Project ID: 297457 **CTA ref:** 03057/0074/001-0001

Name of Researcher:

Name of Participant:

I confirm that I have been given a copy of the Short Professional Legal Representative Information Sheet (Version 1.0 dated 3/11/2021) and I agree as professional Legal Representative on behalf of this stroke patient

- The patient will take part in the TICH-3 study and be given the study medication
- For their medical records to be accessed
- To be followed up at 6 months
- For their GP to be informed
- For their contact details to be collected and used for the purpose of the study
- For their anonymised research data to be used in further research analysis about ICH.

I understand that they are free to withdraw from the study at any point without giving a reason.

For participants who are enrolled following agreement by a professional legal representative as soon as relatives are available or when the patient regains capacity, a detailed information sheet will be provided, and written consent sought for continuation in the trial.

Professional nominee consent - to be completed if participant does not have capacity to consent

Dr. Indi Pendent	01.01.22	I Pendent
Name of Person giving nominee consent	Date	Signature

Relationship to patient (please tick): Healthcare Professional ☐

Dr. ED Doctor	01.01.22	ED Doctor
Name of Person taking consent	Date	Signature

Telemedicine used (please tick if Yes) ☐

Name of Witness if consent taken	Date	Signature

3 copies: 1 for participant, 1 for the project notes and 1 for the medical notes

Professional (Legal Rep) Short Information Sheet and Consent - TICH-3 Draft v0.2 Final v1.0 3/11/2021

[Form to be printed on local headed paper]

You have been asked to act as a professional legal representative to consider if you think that the patient named above should take part in the TICH-3 study.

TICH-3 aims to assess whether the drug tranexamic acid reduces the risk of death and/or improves disability 6 months after stroke due to intracerebral haemorrhage (ICH).

Because intracerebral haemorrhage is an emergency and the potential benefits of the study treatment (tranexamic acid) are likely to be related to how soon after stroke the treatment is given, every minute counts. We need to decide about giving the treatment as quickly as possible. As the patient is not well enough to decide, and no relatives are immediately available you have been asked to decide on their behalf. You are able to make this decision in accordance with emergency consent procedures.

The patient has been identified because they have had a stroke caused by intracerebral haemorrhage - and they fit the requirements for this research project. At present they are not able to tell us whether to take part, so we are asking your opinion. If you do decide they would take part you will be given this information sheet to keep and be asked to sign a consent form. We are inviting approximately 5500 participants with intracerebral haemorrhage to take part from around the UK and worldwide.

Tranexamic acid is approved for use in emergency patients with bleeding after trauma, labour or surgery. The side effects from tranexamic acid are generally mild and can include diarrhoea, low blood pressure and dizziness. Importantly, because the treatment works by stopping bleeding there is a chance it can cause a deep vein thrombosis (DVT) or Pulmonary embolism (PE). However, in previous studies in stroke patients, and in people with emergency bleeding due to trauma, involving many thousands of patients, tranexamic acid at the dose used in this study (2g) was safe and did not increase blood clots.

In this study the treatment (either tranexamic acid or saline) is administered as intravenous infusion through a venous cannula with a loading dose infusion over 10 minutes followed by an infusion over 8 hours.

During the next 7 days members of the clinical and research team will monitor the potential participants condition and record relevant information from their medical notes.

For participants who are enrolled following agreement by a professional legal representative as soon as relatives are available or when the patient regains capacity, a detailed information sheet will be provided, and written consent sought for continuation in the trial.

The participants' decision to withdraw would overrule the decision of either a professional or relative acting as the legal representative.

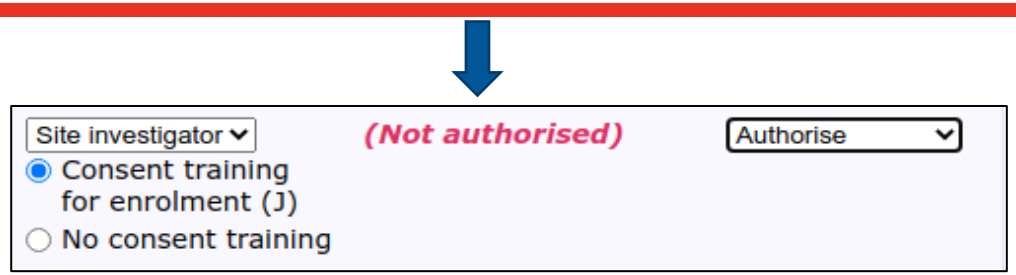
Professional (Legal Rep) Short Information Sheet and Consent - TICH-3 Draft v0.2 Final v1.0 3/11/2021

Delegated roles for consent: J and Z

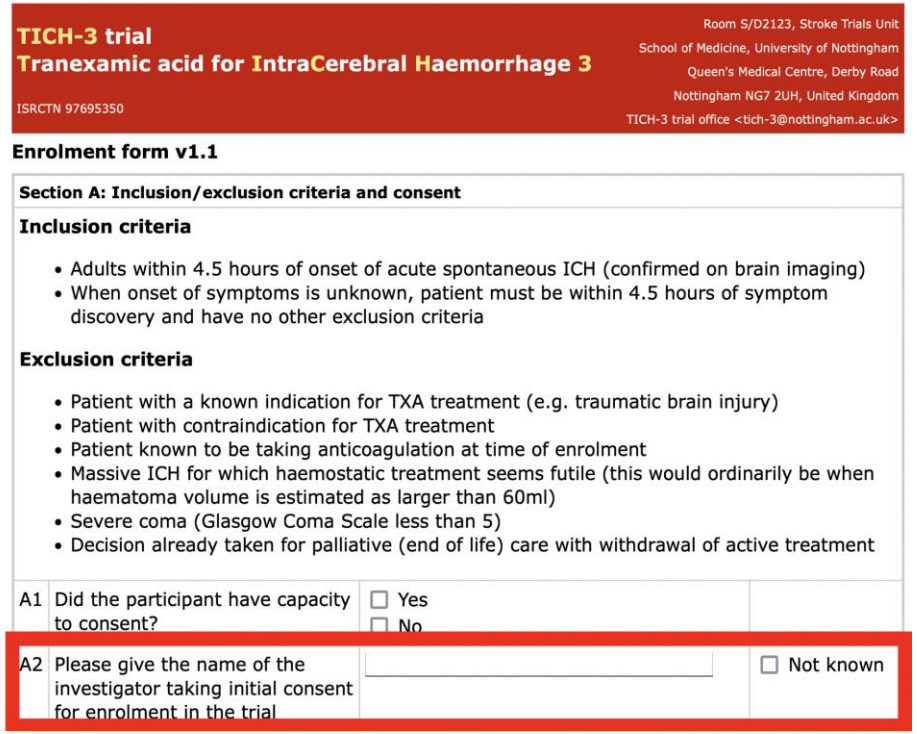
Person taking initial consent must be delegated role J

The PI must select whether code J should be applied as a delegated role.

J. Obtaining consent for enrolment (including oral consent, as appropriate to local policy and practice). **I, PI, DPI**



- Monitoring will check patient was consented by someone on delegation log



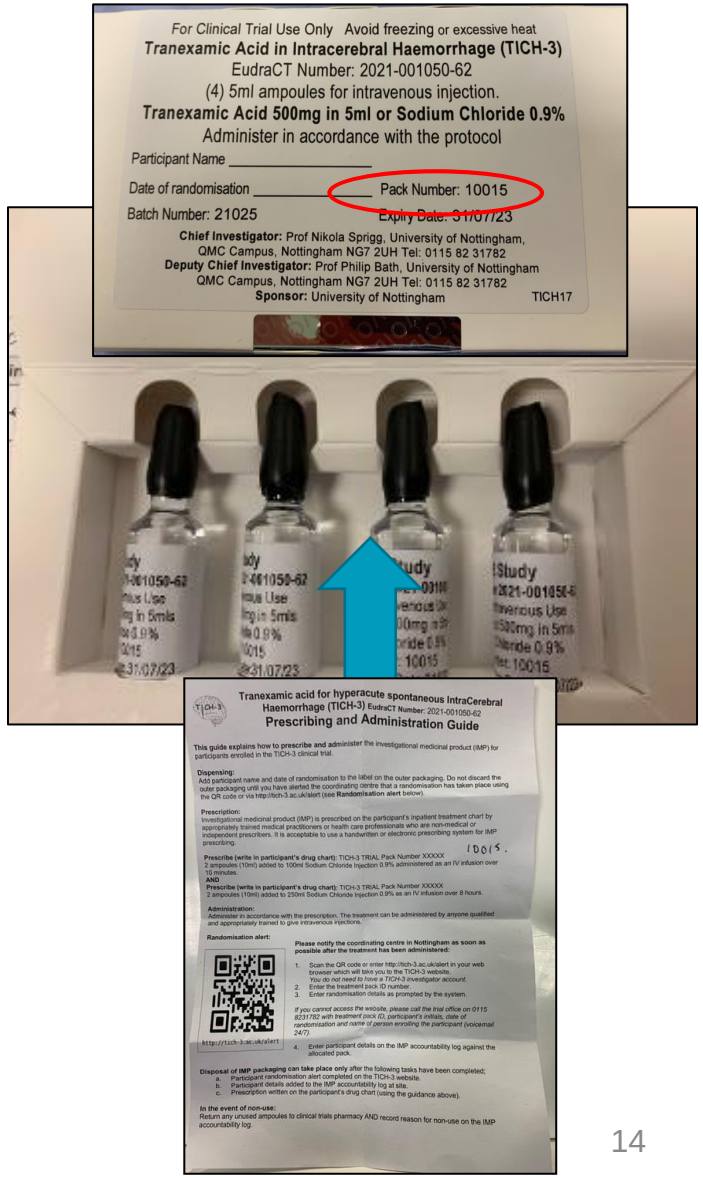
Person taking written consent must be delegated role Z

Z assigned to those with relevant investigator roles (not pharmacists, radiology etc) and confirmed by PI.

Z. Obtaining follow-on written consent (after initial consent) to continue in the study and for follow-up. **I, PI, DPI**

Randomisation

- Blinded treatment packs will be randomly assigned to sites in blocks of 6 treatment packs
- TICH-3 will use simple randomisation
- After confirming eligibility and obtaining consent the investigator selects the treatment pack with the lowest pack number.
- The prescribing and administration guide can be found inside each treatment pack.
- Due to emergency nature of trial randomisation is notified to the coordinating centre after the IMP has been administered by completing the randomisation alert (guidance for this is within the prescribing and administration guide).



Prescribing and Administering the IMP

Prescribing the IMP

Investigational medicinal product (IMP) is prescribed on the participant's inpatient treatment chart by appropriately trained medical practitioners or health care professionals who are non-medical or independent prescribers. It is acceptable to use a handwritten or electronic prescribing system for IMP prescribing.
Do not need to be on delegation log to prescribe

Prescribe (write in participants drug chart):

TICH-3 - TRIAL Pack Number XXXXX

TRANEXAMIC ACID OR PLACEBO

2 ampoules (10ml) added to 100ml Sodium Chloride Injection 0.9% administered as an IV infusion over 10 minutes.

AND

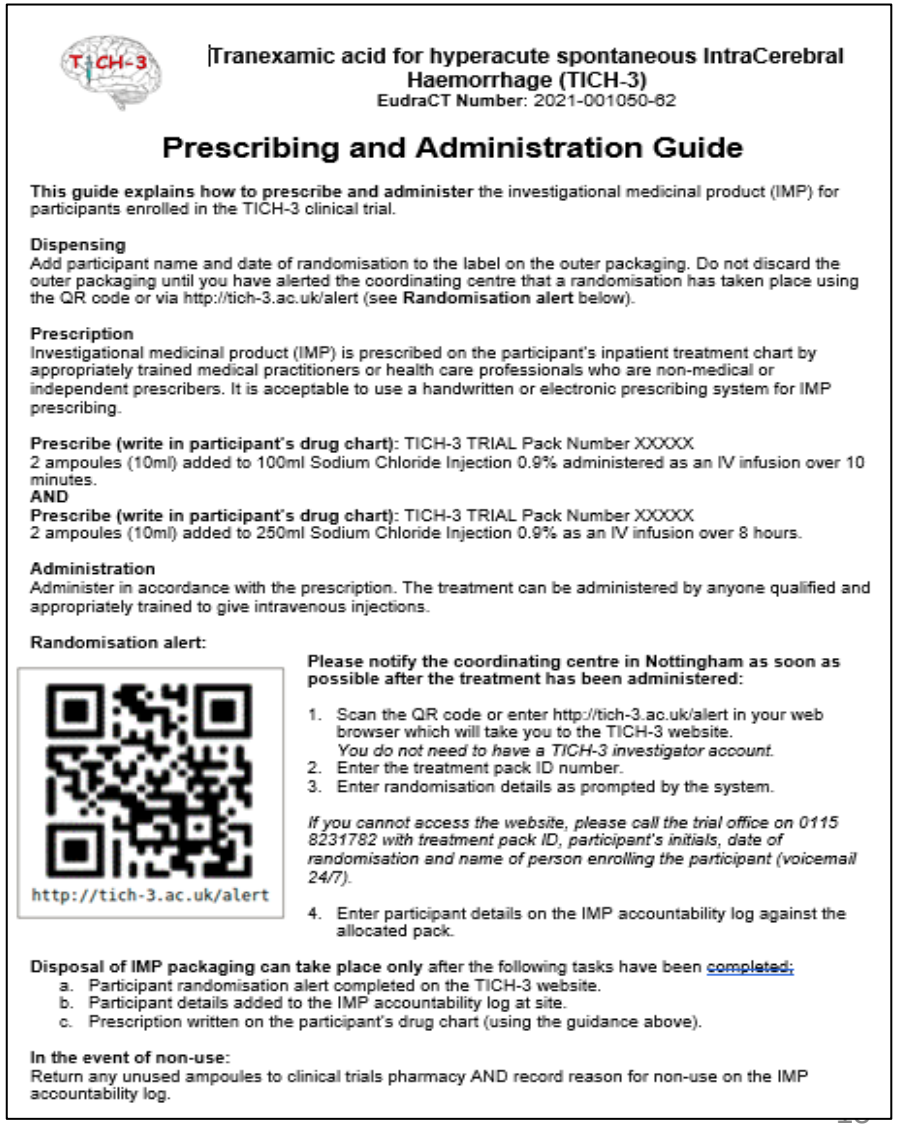
TICH-3 TRIAL Pack Number XXXXX

TRANEXAMIC ACID OR PLACEBO

2 ampoules (10ml) added to 250ml Sodium Chloride Injection 0.9% as an IV infusion over 8 hours.

Administering the IMP

Administer in accordance with the prescription. The treatment can be administered by anyone qualified and appropriately trained to give intravenous injections. ***Do not need to be on delegation log to administer***



Tranexamic acid for hyperacute spontaneous IntraCerebral Haemorrhage (TICH-3)
EudraCT Number: 2021-001050-62

Prescribing and Administration Guide

This guide explains how to prescribe and administer the investigational medicinal product (IMP) for participants enrolled in the TICH-3 clinical trial.

Dispensing
Add participant name and date of randomisation to the label on the outer packaging. Do not discard the outer packaging until you have alerted the coordinating centre that a randomisation has taken place using the QR code or via http://tich-3.ac.uk/alert (see **Randomisation alert** below).

Prescription
Investigational medicinal product (IMP) is prescribed on the participant's inpatient treatment chart by appropriately trained medical practitioners or health care professionals who are non-medical or independent prescribers. It is acceptable to use a handwritten or electronic prescribing system for IMP prescribing.

Prescribe (write in participant's drug chart): TICH-3 TRIAL Pack Number XXXXX
2 ampoules (10ml) added to 100ml Sodium Chloride Injection 0.9% administered as an IV infusion over 10 minutes.
AND
Prescribe (write in participant's drug chart): TICH-3 TRIAL Pack Number XXXXX
2 ampoules (10ml) added to 250ml Sodium Chloride Injection 0.9% as an IV infusion over 8 hours.

Administration
Administer in accordance with the prescription. The treatment can be administered by anyone qualified and appropriately trained to give intravenous injections.

Randomisation alert:

http://tich-3.ac.uk/alert

Please notify the coordinating centre in Nottingham as soon as possible after the treatment has been administered:

1. Scan the QR code or enter http://tich-3.ac.uk/alert in your web browser which will take you to the TICH-3 website.
   You do not need to have a TICH-3 investigator account.
2. Enter the treatment pack ID number.
3. Enter randomisation details as prompted by the system.

If you cannot access the website, please call the trial office on 0115 8231782 with treatment pack ID, participant's initials, date of randomisation and name of person enrolling the participant (voicemail 24/7).

4. Enter participant details on the IMP accountability log against the allocated pack.

Disposal of IMP packaging can take place only after the following tasks have been completed:
a. Participant randomisation alert completed on the TICH-3 website.
b. Participant details added to the IMP accountability log at site.
c. Prescription written on the participant's drug chart (using the guidance above).

In the event of non-use:
Return any unused ampoules to clinical trials pharmacy AND record reason for non-use on the IMP accountability log.

Standard of care for ICH

- All participants should receive standard care for ICH as per the local clinical pathway and guidelines. This is likely to include:

✓Referral to stroke unit

✓**Blood pressure lowering as per clinical guidelines[1] target For patients with BP 150-220mmHg aim for BP 130-140mmg**
x Do not use the same cannula for study drug infusion and blood pressure lowering infusions– need separate IV access line

✓Consideration of referral to neurosurgery or critical care if appropriate

✓Prophylaxis of venous thromboembolism with intermittent compression stockings

Please note tranexamic acid is not standard of care for spontaneous ICH

1: https://www.nice.org.uk/guidance/ng128/chapter/Recommendations

Broken vials:

Broken prior to randomisation e.g. upon receipt in pharmacy

✓Inform the Nottingham coordinating centre and dispose of the pack(s) in accordance with WPD020 (Destruction of IMP).

Broken after randomisation, **before treatment**:

✓Disregard this pack and use the lowest treatment pack ID that is available at your centre

Broken during treatment i.e. Bolus given but infusion vial breaks:

✓Administer as much drug as possible

✓Record on day 7 form that participant does not receive all of the randomised treatment as per protocol and explain why

x Do not open another treatment pack

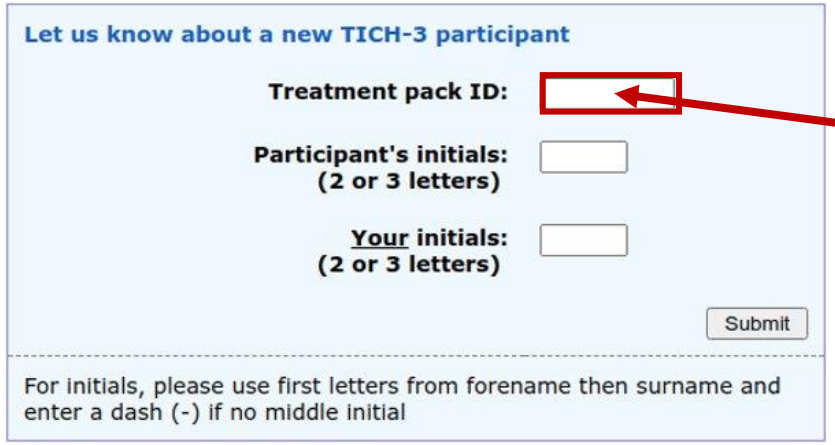
Always record broken vials on the inventory or accountability log as appropriate

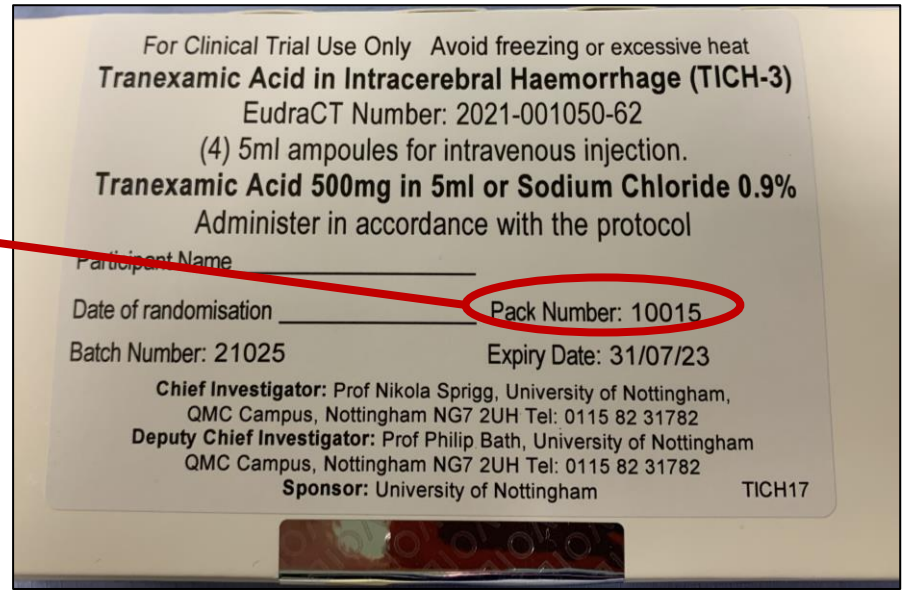
Randomisation Alert

1. Investigator will enter the treatment pack ID (pack number), participant initials and their own initials to alert the coordinating centre to a new randomisation.

SCAN
QR CODE

http://tich-3.ac.uk/



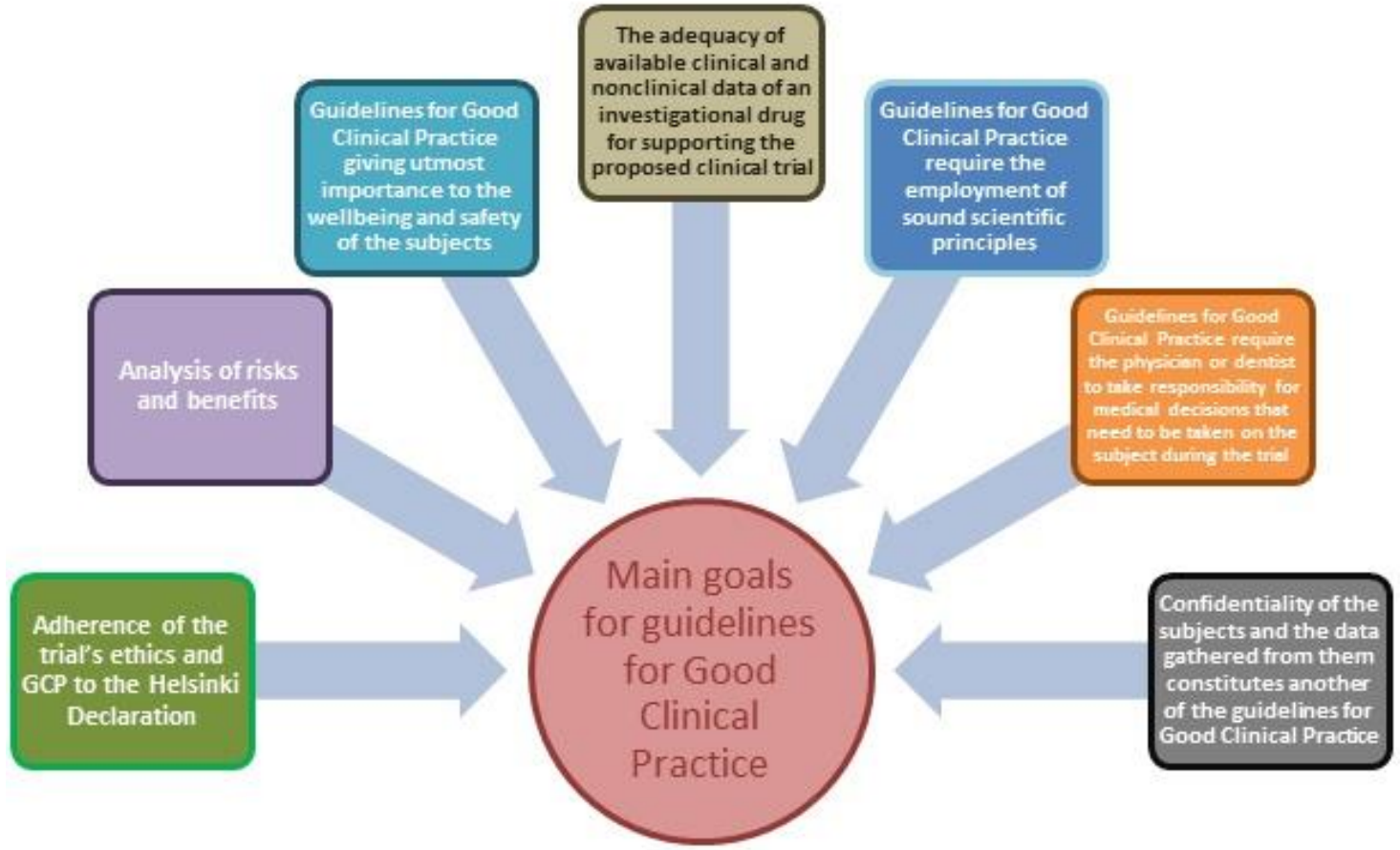


2. Investigator will then confirm that the participant was randomised at the hospital shown in the alert box.

Good Clinical Practice (GCP)

- TICH-3 is to be performed in line with all the principles of good clinical practice
- Investigators must adhere to the protocol at all times
- The safety and rights of the participant are paramount
- Training for investigators should be in proportion to their role within the trial and in accordance with their experience and skills
- The participant has the right to withdraw at any time without giving a reason, without it affecting their medical care
- Investigators eligible for NIHR GCP online training learn account

https://portal.nihr.ac.uk/register



- **Sponsors SOPS can be found on the document page; see TA016 GCP Breach Reporting**

Safety Events, SARS and SUSARS

TXA has an established safety record – we only collect data on focused **safety outcomes** occurring within the **first 7 days or events suspected to be related to the IMP (SAR or SUSAR):**

Safety outcomes: **If a safety outcome (e.g. seizure) occurs during infusion, the infusion must be stopped immediately**

1. Venous occlusive events: VTE (Pulmonary embolism, Deep vein thrombosis)
2. Ischaemic events (arterial thrombosis at any site, ischaemic stroke, transient ischaemic attack peripheral artery embolism, myocardial infarction, acute coronary syndrome)
3. Seizures
4. Fatal events up to discharge from hospital

Serious adverse reactions (SAR) or Suspected Unexpected Serious Adverse Reactions (SUSAR):

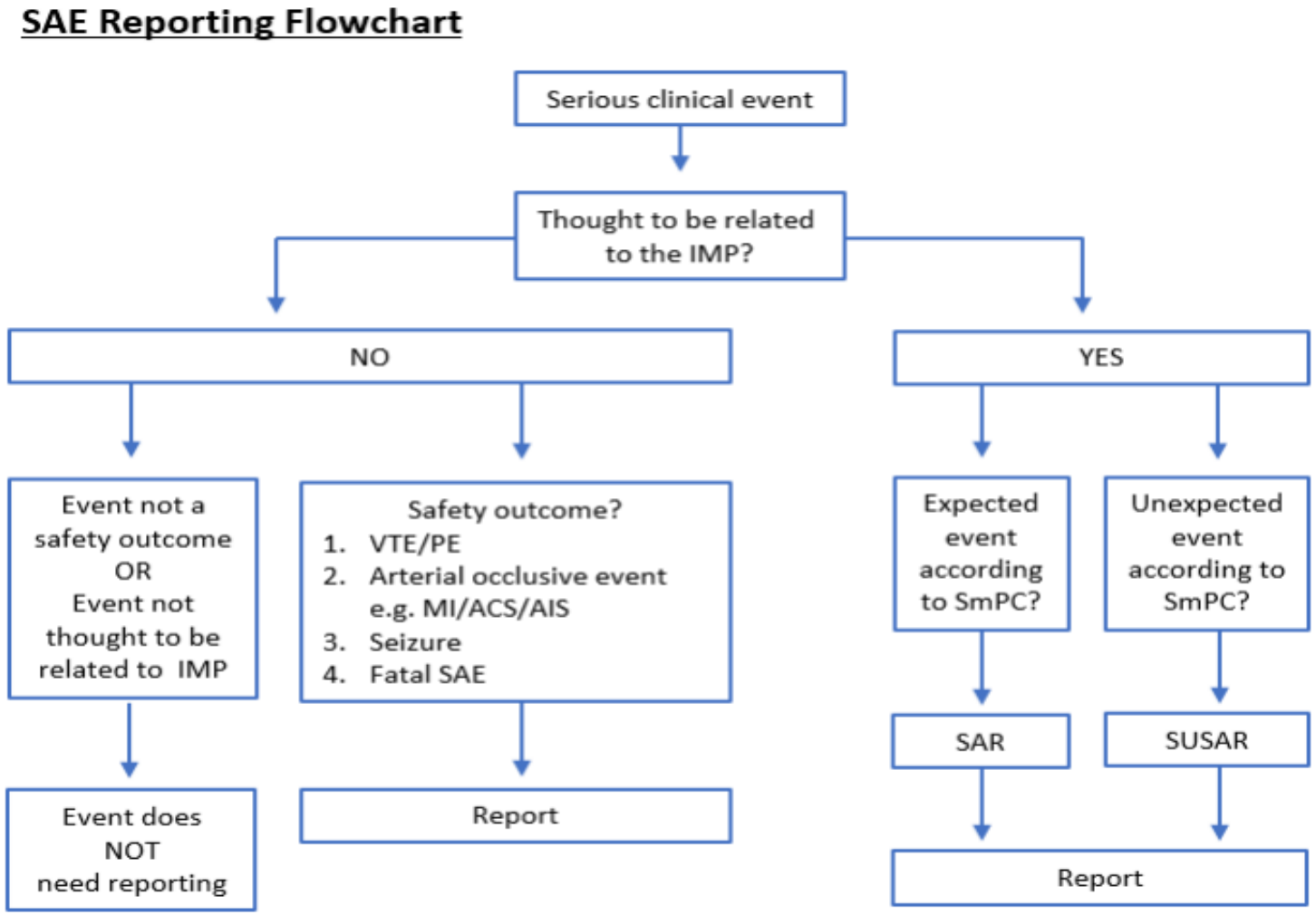
- All events suspected to be related to the IMP will be assessed for seriousness, expectedness and causality by local investigator. Section 4.8 of the SmPC, date of last revision 02 February 2021, will act as the **Reference Safety Information:** Tranexamic Acid https://Tranexamic Acid_SmPC_20210202_REVISION.pdf

Serious Adverse Events (SAEs) that are not safety outcomes, SARS or SUSARS should not be reported

E.g. Neurological deterioration, haematoma expansion, cerebral oedema that is NOT thought to be related to the IMP, and does not result in death does not need to be reported as an SAE

The PI must review and sign off SAE's – recommend print off and file SAE form in site file after sign off by PI

SAE Reporting Flowchart



What to do in Case of Emergency

Safety events during the infusion:

If seizure, thrombosis or arterial occlusion occurs during infusion, the infusion must be stopped immediately. This will be recorded as part of the trial documentation and safety monitoring.

Emergency Unblinding

In general there should be no need to unblind the allocated treatment. If some contraindication to tranexamic acid develops after randomisation (e.g. clinical evidence of thrombosis), the trial treatment should simply be stopped. Unblinding should be done only in those rare cases when the doctor believes that clinical management depends importantly upon knowledge of whether the patient received TXA or placebo. In those few cases when urgent unblinding is considered necessary, the emergency telephone number should be telephoned, giving the name of the doctor authorising unblinding and the treatment pack number. The caller will then be told whether the patient received TXA or placebo.

Eligibility query or any other emergency query:

Call the emergency contact number listed on TICH-3 website

For urgent medical enquiries (including unblinding), and for randomisation problems, you can contact the following emergency mobile numbers. Please ensure that you have these written down (or print them).

+44 (0)7725 580 092 +44 (0)7736 843 592

+44 (0)7798 670 726 +44 (0)7810 540 604

TICH-3 Key Points

- Pragmatic design and methods
- Inclusion criteria – ICH < 4.5 hours,
  Exclusion - massive ICH (low GCS < 5, HV > 60mls), contraindication to tranexamic acid (e.g. seizures)
- Emergency consent – initially oral followed by written consent
- Simple randomisation – use the lowest available treatment pack number
- QR code randomisation alert – inform trial office of enrolment
- Safety monitoring – safety events for 7 days, SAR and SUSAR
  Venous and arterial occlusive events and seizures
- Central postal/telephone follow up at 6 months

ACTION – Return Training Log

- Please complete the investigator training log and return via email to the coordinating centre
  Click here for direct download of training log
- Or use the self referral form: http://tich-3.ac.uk/?ZSelfRef

- Team members who could not attend live training can access training slides from TICH-3 website https://stroke.nottingham.ac.uk/tich-3/docs/#UK_site_training

  There are 3 versions of the training slides

  1. Investigator training which gives a detailed description of the whole trial process, intended for the PI and research nurses/coordinators. There is also a video of this training.
  2. Enrolling investigator training this streamlined training is intended for team members who will only be taking enrolment consent i.e. consultants
  3. Pharmacy training this streamlined training is intended for members of pharmacy team

- A short 3 ½ minute video is available to introduce team members to the TICH-3 trial
  http://tich-3.ac.uk/docs/#Videos

University of Nottingham Trial Team

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THANK YOU!

Any questions?

TICH-3@nottingham.ac.uk

Audit list of updates to training presentations

Previous versions

Version 1.4 25/05/2022

- Broken vials slide changed from protocol violation to 'Record on day 7 form that participant does not receive all of the randomised treatment as per protocol and explain why'
- Added link for ED training video
- Eligibility criteria slide added 'Note - ICH secondary to ischaemic stroke (haemorrhagic transformation of infarct, HTI) or thrombolysis or venous infarct is NOT spontaneous ICH'
- Key points slide - HV < 60mls corrected to HV > 60mls
- Eligibility FAQ slide added Can patients with venous infarction or haemorrhagic transformation of infarct (HTI) be enrolled? No, these are secondary causes of ICH and should not be included. The inclusion criteria requires that thehaemorrhage is thought to be spontaneous at time of enrolment and Can patients that have a bleed after thrombolysis be enrolled? No, this is not a spontaneous haemorrhage

Version 1.5 13/06/2022

- Inform investigators re sponsors SOPS – GCP breach slide 16

This Version 1.6 06/07/2022

- SAE example given e.g. HE

Version 1.7 28/07/2022

- Added SAE flowchart
- Deleted some duplicate FAQ questions and added FAQ recurrent bleeds

This version 2.0 30/01/2023

- Amended wording inclusion to Adults (≥ 18 years) within < 4.5 hours of stroke onset
- Amended exclusion criteria that patients on DOACs at time of ICH are now eligible
- Updated prescription example so its states tranexamic acid or placebo
- Added link for self referral form to get team members onto delegation log
- Added to eligibility FAQs that eligibility must be assessed by a doctor
- Added slide patients on DOACs to fully explain the new inclusion criteria of these participants
- Consent form flowchart and eligibility seizures flowchart added
- Added slide Professional legal representative consent by an independent doctor
- Removed DOAC question from eligibility FAQs
- Eligibility seizures flowchart added