Amendment Tool

v1.6 06 December 2021

For office use

QC: No

Section 1: Project information

Short project title*:	TICH-3
IRAS project ID* (or REC reference if no IRAS project ID is available):	297457
Sponsor amendment reference number*:	SA04_12-09-22
Sponsor amendment date* (enter as DD/MM/YY):	12 September 2022
Briefly summarise in lay language the main changes proposed in this amendment. Explain the purpose of the changes and their significance for the study. If the amendment significantly alters the research design or methodology, or could otherwise affect the scientific value of the study, supporting scientific information should be given (or enclosed separately). Indicate whether or not additional scientific critique has been obtained (note: this field will adapt to the amount of text entered)*:	1.We are submitting a protocol amendment primarily to include patients into the TICH-3 trial that have had an Intracranial haemorrhage (ICH) while on Direct Oral Anticoagulant (DOAC). This was supported by the findings from the TICH- NOAC trial undertaken by Prof Lyrer et al in Switzerland. Enabling this protocol amendment will allow prompt recruitment of patients to the trial that are on DOACs experiencing ICH. 2.We updated Trial Background Information with literature investigation the use of TXA in patients with TXA with three new RCT and 1 ongoing RCT. The references of these trials have also been updated. 3.Correction in inclusion criteria – change of age to include patients that are 18 and above 4.Safety reporting – pregnancies occurring in trial participants or partners of trial participants will not be followed up as TXA has a short half life and TXA is very commonly used during pregnancy. 5.In Appendix 1 – the second event table has been removed as they are common side effects after haemorrhagic stroke and are unnecessary to be reported 6.Health economics outcomes have been moved from the Health economics chapter to secondary outcomes. 7.Layout corrections: a.Remove confidential watermark b.Update SmPC link to approved MHRA version c.EU CTR numbed included in title page d.DOAC added to abbreviations e.References on page 36 have been changed from Vancouver style to Havard style f. Contact details for trial pharmacist, trial manager and new contact details for an EU legal representative has been added.

Project type (select):	**Specific study**			
	Research tissue bank			
	Research database			
Has the study been reviewed by a UKECA-recognised Research Ethics Committee (REC) prior to this amendment?:	**Yes**		No	
What type of UKECA-recognised Research Ethics Committee (REC) review is applicable? (select):	**NHS/HSC REC**			
	Ministry of Defence (MoDREC)			
Is all or part of this amendment being resubmitted to the Research Ethics Committee (REC) as a **modified amendment** (i.e. a substantial amendment previously given an unfavourable opinion)?	Yes		**No**	
Where is the NHS/HSC Research Ethics Committee (REC) that reviewed the study based?:	England	Wales	Scotland	Northern Ireland
	Yes	No	No	No
Was the study a clinical trial of an investigational medicinal product (CTIMP) OR does the amendment make it one?:	**Yes**		No	
EudraCT number*:	2021-001050-62			
Was this clinical trial of an investigational medicinal product (CTIMP) processed under the CTIMP combined review service (formerly known as the Combined Ways of Working (CWoW) pilot)?:	Yes		**No**	
Did the study receive Pharmacy Assurance?:	Yes		**No**	
Was the study a clinical investigation or other study of a medical device OR does the amendment make it one?:	Yes		**No**	

Did the study involve the administration of radioactive substances, therefore requiring ARSAC review, OR does the amendment introduce this?:	Yes		**No**	
Did the study involve the use of research exposures to ionising radiation (not involving the administration of radioactive substances) OR does the amendment introduce this?:	Yes		**No**	
Did the study involve adults lacking capacity OR does the amendment introduce this?:	**Yes**		No	
Did the study involve access to confidential patient information outside the direct care team without consent OR does the amendment introduce this?:	Yes		**No**	
Did the study involve prisoners or young offenders who are in custody or supervised by the probation service OR does the amendment introduce this?:	Yes		**No**	
Did the study involve children OR does the amendment introduce this?:	Yes		**No**	
Did the study involve NHS/HSC organisations prior to this amendment?:	**Yes**		No	
Did the study involve non-NHS/HSC organisations OR does the amendment introduce them?:	Yes		**No**	
	England	Wales	Scotland	Northern Ireland
Lead nation for the study:	**Yes**	No	No	No
Which nations had participating NHS/HSC organisations prior to this amendment?	**Yes**	**Yes**	**Yes**	**Yes**
Which nations will have participating NHS/HSC organisations after this amendment?	**Yes**	**Yes**	**Yes**	**Yes**

Section 2: Summary of change(s)

What do you want to update?:	**Project information**
	New site/PI only

Please note: Each change being made as part of the amendment must be entered separately. For example, if an amendment to a clinical trial of an investigational medicinal product (CTIMP) involves an update to the Investigator's Brochure (IB), affecting the Reference Safety Information (RSI) and so the information documents to be given to participants, these should be entered into the Amendment Tool as three separate changes. A list of all possible changes is available on the "Glossary of Amendment Options" tab. To add another change, click the "Add another change" box.

Change 1				
Area of change (select)*:	Study Design			
Specific change (select - only available when area of change is selected first)*:	Inclusion/exclusion criteria - Significant change (e.g. to age range) likely to affect safety or scientific value of study			
Further information (free text - note that this field will adapt to the amount of text entered):	This amendment allows the recruitment of patient with ICH while on DOAC to the TICH 3 trial. The purpose of this amendment is to allow prompt recruitment of patients and to analyse whether or not TXA will benefit the subset of patients who suffer with ICH while on DOAC.			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	**Yes**	**Yes**	**Yes**
Will all participating NHS/HSC organisations be affected by this change, or only some? (**please note** that this answer may affect the categorisation for the change):	**All**		Some	
			Remove all changes below	

Change 2	
Area of change (select)*:	Study Design
Specific change (select - only available when area of change is selected first)*:	Background information - Change that affects scientific value of study
Further information (free text - note that this field will adapt to the amount of text entered):	We updated Trial Background Information with literature investigation the use of TXA in patients with TXA with three new RCT and 1 ongoing RCT. The references of these trials have also been updated. a)Liu J, Nie X, Gu H, Zhou Q, Sun H, Tan Y et al. Tranexamic acid for acute intracerebral haemorrhage growth based on imaging assessment (TRAIGE): a multicentre, randomised, placebo-controlled trial. Stroke and Vascular Neurology. 2021;6(2):160-1 b)Lyrer P. Treatment Of Intracerebral Hemorrhage In Patients On Non-vitamin K Oral Anticoagulants With Tranexamic Acid (TICH-NOAC). Lyon, France: ESOC; 2022. c)Yassi N, Zhao H, Churilov L, et al Tranexamic acid for intracerebral haemorrhage within 2 hours of onset: protocol of a phase II randomised placebo-controlled double-blind multicentre trial Stroke and Vascular Neurology 2022;7:doi: 10.1136/svn-2021-001070

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	**Yes**	**Yes**	**Yes**
Will all participating NHS/HSC organisations be affected by this change, or only some? (**please note** that this answer may affect the categorisation for the change):	**All**		Some	
			Remove all changes below	

Change 3	
Area of change (select)*:	Study Design
Specific change (select - only available when area of change is selected first)*:	Inclusion/exclusion criteria - Minor change unlikely to affect safety or scientific value of study
Further information (free text - note that this field will adapt to the amount of text entered):	Correction in inclusion criteria – change of age to include patients that are 18 and above

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	**Yes**	**Yes**	**Yes**
Will all participating NHS/HSC organisations be affected by this change, or only some? (**please note** that this answer may affect the categorisation for the change):	**All**		Some	
			Remove all changes below	

Change 4	
Area of change (select)*:	CTIMP safety
Specific change (select - only available when area of change is selected first)*:	Other - Please specify in the free text below
Further information (free text - note that this field will adapt to the amount of text entered):	In the event of a pregnancy occurring in a trial participant or the partner of a trial participant monitoring shall not occur during the pregnancy and after delivery as TXA has a short half life and TXA is very commonly used in pregnancy.

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	No	**Yes**	**Yes**
Will all participating NHS/HSC organisations be affected by this change, or only some? (**please note** that this answer may affect the categorisation for the change):	**All**		Some	
			Remove all changes below	

Change 5	
Area of change (select)*:	Study Documents
Specific change (select - only available when area of change is selected first)*:	Protocol - Non-substantial changes (e.g. not affecting safety or the scientific value of the trial)
Further information (free text - note that this field will adapt to the amount of text entered):	In Appendix 1 – the second table has been removed as they are common side effects after haemorrhagic stroke and are unnecessary to be reported, the protocol specifies the safety events that require collection and reporting.

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	**Yes**	**Yes**	**Yes**
Will all participating NHS/HSC organisations be affected by this change, or only some? (**please note** that this answer may affect the categorisation for the change):	**All**		Some	
			Remove all changes below	

Change 6	
Area of change (select)*:	Study Documents
Specific change (select - only available when area of change is selected first)*:	Protocol - Non-substantial changes (e.g. not affecting safety or the scientific value of the trial)
Further information (free text - note that this field will adapt to the amount of text entered):	Health economics outcomes have been moved from the Health economics chapter to secondary outcomes

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	**Yes**	**Yes**	**Yes**
Will all participating NHS/HSC organisations be affected by this change, or only some? (**please note** that this answer may affect the categorisation for the change):	**All**		Some	
			Remove all changes below	

Change 7	
Area of change (select)*:	Study Documents
Specific change (select - only available when area of change is selected first)*:	Protocol - Non-substantial changes (e.g. not affecting safety or the scientific value of the trial)
Further information (free text - note that this field will adapt to the amount of text entered):	7.Layout corrections: a.Remove confidential watermark b.Update SPCS link to static page c.EU CTR numbed included in title page d.DOAC added to abbreviations e.References on page 36 have been changed from Vancouver style to Havard style f. Contact details for trial pharmacist, trial manager and new contact details for an EU legal representative has been added.

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	**Yes**	**Yes**	**Yes**
Will all participating NHS/HSC organisations be affected by this change, or only some? (**please note** that this answer may affect the categorisation for the change):	**All**		Some	
			Add another change	

Section 3: Declaration(s) and lock for submission

Declaration by the Sponsor or authorised delegate

- I confirm that the Sponsor takes responsibility for the completed amendment tool
- I confirm that I have been formally authorised by the Sponsor to complete the amendment tool on their behalf

Applicant identification:	**Sponsor** Legal representative of the sponsor Person or organisation authorised by the sponsor
Organisation:	University of Nottingham
Name [first name and surname]:*	Angela Shone
Address:	
Telephone number:	
Fax number:	
Purchase Order (PO) number for MHRA invoicing:	4541660
Email address:*	sponsor@nottingham.ac.uk

Lock for submission

Please note: This button will only become available when all mandatory (*) fields have been completed. When the button is available, clicking it will generate a locked PDF copy of the completed amendment tool which must be included in the amendment submission. Please ensure that the amendment tool is completed correctly before locking it for submission.

Lock for submission

After locking the tool, proceed to submit the amendment online. The "Submission Guidance" tab provides further information about the next steps for the amendment.

Section 4: Review bodies for the amendment

Please note: This section is for **information only**. Details in this section will complete automatically based on the options selected in Sections 1 and 2.

Review bodies

	UK wide:						England and Wales:				Scotland:				Northern Ireland:				
	REC	Competent Authority MHRA - Medicines	Competent Authority MHRA - Devices	ARSAC	Radiation Assurance	UKSW Governance	REC (MCA)	CAG	HMPPS	HRA and HCRW Approval	REC (AWIA)	PBPP	SPS (RAEC)	National coordinating function	HSC REC	HSC Data Guardians	Prisons	National coordinating function	Category:
Change 1:	Y	Y				(Y)				(Y)				(Y)				(Y)	A
Change 2:	Y	Y				(Y)				(Y)				(Y)				(Y)	A
Change 3:	N	N				(Y)				(Y)				(Y)				(Y)	A
Change 4:	Y	Y				Y				Y				Y				Y	B
Change 5:	N	N				(Y)				(Y)				(Y)				(Y)	A
Change 6:	N	N				(Y)				(Y)				(Y)				(Y)	A
Change 7:	N	N				(Y)				(Y)				(Y)				(Y)	A
Overall reviews for the amendment:																			
Full review:	Y	Y				Y				Y				Y				Y	
Notification only:	N	N				N				N				N				N	
Overall amendment type:	Substantial for review																		
Overall Category:	A																		