

# Amendment Tool

v1.5 25 Mar 2021

For office use

QC: No

## Section 1: Project information

Short project title*:	SOS Trial: Hyperosmolar therpay in traumatic brain injury			
IRAS project ID* (or REC reference if no IRAS project ID is available):	260350			
Sponsor amendment reference number*:	SA 07			
Sponsor amendment date* (enter as DD/MM/YY):	29 October 2021			
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)*:	See appended summary document for full details. Main changes include: Amendment to protocol to include addition of dosing table, authorship policy, co-enrolment with CTIMPS, allow a rescue dose of hyperosmolar therapy on ICU prior to enrolment, clarifications for consent process and SAE reporting, amendments to follow up process and data collection, and minor clarifications and corrections where required. Revision to Patient Information Sheets to include details on esendex text messaging service, data collection and minor clarifications and corrections. Revision to consent forms to allow follow up data collection from people involved in the patient's care and rehabilitation in addition to their GP. Cover letters to participants and legal representatives for 3, 6 and 12 month follow up questionnaires to encourage return. Revision to 3, 6 and 12 month questionnaires to provide more representative options for who may be completing the questionnaire and removal of GOS-E adjudicators (6 and 12 months). Change of reference safety information (RSI) for Mannitol. The SmPC for 15% Mannitol will be used as the RSI for all three concentrations of Mannitol (10%, 15%, 20%) used in the SOS trial.			
Project type (select):	<input checked="" type="radio"/> Specific study <input type="radio"/> Research tissue bank <input type="radio"/> Research database			
Has the study been reviewed by a UKECA-recognised Research Ethics Committee (REC) prior to this amendment?:	<input checked="" type="radio"/> Yes	<input type="radio"/> No		
What type of UKECA-recognised Research Ethics Committee (REC) review is applicable? (select):	<input checked="" type="radio"/> NHS/HSC REC <input type="radio"/> Ministry of Defence (MoDREC)			
Is all or part of this amendment being resubmitted to the Research Ethics Committee (REC) as a <b>modified amendment</b> (i.e. a substantial amendment previously given an unfavourable opinion)?	<input type="radio"/> Yes	<input checked="" type="radio"/> No		
Where is the NHS/HSC Research Ethics Committee (REC) that reviewed the study based?:	England <input checked="" type="radio"/>	Wales <input type="radio"/>	Scotland <input type="radio"/>	Northern Ireland <input type="radio"/>
Was the study a clinical trial of an investigational medicinal product (CTIMP) OR does the amendment make it one?:	<input checked="" type="radio"/> Yes		<input type="radio"/> No	
EudraCT number*:	2019-001688-66			
Was this clinical trial of an investigational medicinal product (CTIMP) processed under the Combined Ways of Working (CWoW) pilot?:	<input type="radio"/> Yes		<input checked="" type="radio"/> No	
Did the study receive Pharmacy Assurance?:	<input type="radio"/> Yes		<input checked="" type="radio"/> No	
Was the study a clinical investigation or other study of a medical device OR does the amendment make it one?:	<input type="radio"/> Yes		<input checked="" type="radio"/> No	
Did the study involve the administration of radioactive substances, therefore requiring ARSAC review, OR does the amendment introduce this?:	<input type="radio"/> Yes		<input checked="" type="radio"/> 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?:	<input type="radio"/> Yes		<input checked="" type="radio"/> No	
Did the study involve adults lacking capacity OR does the amendment introduce this?:	<input checked="" type="radio"/> Yes		<input type="radio"/> No	
Did the study involve access to confidential patient information outside the direct care team without consent OR does the amendment introduce this?:	<input type="radio"/> Yes		<input checked="" type="radio"/> No	
Did the study involve prisoners OR does the amendment introduce this?:	<input type="radio"/> Yes		<input checked="" type="radio"/> No	
Did the study involve children OR does the amendment introduce this?:	<input type="radio"/> Yes		<input checked="" type="radio"/> No	

Did the study involve NHS/HSC organisations prior to this amendment?:	<input checked="" type="radio"/> Yes	<input type="radio"/> No		
Did the study involve non-NHS/HSC organisations OR does the amendment introduce them?:	<input type="radio"/> Yes	<input checked="" type="radio"/> No		
	England	Wales	Scotland	Northern Ireland
Lead nation for the study:	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Which nations had participating NHS/HSC organisations prior to this amendment?	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Which nations will have participating NHS/HSC organisations after this amendment?	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

Section 2: Summary of change(s)

What do you want to update?:	<input checked="" type="radio"/> Project information
	<input type="radio"/> 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, tick the "Add another change" box.

Change 1				
Area of change (select)*:	CTIMP IMP			
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):	A dosing table to help sites calculate equi-osmoalr doses of Hypertonic Saline (1026 mOsm/L) and Mannitol (1100mOsm/L) has been inserted into the protocol. The dosing table calculates the equi-osmolar doses to be administered for site staff according to the patient's weight (to the nearest 5kg) and the concentration of hypertonic saline and Mannitol they use locally. The osmolarity or concentrations of IMP used has not changed.			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Will all participating NHS/HSC organisations be affected by this change, or only some? ( <b>please note</b> that this answer may affect the categorisation for the change):	<input checked="" type="radio"/> All		<input type="radio"/> Some	

Add another change: ☒

Change 2				
Area of change (select)*:	Study Documents			
Specific change (select - only available when area of change is selected first)*:	Protocol - Substantial changes (e.g. 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):	<div>Changes include: Minor clarifications and typographical errors Co-enrolment to other CTIMP studies Addition of process for obtaining consent from a professional legal representative pre-enrolment Addition of IMP dosing table Addition of authorship policy Amendment to allow patients to be enrolled if they have received a single dose of osmotherapy following ICU admission. Clarification of SAE reporting requirements if participant is discharged prior to end of the 28 day reporting window. Removal of data collection for patient temperature. Inform the REC of previous covid-related changes implemented via a non-substantial amendment during the pandemic.  See appended 'summary of changes' document for list of all changes.</div>			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Will all participating NHS/HSC organisations be affected by this change, or only some? ( <b>please note</b> that this answer may affect the categorisation for the change):	<input checked="" type="radio"/> All		<input type="radio"/> Some	

Add another change: ☒

Change 3				
Area of change (select)*:	Study Documents			
Specific change (select - only available when area of change is selected first)*:	Other significant change to study documents (e.g. information sheets, consent forms, questionnaires, letters) that can be implemented within existing resource in place at participating organisations - Please specify in the free text below			
Further information (free text - note that this field will adapt to the amount of text entered):	<p>Changes to patient information sheets include:            Addition of the use of text message reminders and esendex's privacy policy to ensure transparency of data processing by third party. Esendex is an online text messaging service that will be used to send reminders for follow up questionnaires to patients/legal representatives.            Update to PIS to inform participants/legal representatives that information may also be collected from people involved in the patient's care and rehabilitation.            Minor clarifications and corrections</p> <p>See appended 'summary of changes' document for list of all changes.</p>			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Will all participating NHS/HSC organisations be affected by this change, or only some? ( <b>please note</b> that this answer may affect the categorisation for the change):	<input checked="" type="radio"/> All		<input type="radio"/> Some	

Add another change: ☒

Change 4				
Area of change (select)*:	Study Documents			
Specific change (select - only available when area of change is selected first)*:	Other significant change to study documents (e.g. information sheets, consent forms, questionnaires, letters) that can be implemented within existing resource in place at participating organisations - Please specify in the free text below			
Further information (free text - note that this field will adapt to the amount of text entered):	<p>Clause 5 of consent forms updated to obtain consent from legal representatives/patients for the research team to collect data from people other than their GP who are involved in their care. This has been included to help with the collection of follow up data if the research team are unable to collect it from the patient, legal representative or GP.</p> <p>Removal of reference to the COVID-19 pandemic in the section for documenting witnessed verbal consent on the patient post-enrolment consent form.</p>			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Will all participating NHS/HSC organisations be affected by this change, or only some? ( <b>please note</b> that this answer may affect the categorisation for the change):	<input checked="" type="radio"/> All		<input type="radio"/> Some	

Add another change: ☒

Change 5				
Area of change (select)*:	Study Documents			
Specific change (select - only available when area of change is selected first)*:	Other minor change to study documents (e.g. information sheets, consent forms, questionnaires, letters) that can be implemented within existing resource in place at participating organisations - Please specify in the free text below			
Further information (free text - note that this field will adapt to the amount of text entered):	<p>Minor changes to 3, 6 and 12 month follow up questionnaires to amend the options for who is completing the questionnaire. The option for 'someone who cares for the patient' has been amended to 'relative, friend or carer on behalf of the patient' as if the patient has not regained capacity, the relatives or friends completing the questionnaire on their behalf may not be their carer, or see themselves as the patient's carer.</p> <p>The two GOS-E adjudicators have been removed from the 6 and 12 month questionnaires as an algorithm will be used to automatically calculate the GOS-E score based on the questionnaire responses entered into the trial database.</p>			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Will all participating NHS/HSC organisations be affected by this change, or only some? ( <b>please note</b> that this answer may affect the categorisation for the change):	<input checked="" type="radio"/> All		<input type="radio"/> Some	

Add another change: ☒

Change 6				
Area of change (select)*:	Study Documents			
Specific change (select - only available when area of change is selected first)*:	Other significant change to study documents (e.g. information sheets, consent forms, questionnaires, letters) that can be implemented within existing resource in place at participating organisations - Please specify in the free text below			
Further information (free text - note that this field will adapt to the amount of text entered):	New theory-based cover letters to patients and/or legal representatives for follow up questionnaires. There is a letter to be sent with the initial questionnaire and a further letter to be sent with a second questionnaire if we do not receive a response to the first mailing. The theory-based cover letter will be used to try and encourage questionnaire return and increase participant retention.			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Will all participating NHS/HSC organisations be affected by this change, or only some? ( <b>please note</b> that this answer may affect the categorisation for the change):	<input checked="" type="radio"/> All		<input type="radio"/> Some	

Add another change: ☒

Change 7				
Area of change (select)*:	Study Documents			
Specific change (select - only available when area of change is selected first)*:	IB, SmPC - Non-substantial changes (e.g. that do not affect risk/benefit assessment)			
Further information (free text - note that this field will adapt to the amount of text entered):	On comparison of the undesirable effects listed in section 4.8 of the SmPCs for 10%, 15% and 20% Mannitol, the list of undesirable effects are more comprehensive in the 10% and 15% SmPCs than the 20% SmPC. Therefore, as all three products are being used in the same patient population for the SOS trial (sites use whichever concentration of mannitol they usually use locally), it would be assumed that the 20% mannitol would exhibit similar ADRs to the lower mannitol concentrations. As section 4.8 of the 15% mannitol SmPC is the most			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Will all participating NHS/HSC organisations be affected by this change, or only some? ( <b>please note</b> that this answer may affect the categorisation for the change):	<input checked="" type="radio"/> All		<input type="radio"/> Some	

Add another change: ☐

Section 3: Declaration(s) and lock for submission

<b>Declaration by the Sponsor or authorised delegate</b>	
<ul style="list-style-type: none"><li>I confirm that the Sponsor takes responsibility for the completed amendment tool</li><li>I confirm that I have been formally authorised by the Sponsor to complete the amendment tool on their behalf</li></ul>	
Applicant identification:	<input checked="" type="radio"/> Sponsor <input type="radio"/> Legal representative of the sponsor <input type="radio"/> Person or organisation authorised by the sponsor
Organisation:	University of Warwick
Name [first name and surname]*:	Mathew Gane
Address:	
Telephone number:	
Fax number:	
Purchase Order (PO) number for MHRA invoicing:	
Email address*:	sponsorship@warwick.ac.uk

<b>Lock for submission</b>
<p><b>Please note:</b> 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.</p>
<div>Lock for submission</div>



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:	Y	N				Y				Y				Y				Y	C
Change 4:	Y	N				Y				Y				Y				Y	C
Change 5:	N	N				(Y)				(Y)				(Y)				(Y)	C
Change 6:	Y	N				Y				Y				Y				Y	C
Change 7:	N	N				(Y)				(Y)				(Y)				(Y)	C
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																		