Amendment Tool

v1.6 06 December 2021

For office use

QC: No

Section 1: Project information

Short project title*:	MACE-ICH			
IRAS project ID* (or REC reference if no IRAS project ID is available):	1004870			
Sponsor amendment reference number*:	SA_01_23			
Sponsor amendment date* (enter as DD/MM/YY):	30 June 2023			
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) Co-enrolment information updated throughout documents, including protocol, participant/legal representative pictorial and full information sheet and consent forms to indicate that participants may be approached about taking part in other studies that have a co-enrolment agreement in place, and to add clarification regarding SAE management for co-enrolment. The MACE-ICH website has also been added to the PIS documents, which will show all trials that participants could co-enrol in. (2) Consent forms and pictorial information sheets (both participant and legal representative) updated with CTA reference and space to record whether telemedicine and/or a witness was used during the consent process. (3) mNCA updated to the most recent HRA template; schedule 2 updated to reflect responsibilities; financial arrangements added. (4) Month 6 follow up postal form replaces previously approved word document. The updated version includes changes to formatting and wording of questions throughout to align with the Month 6 follow-up form completed centrally on the trial database. Other changes include: Zung depression scale now the shortened version (section F), addition of hospitalisation questions (items B2a/b), and COVID-19 items (section G). (5) Protocol updates: minor corrections to spelling/punctuation/grammar throughout; trial registry details added; 'confidential' removed from footer; updates to trial staff contact details; clarified that the legal representative information sheet and legal representative consent form need to be used for professional legal representative consent; trial procedures and assessments schedule table updated to indicate that GCS/NIHSS/ also collected at day 1 and 2 follow up, blood sample analysis at day 28 or discharge, column names amended, and row added to indicate data collection points for mortality; correction of wording to indicate that participants will not have serum osmolality calculated before infusion, as explained in the response to MHRA; clarified that TSC meetings may take place via Teams videoconference. Further information regarding co-enrolment and SAE reporting for co-enrolment as per change 1 above. (6) Site PI update for Addenbrookes Hospital. (7) The sponsor contact details are being updated due to changes in staff within the sponsor organisation.			
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*:	2022-000283-22			
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 have Radiation Assurance OR is Radiation Assurance being sought for the first time because of this amendment?:	**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**	No	**Yes**	No
Which nations will have participating NHS/HSC organisations after this amendment?	**Yes**	No	**Yes**	No

Section 2: Summary of change(s)

What do you want to update?:	Chief Investigator Sponsor Group Administrative **Project information**

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 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):	Co-enrolment information updated throughout documents, including protocol, to indicate that participants may be approached about taking part in other studies that have a co-enrolment agreement in place, and to add clarification regarding SAE management for co-enrolment. Protocol being submitted is 1004870_MACEICH_Protocol_v2.0_27Jul2023 (TC and Cln)			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	No	**Yes**	No
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 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
	Co-enrolment information updated throughout documents, to indicate that participants may be

Further information In particular, please describe why this change can be implemented within the existing resource in place at the participating organisations (free text - note that this field will adapt to the amount of text entered)*	approached about taking part in other studies. Co-enrolment clause added to each consent form and pictorial information sheet to indicate that the participant/legal representative may be approached about other studies and data shared according to GDPR and Data Protection Act. The study website has been added to the PIS so that participants can see a list of studies they can be co-enroled into. Participant information sheet and legal representative information sheet updated with co-enrolment information to explain that participants may be approached to take part in other studies. Documents being submitted: 1004870_MACE ICH_PIS_v2.0_27Jul2023 (TC and Cln); 1004870_MACE ICH_Participant Pictorial Info Sheet_v2.0_27Jul2023 (TC and Cln); 1004870_MACE-ICH_Legal Representative Information Sheet_v2.0_27Jul2023 (TC and Cln); 1004870_MACE-ICH_Legal Representative Pictorial Information Sheet_v2.0_27Jul2023 (TC and Cln); 1004870_MACE ICH_ICF_v2.0_27Jul2023 (TC and Cln); 1004870_MACE ICH_Legal Rep Consent Form_v2.0_27Jul2023 (TC and Cln).

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	No	**Yes**	No
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 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 In particular, please describe why this change can be implemented within the existing resource in place at the participating organisations (free text - note that this field will adapt to the amount of text entered)*	Minor grammatical corrections/updates to information sheets. Month 6 follow up postal form (1004870_MACE-ICH_Month_6_follow-up_20230621_v1.1_postal) to replace the previously approved word document (11 - 1004870 MACE-ICH_CRF_6mth postal questionnaire_v1.0_22Jun2022). The updated version includes changes to formatting and wording of questions throughout to align with the Month 6 follow-up form completed centrally on the trial database. Other changes include: Zung depression scale now the shortened version (section F), addition of hospitalisation questions (items B2a/b), and COVID-19 items (section G).

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	No	**Yes**	No
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)*:	Study Management
Specific change (select - only available when area of change is selected first)*:	Contract/agreement arrangements
Further information (free text - note that this field will adapt to the amount of text entered):	mNCA updated to the most recent HRA template; schedule 2 updated to reflect responsibilities; financial arrangements added - 1004870_MACE ICH_mNCA_DoR_UoN+NUH_20230623 (TC and Cln)

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	No	**Yes**	No
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):	Protocol updates: minor corrections to spelling/punctuation/grammar throughout; trial registry details added; 'confidential' removed from footer; updates to trial staff contact details; clarified that the legal representative information sheet and legal representative consent form need to be used for professional legal representative consent; trial procedures and assessments schedule table updated to indicate that GCS/NIHSS/ also collected at day 1 and 2 follow up, blood sample analysis at day 28 or discharge, column names amended, and row added to indicate data collection points for mortality; correction of wording to indicate that participants will not have serum osmolality calculated before infusion, as explained in the response to MHRA; clarified that TSC meetings may take place via Teams videoconference.

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	No	**Yes**	No
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)*:	Researchers
Specific change (select - only available when area of change is selected first)*:	PI - New PI, or temporary arrangements to cover the absence of a PI
Further information (free text - note that this field will adapt to the amount of text entered):	Addenbrooke's Hospital: PI previously Dr Smriti Agarwal. Site confirmed 27/05/23 that the new PI is Dr Mathilde Pauls.

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	No	No	No
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 Management
Specific change (select - only available when area of change is selected first)*:	Sponsor delegations - Changes to the internal organisation of the sponsor or persons/organisations to whom tasks have been delegated
Further information (free text - note that this field will adapt to the amount of text entered):	Section B "Identification of the sponsor responsible for the request", questions B1-2-1 and B1-2-3 are updated from Maria Koufali, to Tom Smith, respectively. Question B5-2 is updated to Alison Lloyd.

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	**Yes**	No	**Yes**	No
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

	Sponsor
Applicant identification:	Legal representative of the sponsor Person or organisation authorised by the sponsor

Organisation:	Nottingham University Hospitals NHS Trust
Name [first name and surname]:*	Alison Lloyd
Address:	Queens Medical Centre, Derby Road, Nottingham, NG7 2UH
Telephone number:	0115 9249924
Fax number:	N/A
Purchase Order (PO) number for MHRA invoicing:	200738905
Email address:*	Alison.Lloyd@nuh.nhs.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, amendments to trials processed under the combined review service should be made using the new part of IRAS. Further information can be found on the "Submission Guidance" tab.

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)					A
Change 2:	Y	N				Y				Y				Y					C
Change 3:	N	N				(Y)				(Y)				(Y)					C
Change 4:	N	N				Y				Y				Y					A
Change 5:	N	N				(Y)				(Y)				(Y)					A
Change 6:	N	N				(Y)				(Y)				N					B
Change 7:	N	N				Y				Y				Y					A
Overall reviews for the amendment:																			
Full review:	Y	Y				Y				Y				Y					
Notification only:	N	N				N				N				N					
Overall amendment type:	Substantial for review																		
Overall Category:	A																		