Amendment Tool

v1.6 06 December 2021

For office use

QC: No

Section 1: Project information

Short project title*:	EVIS
IRAS project ID* (or REC reference if no IRAS project ID is available):	307862
Sponsor amendment reference number*:	Substantial Amendment 07
Sponsor amendment date* (enter as DD/MM/YY):	10 October 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). Non-Substantial Changes to the Protocol: (A) Administrative updates: versioning. (B) Update to the sponsor representative contact. (C) SMG updated to TMG throughout the protocol for consistency. (D) Schedule of Assessments updated for consistency with the study visits. (E) SOFA score changed from a secondary outcome to an exploratory outcome. As routine bloods are optional at all time points apart from at baseline, data collection for the SOFA score is not mandatory and therefore has been changed to an exploratory outcome only. (F) Clarity added to the inclusion and exclusion criteria regarding assessing eligibility. (G) Additions to the description of the consent process to add additional clarifications. (H) Clarity added regarding randomisation and eligibility assessment. Further information provided in relation to time frames for the measurement of vital signs and the serum lactate used for determining eligibility. (I) Study Visits updated for consistency to match the updated schedule of assessments table. 2). Minor update to the clinical information sheets for the standard of care arm, to match the updated protocol wording. 3). Clinical information sheet for the intervention arm updated for the Sandwell and West Birmingham NHS Trust sites, to match their local policy for the preparation and administration of peripheral norepinephrine. Local policy for norepinephrine preparation will be used at site rather than that contained in EVIS protocol i.e. at SWB norepinephrine will be prepared as a solution containing 20 micrograms/ml solution with a final volume of 50ml presented in a syringe for administration via a syringe driver. This variation is permitted within the current approved EVIS protocol. All other aspects of dosing and administration will be as per the study protocol; that is no change to the minimum and maximum permitted norepinephrine doses etc. 4). Minor updates to the; Main PIS/ICF, PIS Summary, Welfare Attorney/Guardian, Professional Legal Rep (Scotland & England) and Personal Legal Rep, to remove an additional date and signature panel which was included in error in the original submission. 5). Removal of Royal Devon & Exeter Hospital as a participating site. 6). Addition of John Radcliff Hospital, Oxford as a participating site, PI Dr. Deon Louw. 7). Addition of Fairfield General Hospital as a participating site, PI Dr. Scott Houston. 8). Addition of University Hospital, Lewisham as a participating site, PI Dr Anna Colclough. 9). Addition of Sandwell Hospital, West Bromwich as a participating site, PI Dr Hema Patel. 10). Addition of City Hospital, Birmingham as a participating site, PI Dr Hema Patel. 11) Addition of Royal Liverpool University as a participating site, PI Dr. Ned Gilbert-Kawai

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
	No	No	**Yes**	No
Was the study a clinical trial of an investigational medicinal product (CTIMP) OR does the amendment make it one?:	**Yes**		No	
EudraCT number*:	2021-006886-39			
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:	No	No	**Yes**	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 - 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):	1). Non-Substantial Changes to the Protocol: (A) Administrative updates: versioning. (B) Update to the sponsor representative contact. (C) SMG updated to TMG throughout the protocol for consistency. (D) Schedule of Assessments updated for consistency with the study visits. (E) SOFA score changed from a secondary outcome to an exploratory outcome. As routine bloods are optional at all time points apart from at baseline, data collection for the SOFA score is not mandatory and therefore has been changed to an exploratory outcome only. (F) Clarity added to the inclusion and exclusion criteria regarding assessing eligibility. (G) Additions to the description of the consent process to add additional clarifications. (H) Clarity added regarding randomisation and eligibility assessment. Further information provided in relation to time frames for the measurement of vital signs and the serum lactate used for determining eligibility. (I) Study Visits updated for consistency to match the updated schedule of assessments table.

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 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)*	2). Minor update to the clinical information sheets for the standard of care arm, to match the updated protocol wording.

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 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 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)*	3). Clinical information sheet for the intervention arm updated for the Sandwell and West Birmingham NHS Trust sites, to match their local policy for the preparation and administration of peripheral norepinephrine. Local policy for norepinephrine preparation will be used at site rather than that contained in EVIS protocol i.e. at SWB norepinephrine will be prepared as a solution containing 20 micrograms/ml solution with a final volume of 50ml presented in a syringe for administration via a syringe driver. This variation is permitted within the current approved EVIS protocol. All other aspects of dosing and administration will be as per the study protocol; that is no change to the minimum and maximum permitted norepinephrine doses etc.

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 4	
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)*	4). Minor updates to the; Main PIS/ICF, PIS Summary, Welfare Attorney/Guardian, Professional Legal Rep (Scotland & England) and Personal Legal Rep, to remove an additional date and signature panel which was included in error in the original submission.

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)*:	Participating Organisations
Specific change (select - only available when area of change is selected first)*:	Early closure or withdrawal of research sites
Further information (free text - note that this field will adapt to the amount of text entered):	5). Removal of Royal Devon & Exeter Hospital as a participating site.

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 6				
Area of change (select)*:	Participating Organisations			
Specific change (select - only available when area of change is selected first)*:	Addition of sites undertaking the same activities as existing sites			
Further information (free text - note that this field will adapt to the amount of text entered):	6). Addition of John Radcliff Hospital, Oxford as a participating site, PI Dr. Deon Louw.			
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)*:	Participating Organisations			
Specific change (select - only available when area of change is selected first)*:	Addition of sites undertaking the same activities as existing sites			
Further information (free text - note that this field will adapt to the amount of text entered):	7). Addition of Fairfield General Hospital as a participating site, PI Dr. Scott Houston.			
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 8				
Area of change (select)*:	Participating Organisations			
Specific change (select - only available when area of change is selected first)*:	Addition of sites undertaking the same activities as existing sites			
Further information (free text - note that this field will adapt to the amount of text entered):	8). Addition of University Hospital, Lewisham as a participating site, PI Dr Anna Colclough.			
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 9				
Area of change (select)*:	Participating Organisations			
Specific change (select - only available when area of change is selected first)*:	Addition of sites undertaking the same activities as existing sites			
Further information (free text - note that this field will adapt to the amount of text entered):	9). Addition of Sandwell Hospital, West Bromwich as a participating site, PI Dr Hema Patel.10). Addition of City Hospital, Birmingham as a participating site, PI Dr Hema Patel.			
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 10				
Area of change (select)*:	Participating Organisations			
Specific change (select - only available when area of change is selected first)*:	Addition of sites undertaking the same activities as existing sites			
Further information (free text - note that this field will adapt to the amount of text entered):	11) Addition of Royal Liverpool University as a participating site, PI Dr. Ned Gilbert-Kawai			
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**	

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

Name [first name and surname]:*	Alison Hamilton
Email address:*	alison.hamilton@ggc.scot.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:	N					(Y)				(Y)				(Y)					A
Change 2:	N					(Y)				(Y)				(Y)					C
Change 3:	Y					Y				Y				N					C
Change 4:	N					(Y)				(Y)				(Y)					C
Change 5:	N					(Y)				(Y)				N					B

Change 6:	N					(Y)				(Y)				(Y)					New site
Change 7:	N					(Y)				(Y)				(Y)					New site
Change 8:	N					(Y)				(Y)				(Y)					New site
Change 9:	N					(Y)				(Y)				(Y)					New site
Change 10:	N					(Y)				(Y)				(Y)					New site
Overall reviews for the amendment:																			
Full review:	Y					Y				Y				N					
Notification only:	N					N				N				Y					
Overall amendment type:	Substantial for review																		
Overall Category:	A																		