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 05
Sponsor amendment date* (enter as DD/MM/YY):	20 December 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). Substantial Changes to protocol: (A) Updated risk assessment of extravasation with peripheral vasopressor administration, namely updated safety information and stopping criteria, allowing for peripheral norepinephrine infusion to be restarted at a different PVC site in the cases where Extravasation resulted in temporary tissue injury (grade 1 or 2). (B) A new appendix has been inserted (Appendix B) that includes an extravasation assessment score. (C) Specification of key secondary outcomes. (D). Section added on concomitant administration of IMPs with interventions for management of COVID-19. (E). Revision to dose titration requirements to allow for delay to treatment start and/or temporary halt to peripheral vasopressor administration in the event that the target MAP > 65 mmHg is achieved. (F). Revision to the guidance for the administration of rescue vasopressors. (G). Updates to the statistics and data analysis section of the protocol, in line with the specifics now to be captured in a separate statistical analysis plan.(H) Inclusion that The University of Edinburgh will act as sole data controller for the purposes of data linkage only. Clarification on how data linkage will be conducted, which linkers will be collected and which specific NHS departments this information will be shared with. 2) Non-Substantial Changes to protocol: (A) Administrative updates: versioning. (B) Clarification regarding CTIMP to Non-CTIMP co-enrolment. (C) Updated instructions in regards to archiving in line with sponsor SOP's. (D) Updated appendix A for dosing guidance. (E) Updated appendix E for SOFA score. (F) Standardisation of MAP > 65 mmHG. 3). Withdrawal of St Johns, Edinburgh as a participating site. 4). Withdrawal of Royal Victoria Infirmary, Newcastle as a participating Site. 5). Addition of Petersborough City Hospital as a participating site, PI Dr. Christopher Edmunds 6). Change of PI at participating site 26. Leicester Royal Infirmary from Dr. Scott Knapp to Dr Ravindra Pochiraju. 7). Substantial updates to the PIS/ICF's to reflect all applicable protocol changes (i.e information on data linkage, data controlship for data linkage purpose and how it will be conducted). Correction of a previous error, from 180 day follow up to 90 days for the completion of the health questionnaire, in line with the protocol. 8). Minor updates to the clinical information sheets for the intervention and standard of care arms, to match the updated protocol wording.

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?:	**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 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):	1). Substantial Changes to protocol: (A) Updated risk assessment of extravasation with peripheral vasopressor administration, namely updated safety information and stopping criteria, allowing for peripheral norepinephrine infusion to be restarted at a different PVC site in the cases where Extravasation resulted in temporary tissue injury (grade 1 or 2). (B) A new appendix has been inserted (Appendix B) that includes an extravasation assessment score. (C) Specification of key secondary outcomes. (D). Section added on concomitant administration of IMPs with interventions for management of COVID-19. (E). Revision to dose titration requirements to allow for delay to treatment start and/or temporary halt to peripheral vasopressor administration in the event that the target MAP > 65 mmHg is achieved. (F). Revision to the guidance for the administration of rescue vasopressors. (G). Updates to the statistics and data analysis section of the protocol, in line with the specifics now to be captured in a separate statistical analysis plan. (H). Inclusion that The University of Edinburgh will act as sole data controller for the purposes of data linkage only. Clarification on how data linkage will be conducted, which linkers will be collected and which specific NHS departments this information will be shared with.

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)*:	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):	2) Non-Substantial Changes to protocol: (A) Administrative updates: versioning. (B) Clarification regarding CTIMP to Non-CTIMP co-enrolment. (C) Updated instructions in regards to archiving in line with sponsor SOP's. (D) Updated appendix A for dosing guidance. (E) Updated appendix E for SOFA score. (F) Standardisation of MAP > 65 mmHG.			
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)*:	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):	3). Withdrawal of St Johns, Edinburgh 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?*:	No	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)*:	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):	4). Withdrawal of Royal Victoria Infirmary, Newcastle 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 5				
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):	5). Addition of Petersborough City Hospital as a participating site, PI Dr. Christopher Edmunds			
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)*:	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):	6). Change of PI at participating site 26. Leicester Royal Infirmary from Dr. Scott Knapp to Dr Ravindra Pochiraju.			
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 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 will have additional resource implications for participating organisations - Please specify in the free text below			
Further information In particular, please describe the additional resource arrangements that participating organisations will need to have in place to implement this change (free text - note that this field will adapt to the amount of text entered)*:	7) Substantial updates to the PIS/ICF's to reflect all applicable protocol changes (i.e information on data linkage, data controlship for data linkage purpose and how it will be conducted). Correction of a previous error, from 180 day follow up to 90 days for the completion of the health questionnaire, in line with the protocol			
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 8				
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)*	8). Minor updates to the clinical information sheets for the intervention and standard of care arms, 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	
			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:	R&I NHS GG&C
Name [first name and surname]:*	Pamela Sandu
Address:	Ward 11, Dykebar Hospital, Grahamston Road
Telephone number:	
Fax number:	
Purchase Order (PO) number for MHRA invoicing:	
Email address:*	pamela.sandu@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, 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)					A
Change 2:	N	N				(Y)				(Y)				(Y)					A
Change 3:	N	N				(Y)				N				(Y)					B
Change 4:	N	N				(Y)				(Y)				N					B
Change 5:	N	N				(Y)				(Y)				(Y)					New site
Change 6:	N	N				(Y)				(Y)				N					B
Change 7:	Y	N				Y				Y				Y					A
Change 8:	N	N				(Y)				(Y)				(Y)					C
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																		