Amendment Tool

v1.6 06 December 2021

For office use

QC: No

Section 1: Project information

Short project title*:	PhEAST
IRAS project ID* (or REC reference if no IRAS project ID is available):	304658
Sponsor amendment reference number*:	SA_02_22
Sponsor amendment date* (enter as DD/MM/YY):	29 June 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)*:	This amendment comprises of the addition of a cognitive sub-study, which introduces further follow up time points at day 180 and day 365, with cognitive scales being used at each follow up point, as well as the scales being used previously in the trial protocol. The day 7 follow up has also been removed as this data will be collected after treatment on days 1-6. This amendment also comprises various administrative changes, such as wording changes and sentences added for clarification. Appendix M has been added to outline the cognition sub study scales, and appendix N has been added to outline the IQCODE scale. All patient facing documents (information sheets, consent forms and GP letter) have been updated with the follow up time points, and cognition has been added in as a follow up measure. This amendment will also add a postal follow up, should we not be able to contact a participant by telephone to complete the follow up. Finally, this amendment introduces an informant information sheet and consent form, as well as an aphasia friendly information sheet and consent form.

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**	
Was the study a clinical investigation or other study of a medical device OR does the amendment make it one?:	**Yes**		No	
Does this clinical investigation or other study of a medical device require a Notice of No Objection from MHRA Devices?:	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)

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)*:	Participant Procedures
Specific change (select - only available when area of change is selected first)*:	Participant procedures - significant change that can be implemented within existing resource 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)*	We expect most patients with post-stroke dysphagia in the PhEAST trial will have severe stroke, and so the PhEAST cognition sub-study will assess cognition at days 0 (baseline), day 14 (timing of main study primary outcome), day 90 (timing of main study secondary outcomes) and day 180 and day 365 after randomisation. Dysphagia measures at day 180 and day 365 will be collected as well as the cognition measures. The measures used for the cognition sub-study will be: •Cognition (participant): 7- and 4-level ordinal cognition scales, t-MoCA, t-TICS, t-MMSE, semantic verbal fluency (animal naming), phonemic verbal fluency (letter F), clinical diagnosis of dementia (from participants or carers/informants) • Cognition (from informant): IQCODE. • Dependency and disability (necessary for diagnosis of dementia): modified Rankin scale (mRS), 9,10 and Barthel index (BI). •Frailty: clinical frailty index (CFI). • Mood/depression (which complicates PSCI/PSD diagnosis): Zung. •Health economics: EuroQol - EQ-5D-5L, EQ-VAS •Global: stroke impact scale. • Recurrent stroke after index event. Sites will be able to complete the additional cognition scales at baseline and day 14, we the coordinating centre will complete the additional scales and follow up points at day 90, day 180 and day 365.

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 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):	Table of contents page numbers have been changed to reflect changes. Device disposition log supplied by Phagensis – this has been changed to UoN. New logo added in. Outcome measures table and secondary endpoint on page 25 amended to include new scales being used for cognitive sub study i.e., MoCA, TICS, MMSE, semantic verbal fluency, phonemic verbal fluency, clinical diagnosis of dementia, cognition from informant, IQCODE, frailty (CFI), mood/depression (Zung), global (Stroke Impact Scale). Day 180 and Day 365 follow up has been added to outcome measures table and secondary endpoint on page 25 alongside the scales that will be being used. Additional time points have been added for collection of health care resource with it now being completed at discharge, day 90, day 180 and day 365. Wording change on page 24 'outcome assessment will be assessed by dysphagia trained SLTs who are not involved in the treatment (or research nurse/coordinator if appropriate). Section added to page 26 on Cognition sub study. Sentenced added to page 27 on stopping treatment 'investigators may also choose to discontinue further PES, e.g., removal of catheter before PES treatment if patient is ready for discharge or unless the patient cannot tolerate the tube or removes it'. Number change to page 30 and SAE adjudication, 'we will adjudicate all serious adverse events up to 9 days and fatal SAEs for 10 days, and all procedure/device related (serious) adverse events day 0-14'. Sentence added to page 30 'treating investigators will receive face-to-face training with a Phagenesis training representative. Table on page 36 updated to include new time points for data collection and new scales being used to collect patient data. Duration wording changed on page 37 to 'final follow-up on day 365'. Page 38 wording added to include 'LOT number'. Wording added to page 40 and 41 to reflect data management plan, data capture and data queries for cognition sub study. Wording added to page 44 'Day 180 and Day 365: Day 90:EQ5D-5l (VAS and form), Resource use. Wording added to page 45 and 46 to add in extra time points and scales being used.

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 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):	Appendix M added to outline the cognition sub study scales. Appendix N added to outine the IQCODE scale.			
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)*:	Study Documents			
Specific change (select - only available when area of change is selected first)*:	Correction of typographical errors			
Further information (free text - note that this field will adapt to the amount of text entered):	In inclusion criteria, 35 litres of oxygen has been updated to 35 % oxygen - typo error in protocol version 3.0			
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 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 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)*	All consent forms and information sheets have been updated with the new follow up time points and wording regarding collecting information on cognition. The GP letter has also been updated.			
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)*:	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)*	We have added in an informant information sheet and consent form, so we can consent relatives or close friends to complete a questionnaire regarding the participant. A sentence regarding this has also been added into the protocol. We have also added an aphasia friendly information sheet and consent form, to aid with the consent process in patients presenting with aphasia.			
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)*:	Participant Procedures
Specific change (select - only available when area of change is selected first)*:	Participant procedures - minor change that can be implemented within existing resource 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)*	The day 7 follow up has been removed from the protocol, as this information will be collected after treatment on days 1-6.

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

Name [first name and surname]:*	Anglea Shone
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	C
Change 2:	Y					Y				(Y)				(Y)				(Y)	A
Change 3:	Y					Y				(Y)				(Y)				(Y)	A
Change 4:	N					N				N				N				N	N/A
Change 5:	N					(Y)				(Y)				(Y)				(Y)	C
Change 6:	Y					Y				Y				Y				Y	C
Change 7:	N					(Y)				(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																		

Overall Category:	A