Amendment Tool

v1.6 06 December 2021

For office use

QC: No

Section 1: Project information

Short project title*:	SCN1A Horizons: A natural history study of SCN1A epilepsies in the UK			
IRAS project ID* (or REC reference if no IRAS project ID is available):	295069 (Eng/Wales) 316675 (Scotland)			
Sponsor amendment reference number*:	SA 03			
Sponsor amendment date* (enter as DD/MM/YY):	01 August 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)*:	Proposed changes ahead of start of study recruitment.			
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**	
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**	**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)*:	Study Design
Specific change (select - only available when area of change is selected first)*:	Other minor change to study design 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)*:	A new version of the Bayley Scale of Infant Toddler Development (BSID) neurodevelopmental assessment tool has been validated for use within our participant sample and released within the UK. We seek to amend our study procedure to implement version 4 of this assessment tool in to this study which is the most up to date version and has recently become available for purchase within the UK (first published in USA 2019). BSID-4 has been found to be time-saving and has better sensitivity and accuracy when compared with version 3 (BSID-III). As this tool is a very newly released update on the BSID-III version which is currently specified within protocol v1.4, the rater will also endeveour to calculate scoring for both the BSID-III and BSID-4, with the addition of five physical items to the testing procedure from the BSID-III kit. No extra assessment time burden is anticipated as the BSID-4 has a shorter admininistration time than the currently specified BSID-III. Calculating both scores will allow this study to ensure the results are also comparable to similar study populations where the BSID-III has been utilised. The BSID-III was first published in 2005 and continues to be used within research and clinical contexts, during a period of transition to the BSID-4. Raters will undergo the relevant training and supervision to ensure they are competent in scoring and conducting the assessment in accordance with the changes detailed here.

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 - 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):	Additional text has been implemented within the protocol (Protocol v2.0 010823 TRACKED) to reflect the conduct of the neurodevelopmental assessment, Bayley Scales of Infant and Toddler Development 4th Edition (BSID-4); Page 6 –alphabetised abbreviation list; Page 9 – neurodevelopmental endpoints; Page 12 –Table 1: Schedule of Assessments- Comprehensive study arm and to table abbreviations; Page 13 – table 1 legend point 2 and point 7; Page 16 – table 2 legend point 5; Page 22 –primary outcomes and secondary outcomes; Page 30 –list of participant-based assessments; Page 31/32 – table 3-time allocations and table abbreviations; Page 36/37 –section 11.10, Developmental and Cognitive Scale Selection and figure 3: Cognitive Testing Algorithm diagram and abbreviation list; Page 38/39 –section added, detailing tool and cognitive testing algorithm figure 3 updated; Page 40 – Cognitive Testing Algorithm diagram updated to incorporate update to BSID-4. The text within the protocol has been updated to specify that it will be the 2nd Edition of the Autism Diagnostic Observational Schedule (ADOS-2) which will be used within this study, as the most up to date version of this assessment, published in May 2012. This was referred to simply as “ADOS” in previous protocol versions, without specifying edition. Changes have been made to the text regarding the HCRUQ assessment to make it clear this will take place at each clinical visit, and not as part of the neuropsychology visit; Study Protocol v2.0 010823 TRACKED page 12, 13, 16, 30, 31,46. As per change 8 detailed below, the protocol has been updated to remove inclusion of the Motor Development Milestones assessment. Study Protocol v2.0 010823 TRACKED page 6, 12, 13, 31, 42. As per change 9 detailed below, the protocol has been updated provide detail of the British Paediatric Neurology Surveillance Unit (BPNSU) as a route to participant identification. Study Protocol v2.0 010823 TRACKED page 27.

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)*:	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 propose a change to the volume of blood sample collected at baseline from 5ml to 8ml. An important part of the SCN1A Horizons natural history study is the identification of potential disease biomarkers, including blood derived DNA, to inform future diagnostics and therapeutics as detailed in the study protocol, section 11.9 Clinical Laboratory Tests. The original study protocol included the option to take repeated blood samples throughout the study to account for any technical difficulties extracting DNA from study participants. This had been approved by England/Wales REC, however Scotland A REC suggested that this is changed to only collect a single blood sample at baseline. Rather than collecting repeated blood samples we wish to increase the amount of blood collected from 5ml to 2x 4ml EDTA blood at baseline. This is deemed as the most acceptable, safe and reliable quantity and method of blood sample collection to ensure successful extraction, as informed by our local genetics lab who will be carrying out the extraction. This will be collected within a single sample collection at baseline, in line with the study procedures currently detailed within the protocol. Taking a small amount of extra blood should not lead to further burden for the study participant or member of staff collecting and processing the sample. This will allow the study to collect a sufficient amount of DNA to undertake future genetic testing as per study protocol. We hope that this is acceptable.				
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)*:	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):	Additional text has been implemented within the protocol to reflect the collection of 2x 4ml EDTA blood sample during baseline visit, rather than 5ml sample within section 14.7, page 57.				
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)*:	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 would like to highlight that as per best practice, we will video record participants carrying out participant administered neurodevelopmental assessments. This will assist the rater in scoring of these assessments and allow for review with the neuropsychologist supervisor, following assessment, if required. For example, in the case of the ADOS-2 assessment, video recording and assessor review of these assessments is recommended as an efficient and effective way to ensure skilled and reliable conduct and scoring of this assessment. It is also recommended as good practice to video the other patient-directed neurodevelopmental assessments, within the specified population. This will also allow for the assessment of interrater reliability on a sub-section of the assessments carried out by study raters.The assessments outlined within the Cognitive Testing Algorithm (page 38 protocol v2.0) as well as the ADOS-2 will be video recorded, with the written consent of the relevant individual, as per the relevant ICF. Videos will solely be used for research purposes, in line with the handling of all data within this study and will not be shared in public forums.

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)*:	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):	Text added to protocol detailing use of video recording for participant-administered neurodevelopmental assessment including information about storage, video data handling and equipment requirements. Page 39 (BSID-4), page 40 (WPPSI-IV & WISC-V), page 41 (WAIS-IV), page 43 (ADOS-2). Also, text relating to video recordings added to page 61 & 62 within data collection section. Furthermore, the Data Protection Impact Assessment has been updated and authorised 27/07/2023.

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)*:	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)*	Wording updated within each version of the PIS to explain use of video recording as an optional part of study participation. An extra item has been added to each version of the ICF, to specifically consent to video recording for neuropsychological assessment. Participant PIS ICF v2.0 010823 TRACKED page 3 & 10 (PIS) and page 13 (ICF) PIS ICF Nominated Consultee v2.0 010823 TRACKED page 3 & 10/11 (PIS) and page 15 (ICF) PIS ICF Parent_Legal Guardian v2.0 010823 TRACKED page 3 & 10 (PIS) and page 13 (ICF) PIS ICF Personal Consultee v2.0 010823 TRACKED page 3 & 10 (PIS) and page 15 (ICF) PIS ICF WG.WA.NR v2.0 010823 TRACKED page 3/4 & 11 (PIS) and page 15 (ICF)

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 8	
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 study team have decided to remove the Motor Development Milestones(MDM) assessment following review of standard of care information collection as well as review of the assessments being carried out by the research assistant. Inclusion of the MDM would lead to duplication of data and unnecessary participant burden.

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 9					
Area of change (select)*:	Participating Organisations				
Specific change (select - only available when area of change is selected first)*:	PICs - Addition of Participant Identification Centres for the first time, or a change to activities undertaken by existing PICs				
Further information (free text - note that this field will adapt to the amount of text entered):	We plan to utilise the British Paediatric Neurology Surveillance Unit (BPNSU) as a route to participant identification. The BPNSU encompasses a registry of Consultant members of the British Paediatric Neurology Association. By registering this study with the BPNSU, members will be alerted to inform the research team if they have a patient who may be an eligible study participant, based on eligibility criteria outlined within the study protocol.				
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 10					
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)*	The wording of PIS/ICF versions relevant to Scotland have been updated to include chi number (alongside the use of "NHS number" which is the equivalent within the other UK nations); Participant PIS ICF v2.0 010823 – page 2 & 3 PIS IC Parent_Legal Guardian v2.0 010823 – page 3 PIS ICF WG.WA.NR v2.0 010823 – page 3 & 4 All versions of the PIS updated to include note of the participants GP being notified of study participation (page 4/5), in line with existing text within the consent form. The “Additional Information on Neuropsychology Assessments and Patient/Caregiver Assessments” section on the final page of each PIS/ICF version has been updated to include the full list of participant/caregiver assessments, as specified within the protocol. All versions of PIS updated to reflect the access of personal data by the neuropsychology research assistant for neuropsychology visit purposes within the "Who collects this information?" section, page 3/4 of each updated PIS version.				
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	

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, 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:	N					(Y)				(Y)				(Y)				(Y)	A
Change 2:	N					(Y)				(Y)				(Y)				(Y)	A
Change 3:	Y					Y				Y				Y				Y	C
Change 4:	Y					Y				(Y)				(Y)				(Y)	A
Change 5:	Y					Y				Y				Y				Y	C
Change 6:	Y					Y				(Y)				(Y)				(Y)	A
Change 7:	Y					Y				Y				Y				Y	C
Change 8:	N					(Y)				(Y)				(Y)				(Y)	C
Change 9:	N					Y				Y				Y				Y	A
Change 10:	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																		