**PhEAST – Working Practice Document**

**Title: Site Closedown, no. 014**

**Introduction**

To ensure that the PhEAST trial is closed down in accordance with Good Clinical Practice (GCP) and regulatory requirements, it is mandatory for each centre to follow the closedown procedures as described in this document. The Sponsor of PhEAST (University of Nottingham) has agreed a procedure to allow the close down of PhEAST centres remotely, using the PhEAST Closedown Checklist (Appendix 1).

**Purpose of this document**

To define the procedure for closing out centres participating in the PhEAST trial and ensure all essential documentation for PhEAST is complete and archived to demonstrate compliance with GCP. To outline the responsibilities of the PI to ensure the requirements have been met.

**Scope of this document**

This document is applicable to all PIs, principal contacts or staff from the Trial Co-ordinating Centre delegated the responsibility of ensuring that the closedown procedures outlined in this document are carried out in accordance with Sponsor requirements and GCP.

**Essential documentation and archiving**

It is a GCP requirement that the essential documentation is reviewed prior to the closedown visit (where appropriate);

*“trial master files should be established at the beginning of the trial, both at the investigator/institution site and at the sponsor’s office” ICH-GCP-E6*

The trial Sponsor Standard Operating Procedure (SOP QA005 Archiving) defines that for a multi-centre trial “documents and electronic data should be retained locally to allow reconstruction of the trial at that site. Only one copy of each document needs to be retained. Electronic documents and databases should be transferred onto a suitable storage medium and archived as for paper documents”.

**Archiving**

The trial Sponsor Standard Operating Procedure (SOP QA005 Archiving) states that “archiving of research data shall be for a **minimum of seven years after the date of any publication that is based on them**”. PhEAST is planned to close in June 2025, with publication likely to be in late 2025/2026. Therefore, documents must be archived until 2032 in accordance with local archiving protocols. Sites will be notified in advance if this date is extended. Please note that the PI at each hospital site will need to ensure that responsibility for archiving is delegated to a named individual. The PI is also obliged to notify R&D of any change of ownership of the Investigator Site File (ISF). Audits by trial sponsors, competent authorities or local boards can occur for this trial for the duration of the archiving period.

**End of randomisation**

A trial centre will not be closed until all trial data is completed and queries have been resolved for all patients randomised into the trial. Any final per patient payments due will only be paid once all documentation is received.

**Returning of trial devices**

All PhEAST base stations, catheters and other unused consumables will be returned to Phagenesis Ltd. A representative from the Phagenesis team will contact the site to arrange the return of the devices, once confirmation of trial close-out is provided to the site. Additionally, all data should be exported from the base stations via USB before they are returned, and these USBs should be retained within the trial ISF prior to archiving.

**Payments**

Any centre payments due will only be paid once all documentation is received.

**Closedown procedure**

The attached PhEAST Closedown Monitoring Checklist must be completed, signed and returned to the Trial Coordinating Centre (pheast@nottingham.ac.uk) to confirm that all the essential documentation is present and ready to be archived.

The PI is responsible for all patient related data, regulatory and trial correspondence and patient records being archived appropriately. The responsibility may be delegated but the list must be checked and signed off by the PI.

Every attempt should be made to ensure that all missing documents are found and present in the file before archiving. If a document is deemed to be unrecoverable a file note should be added to the appropriate section and noted on this document.

Once the end point of the trial has been reached, the PI must notify R&D or any other appropriate bodies.

Please note that whilst we intend to ensure that all data checks are complete prior to closedown, please be aware that there may still be some outstanding queries that will require your attention after the closedown paperwork has been submitted. We will do our best to ensure that these are, if any, kept to a minimum.

**Appendix 1**

**PhEAST Closedown Monitoring Checklist**

This checklist must be completed by a person delegated this role on the PhEAST trial delegation log. The PI (or a responsible person in R&D if no PI remains) must countersign the form and return it to the Trial Coordinating Centre (pheast@nottingham.ac.uk) in order to complete closedown for your site. Each item must be initialled. Once completed and signed, this checklist provides documented proof that all activities required for your centre closedown are completed and copies of all essential documents are held in the appropriate files in accordance with Good Clinical Practice and sponsor requirements.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Yes | No | N/A | Comments |
| (please initial) | | |
| Is there an Investigator Site File? |  |  |  |  |
| Does it contain the following: |  |  |  |  |
| a. Cover sheet  b. Trial office contact sheet V3.0 20240404  c. Investigator site file index |  |  |  |  |
| Section A Pre-Trial Opening | | | | |
| A.1 Trial Development Documentation   1. File note (this section is not applicable for the TSF and will be stored in the TMF at the coordinating centre). |  |  |  |  |
| A.2 Study protocol and associated documents – current versions    a. Signed Protocol  Current: v10.0 20240508  Superseded, *if applicable*:  v2.0 20211202  v3.0 20220225  v4.0 20220624  V5.0 20220809  v6.0 20221219  v7.0 20230328  v8.0 20231015  v9.0 20231121   1. Information Sheets and Consent Forms on local headed paper:   Current:  England   |  | | --- | | 1. Participant information sheet v4.0 20220809 | | 1. Participant consent form v3.0 20220513 | | 1. Aphasia Friendly PIS and ICF v2.0 20220809 | | 1. Consultee information sheet v6.0 20230328 | | 1. Consultee declaration form v4.0 20230328 | | 1. Consultee tel declaration form v3.0 20220513 | | 1. Participant re-consent form v3.0 20220513 | | 1. GP letter v3.0 20220513 | | 1. Informant information sheet v1.0 2022 20220624 | | 1. Informant consent form v3.0 20221219 | | 1. Informant tel consent form v3.0 20221219 |   Superseded *if applicable*:  England   |  | | --- | | 1. Participant information sheet v2.0 20211202 2. Participant information sheet v3.0 20220513 | | 1. Participant consent form v2.0 20211202 | | 1. Participant Short pictorial PIS v.0 v2.0 20211202 2. Participant aphasia friendly PIS and ICF 20220624 | | 1. Consultee information sheet v2.0 v2.0 20211202 2. Consultee information sheet V3.013/05/2022 3. Consultee information sheet V4.009/08/2022 4. Consultee information sheet v5.0 20221219 | | 1. Consultee declaration form v2.0 v2.0 20211202 2. Consultee declaration form v3.0 20220513 | | 1. Consultee tel declaration form v2.0 v2.0 20211202 | | 1. Participant re-consent form v2.0 v2.0 20211202 | | 1. GP letter v2.0 20211202 2. Informant consent form v1.0 20220627 3. Informant tel consent form v1.0 20220627 |   Current:  Scotland   |  | | --- | | 1. Participant information sheet v6.0 20230307 | | 1. Participant consent form v4.0 20230307 | | 1. Aphasia Friendly PIS and ICF v2.0 20221027 | | 1. Legal representative information sheet v6.0 20230307 | | 1. Legal representative consent form v5.0 20230307 | | 1. Legal representative telephone consent v5.0 20230307 | | 1. Participant re-consent form v5.0 20230307 | | 1. GP letter v3.0 20221027 | | 1. Informant consent form v2.0 20230307 | | 1. Informant information sheet v1.0 20220624 | | 1. Informant tel consent form v1.0 20220624 |   Superseded:  Scotland   |  | | --- | | 1. Participant information sheet v3.0 20220204 2. Participant information sheet v4.0 20220513 3. Participant information sheet v5.0 20221027 | | 1. Participant consent form v2.0 20220204 2. Participant consent form v3.0 20220513 | | 1. Participant Short pictorial PIS v.0 v2.0 20220204 2. Aphasia Friendly PIS and ICF v1.0 20220629 | | 1. Legal representative information sheet v3.0 20220204 2. Legal representative information sheet v4.0 20220513 3. Legal representative information sheet v5.0 20221027 | | 1. Legal representative consent form v2.0 20220104 2. Legal representative consent form v3.0 20220204 3. Legal representative telephone consent v4.0 20220513 | | 1. Legal representative telephone consent v3.0 20220204 2. Legal representative telephone consent v4.0 20220513 | | 1. Participant re-consent form v3.0 20220204 2. Participant re-consent form v4.0 20220513 | | 1. GP letter v2.0 20220104 2. Informant consent form v1.0 20220624 | |  |  |  |  |
| A.3 Approval and Agreements  a. Initial REC approval letter  England: dated 06/12/2021  Scotland: dated 09/02/2022  b. Initial HRA Approval letter 07/01/2022  c. Site-specific approvals  (i) Sponsor Regulatory Greenlight  (ii) R&D approval  (iii) Signed non-commercial research agreement  (iv) Organisation Information Document (OID) *(if applicable)*  d. Additional HRA documents  (i) SoECAT (authorised 13/06/2023)  (ii) SoECAT (authorised: 11/03/2020) (superseded)  e. Original IRAS form  304658 dated 04/10/2021  f. Sponsorship statement 04.10.2021  g. Letters of Insurance, dated:  (i) 1st Aug 2021 – 31st July 2022  (ii) 1st Aug 2022 – 31st Aug 2023  (iii) 1st Aug 2023 - 31st Jul 2024  (iv) 1st Aug 2024 – 31st Jul 2025 |  |  |  |  |
| A.4 Staff Participation  a. File Note A4 Site File – Delegation Logs  b. Signed and dated CVs and GCP (in date) updated as per site’s policies and procedures for all staff on the delegation log   1. Attendance at Investigator Training (RF1 TA008) signed by all staff on the delegation log 2. Phagenesis Training Log (RF1TA008) 3. Training slides: 4. V8.0 20231122 5. V7.0 20230503 (superseded) 6. V6.0 20230127 (superseded) 7. V5.0 20221214 (superseded) 8. V4.0 20221027 (superseded) 9. V3.0 20220811 (superseded) 10. V2.0 20220328 (superseded) 11. V2.1 20220412 (superseded) 12. V2.2 20220504 (superseded) 13. V2.3 20220527 (superseded)   **OR FILE NOTE TO STATE WHERE LATEST VERSION IS KEPT (I.E WEBSITE)**  g. FAQS  **OR FILE NOTE TO STATE WHERE LATEST VERSION IS KEPT (I.E WEBSITE)** |  |  |  |  |
| A.5 Medical Testing and Pharmacy *(where applicable)*  Confirmation of MPE approval |  |  |  |  |
| A.6 Randomisation and Blinding  a. Coordinating centre file note v1.0 20231301 |  |  |  |  |
| A.7 Database Build  a. Coordinating centre file note – not applicable for the TSF (stored in the TMF at the coordinating centre) |  |  |  |  |
| Section B: Ongoing Trial | | | | |
| B.1 Study Protocol Amendments and Approvals  a. RF1 TA013 Amendment Log |  |  |  |  |
| B.2 Staff Participation (ongoing trial)  Updated training logs |  |  |  |  |
| B.3 Informed Consent  a. Signed informed consent forms *(or file note to state these are stored within patient files)1*  b. Signed GP letters *(or file note to state these are stored within patient files)1*  d. Participant screening and enrolment log (RF1 TA011) |  |  |  |  |
| **B.4 Medical Testing and Pharmacy**  a. Evidence that base station has been approved for use internally.  b. Supplies log V1.0 20220308 |  |  |  |  |
| **B.5 CRFs and Source Documents**  File note documenting where source documents and patient files1 are kept. |  |  |  |  |
| B.6 Serious Adverse Events  a. SAE report forms signed and dated by PI (where applicable – may be electronic on REDCap) (Check all SAEs on website have been printed and signed by PI, report as all seen or otherwise report those missing which need adding).  b. Safety reporting notifications (where applicable)  c. Protocol violation report forms (where applicable) |  |  |  |  |
| B.7 Biological Materials  a. Coordinating centre file note v1.0 20230201 |  |  |  |  |
| B.8 Audit and Reporting   1. Site Visit Log (1.0 20220217) 2. Monitoring reports for previous visits (if applicable) 3. Completed monitoring visit action lists (if applicable) |  |  |  |  |
| B.9 Miscellaneous   1. Relevant, important correspondence. 2. File note template (V1.0 20220218). 3. Completed file notes. 4. WPDs *(or file note to say these are viewed on PhEAST documents website):* 5. 001 Screening and Enrolment Log 6. 002 Consent 7. 003 Manual Randomisation 8. 004 Decontamination of Equipment 9. 005 Site Monitoring 10. 008 blinding 11. 009 Document Preparation 12. 010 Secure Vault Uploads 13. 011 Cognition Sub-study 14. 012 Randomisation   e. Newsletters |  |  |  |  |

1 Trial patient files must be retained and archived along with the ISF.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Data entry is completed for all participants, and all data reflects source documentation:** | | **Initials** | | |
| YES | NO | N/A |
| 1 | Eligibility. |  |  |  |
| 2 | Baseline data (Day-000; Day-000 Clinical; Day-000 EQ-5D-5L; Day-000 Cognition; Day-000 IQCODE). |  |  |  |
| 3 | PES Treatments 1-6. |  |  |  |
| 4 | Day-14 data (Day-14 Primary Outcome; Day-14 EQ-5D-5L; Day-14 Cognition). |  |  |  |
| 5 | Discharge or death *(if applicable).* |  |  |  |
| 6 | Withdrawal *(if applicable).* |  |  |  |
| 7 | Device deficiency *(if applicable).* |  |  |  |
| 8 | Protocol violations and protocol deviations *(if applicable).* |  |  |  |
| 9 | SAEs *(if applicable).* |  |  |  |

Further comments:

I can confirm that all queries relating to any trial participant involvement have been resolved and all essential documentation is in place before archiving.

Principal Investigator Signature: ………………………………………………

Name (block capitals): ……………………………………………………….....

Signature of those who have initialled work as completed:

Name Signature Initials Date

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**Please note that archiving of all the documents cannot take place until after the publication of results.**