Introduction

To ensure that the TARDIS 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. Due to the number of centres and the resources available, the Sponsor of TARDIS (University of Nottingham) has agreed a procedure to allow the close down of all TARDIS centres which have not recruited any participants, remotely, using the TARDIS Closedown Checklist (Appendix 1),

Purpose of this document

To define the procedure for closing out centres participating in the TARDIS trial and ensure all essential documentation for TARDIS 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**". TARDIS is likely to be published in March 2016 therefore documents must be archived until March 2025 in accordance with local archiving protocols. 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

The last day of randomisation for TARDIS was 12 April 2016 - .the web randomisation was closed to recruitment at midnight (24:00hours; GMT) on this date.

A centre will not be closed until all trial data, scans and queries have been received for all patients randomised into the trial. Any final per patient payments due will only be paid once all documentation is received. This needs to be received by the end of June 2017 otherwise the grant account will have ceased to be operational.

Reconciliation of Investigational Medicinal Product (IMP)

All aspirin, dipyridamole and clopidogrel for use in the TARDIS trial must be removed from clinical areas following the end of trial recruitment. All unused stock must be returned and accounted for by the Responsible Trial Pharmacist.

Payments

Any centre payments due will only be paid once all documentation is received. This needs to be received by the end of June 2017 otherwise the grant account will have ceased to be operational.

Closedown procedure

The attached TARDIS Closedown Monitoring Checklist must be completed, signed and returned to the Trial Coordinating Centre to confirm that all the essential documentation is present and ready to be archived at your site.

For centres which have randomised participants, an on-site closedown visit will be made by a UK Trial Co-ordinator and the form will be commenced at this time by the Co-ordinator and the site investigator involved in the visit.

Any outstanding items after the visit must be resolved before sending the completed form back to the Co-prdinating Centre in Nottingham.

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

TARDIS Closedown Monitoring Checklist

This checklist must be completed by a person delegated this role on the TARDIS 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 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.

Centre Name: …… **Centre Number: C……** **Name of PI: ……**		**Number of TARDIS Patients recruited** _____ **(See online recruitment list)**		
Reason for closedown:			**Initials**	
Essential documentation required for closedown and archiving		YES	NO	N/A
INVESTIGATOR SITE FILE (ISF) contains:				
• Latest contact details of trial office & emergency numbers.				
• Latest Trial delegation log • All 'old' versions' of delegation log				
• Signed & dated CVs (for everyone listed on the delegation log)				
• GCP certificates for all investigators on the delegation log. (These must cover the duration of teach investigator's role in the trial)				
• Signed & dated current protocol V1.5				
• Relevant archived protocols (since commencing the trial)	List:			
• All current approved Information Sheets and Consent Forms. (V1.5) (On hospital headed paper)				
• Relevant archived Information Sheets and Consent forms				

• Current approved GP letter (V1.3a)				
• Archived approved GP letters				
• Local R&D approval letters (from initial approval to take part and for all subsequent substantial amendments approved).				
• Copies of correspondence with Ethics (commencing with initial approval letter for trial, approval for site and all subsequent substantial amendments relating to changes of protocol, consent forms, information sheets and GP letters).				
• MHRA approval and amendments (As ethics above)				
• Sponsor letters				
• Insurance letters (to cover the duration of your site taking part in the trial).				
• Signed contract (between University of Nottingham as Sponsor and your hospital)				
• Completed Trial Drug Accountability log(s)				
• SmPCs for IMP				
• Screening log(s)				
• Filenote stating where CRFs can be found.				
• SUSAR information				
• SAE reports signed/dated by PI				
• Site monitoring reports				
• Annual reports (R&D)				
• Ward Temperature monitoring logs (where IMP held on the ward)				
• Lab Accreditation certificates filed				
• Normal Lab ranges filed				
• Completed Trial blood sample freezer log				

• Freezer log sent to Co-ordinating Centre to arrange collection				
• All blood samples collected by Coordinating centre				
• Patient contact details (may be stored separately, from the ISF) **Patient contact details must be kept until all the trial paperwork is actually archived, then they must be destroyed as per protocol.**				
• Master Signed Consent forms for the Main Trial (and DNA where applicable) for all participants. (if stored separately raise a trial filenote to indicate the name of the file and where it can be found)				
• TARDIS CLINICAL TRIAL FINAL REPORT	The report will be available on our investigator website, to be downloaded and filed prior to archiving trial documents.			
CLOSEDOWN DOCUMENTS HRA/Ethics/MHRA and signed/completed Wpd040				
ALL PARTICIPANT TRIAL FILES contain anonymised versions of the following where applicable:				
• CT/MR/carotid reports				
• Completed up to date paper CRFs (or printout reports if data entered directly onto the website)				
• Any completed SUSAR forms				
• Completed protocol deviation & violation forms				
• Completed data correction forms				
• Source documents (medical records for all trial patients have been labelled that the patient is in TARDIS trial and will be required to be archived – kept until 7 years after publication of trial)				

DATA ENTRY is completed for all:				
• Randomisation				
• Baseline				
• Day 7 follow-up				
• Day 35 follow-up				
• Hospital event				
• SAE/Outcome events • SUSARS				
All radiology scans for the participants randomised have been uploaded to the TARDIS website (or sent on CD).				
PHARMACY SITE FILE (ISF) and contents				

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
…….	……..	…….	…….
…….	……..	…….	…….
…….	……..	…….	…….
…….	……..	…….	…….

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