

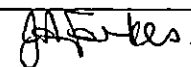
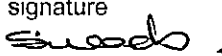

# Trial Delivery 04 – End of Trial procedures – Close Down

**IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED**

All staff should regularly check the Research & Development Webpage for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded version are promptly withdrawn from use unless notified otherwise by the SOP Controller.

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<http://www.gloshospitals.nhs.uk/en/About-Us/Research--Development/>

<b>SOP reference:</b>	R&D SOP TD04	
<b>Version:</b>	3.0	
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<b>Reviewed by Associate Director of R&amp;D</b>	Julie Hapeshi 27/03/2018	
<b>Implementation date of current version:</b>	31/03/2018	
<b>Date of Review:</b>	01/10/2018	

The Gloucestershire Hospitals NHS Foundation Trust wishes to acknowledge York Hospitals NHS Foundation Trust and University Hospitals Bristol NHS Foundation Trust who gave permission to use their templates in the development of these SOPs.

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## VERSION HISTORY LOG

This area will be updated with details of all changes made to the SOP whether due for full review or not.

Version	Details of Change	Date Implemented
1.0	Original SOP	29/12/2014
2.0	Review and update on storage of information in Pharmacy files trials which do not recruit a participant	03/02/2017
3.0	Rebranding to GHNHSFT, updating of contact details and reference documents	31/03/2018

This SOP will be reviewed every two years unless changes to any relevant legislation require otherwise

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## 1. Introduction, Background and Purpose

The purpose of this SOP is to set out the matters to be considered upon the completion of a trial and the steps to be taken, including the notification of relevant bodies.

In this SOP the phrase 'Close Down' will be used throughout and is synonymous with 'Close Out' and 'Completion'. Typically 'Close Out' refers to the official visit of the Sponsor or delegated representative to a participating site to review documentation before formally closing the trial at that site.

There are three written documents which are produced at the end of the trial:

- 1) Declaration of End of Trial ( see appendices 1,2,3 and 4)
- 2) End of Trial Report - there is no proforma for this but guidance states that it should include whether the study achieved its objectives, the main findings, and arrangements for publication or dissemination of the research, including any feedback to participants.

At the end of the trial, commitments made to research participants must be fulfilled. 'Care after research' (See HRA website) states that responsible transition of participants out of the trial may include:

- Making arrangements for aftercare;
- Ensuring safety;
- Communicating with caregivers;
- Sharing information with participants: aggregate results and, as appropriate, individual results and incidental findings;
- Showing appreciation; and
- Resolving any deception.

- 3) Clinical Study Report (CSR)/ Publication

This document accurately reflects the objectives of the trial the summary of what happened and the outcome or results. (See information on the NIHR Clinical trial toolkit)

## 2. Who should use this SOP

### 2.1 Trust Sponsored or Co-sponsored Trials

- Sponsor
- Chief Investigators (CIs),
- Research Nurses
- Trial co-ordinators,
- Clinical Study Officers
- Health professionals
- Administrative research staff
- Research links in support departments
- R&D team

- Any contracted CROs

The Sponsor may delegate the tasks involved in trial completion to the CI or external vendor but must have mechanisms in place to maintain oversight of the delegated activities.

## **2.2 Trust hosted trials**

- Principal Investigators (PIs)
- Research Nurses
- Trial co-ordinators,
- Clinical Study Officers
- Health professional
- Administrative research staff
- Research links in support departments
- R&D team

The PI may delegate the responsibility for trial completion activities to members of the research team duly documented on the delegation log.

## **3. When this SOP should be used?**

This SOP will be used at the end of the trial as defined in the trial protocol (the end of the recruitment period does not automatically signify the end of the trial). It will be used for all the following types of research:

- a CTIMP or a non-CTIMP that is sponsored or co-sponsored by the Trust
- a CTIMP or a non-CTIMP hosted by the Trust taking into consideration an SOP for this purpose provided by the trial Sponsor SOP

## **4. Process for close down of Trust sponsored trials**

### **4.1 Who is responsible for the Declaration of the end of trial**

- It is the responsibility of Sponsor, to notify the main REC, the MHRA, EuDRACt and the CI and every participating site of the end of the trial. ( Appendix 1 Trial Completion Declaration MHRA notification forms; NHS HRA website for REC notification; EuDRACt documentation ). Note that once the declaration of the end of a clinical trial form has been received by the competent authority only the clinical trial summary report will be accepted no further amendments can be submitted.
- The Sponsor may delegate this task to the CI.
- Where there has been a clinical trial of an investigational medical device the manufacturer will notify the MHRA.

## **4.2 Final analysis of data and locking of database**

- Final analysis of data will take place promptly after the appropriate follow-up period, following the details in the trial protocol and or the Statistical Analysis Plan (SAP).
- Analysis of the data will be recorded in an analysis plan with all the outcome measures set out in the protocol fully addressed. The analysis will be discussed by the trial management group (if applicable) to assist with interpretation and discuss findings
- The trial database will then be locked at this stage and no further modification or manipulation

## **4.3 Time lines for end of trial reporting**

### **4.3.1 At the conclusion of the trial**

The Sponsor/ CI must notify the competent authorities that the clinical trial has ended within 90 days of the conclusion of the trial as defined in the protocol. All this information can be sent by email to both the REC and MHRA. Note that the MHRA can be informed separately by email of the end of the trial in the UK when other non-UK sites remain active in order to terminate the annual service charge, however this is a separate process from the formal notification of the end of trial ( refer to MHRA website for details).

### **4.3.2 Early termination of the trial**

If the trial is terminated early the competent authorities must be notified immediately and at the latest within 15 days after the trial is halted. This applies to early termination due to safety measures, financial or business difficulties or very slow recruitment. This does not apply to a trial which has reached full recruitment early. A notice of substantial amendment can be submitted alongside a declaration of early termination where it is necessary to seek ethical review of related actions such as informing trial participants of the early closure and arranging continuing care and follow up outside the trial setting.

### **4.3.3 Abandoned Trials**

If a trial is abandoned prior to recruitment starting the Sponsor/ CI will notify the competent authorities by letter outlining the reasons for abandoning the trial.

### **4.3.4 End of Trial Report to R&D**

The CI is must submit an end of trial report to the Trust Senior Research Manager within 10 months of the date of the end of trial.

#### **4.3.5 End of Trial Report to Competent Authorities**

The CI, acting on behalf of the Sponsor is responsible for submitting the end of trial report to the REC and MHRA to arrive within 12 months of the date of the end of the trial.

#### **4.3.6 Clinical Study Report (CSR) / Publications**

The production and quality control (QC) of the CSR/ Publication will be defined and approved by the Sponsor and overseen by the Trial Management Committee (TMC).

The CSR and/or Publication will reflect the conduct of the trial and provides a summary of the results including a list of all the significant non-compliances (see R&D SOP Ph04 Non-Compliance Serious Breaches) that occurred during the trial and how these have contributed to the analysis of the trial data.

A statement of compliance with GCP will be included in the CSR/ Publication.

#### **4.4 Close down and essential documentation**

- In the case of a multi-centre trial the Sponsor/ CI and the central team will arrange a Close-Down monitoring visit for each site. Support departments (e.g. pharmacy) should also be notified in order that they can prepare for Close-Down.
- All essential documentation for a particular site must be confirmed to be in the appropriate files which provide clear audit trails of the trial conduct at the site. All issues raised in previous monitoring reports must be resolved and fully documented in reports and site file notes.
- Before close down all site data will be collected, entered and validated. All data queries will be resolved where feasible.
- All unused trial supplies will be returned or destroyed according to the trial protocol and trial agreement.
- Final drug accountability will be fully documented at site (TPF) and in the TMF. Drugs will be returned or destroyed at site according to the trial protocol and site agreement and certificates of destruction files in the site file.
- Where regulatory authority approval is in place participants samples or data will be contributed to existing bio-bank or data-sharing repositories.
- All financial matters will be resolved and site payments are complete as agreed and documented in the site agreement.
- The Trial Master File (TMF) must be organized ensuring all necessary documents are present (see R&D SOP TD 01 Managing Trial Master File, Trial Site File and Trial Pharmacy File).

- The CI site will not be closed until all participating sites have been closed down.
- Instigate archiving procedures (see R&D SOP TD 05 Trial Archiving)

## 5. Trust Hosted Trials

### 5.1. PI responsibilities

- The PI or delegated senior member of the research team must confirm that all trial related activities have stopped.
- The PI or delegated senior member of the research team must ensure a full in-house reconciliation of all documentation has been performed.
- A complete Quality Assurance review of the study must be performed, and any corrective action, including the addition of file notes must be performed and documented prior to transfer for archiving.
- For some trials, the trial office / sponsor may send a representative to the site to complete a final close down visit to confirm that all procedures have been completed correctly prior to archiving of study documentation.

### 5.2 Whole Site Responsibilities

All departments that have collected or generated documents during the conduct of the trial must transfer upon request these documents to the responsible senior member of the research team for the final reconciliation of the ISF.

#### 5.2.1 Pharmacy

The pharmacist responsible for the trial will review and document the final accounting of IMP(s) received at the site, dispensed to subjects, returned to sponsor, or the method and date of destruction of unused IMP(s) at site as detailed in the trial protocol and site agreement.

When all essential documents have been filed in the Trial Pharmacy File (TPF) it is to be returned to the delegated senior member of the research team for archiving alongside the ISF. In some circumstances, the TPF may be archived by the Pharmacy Department, depending on the protocol. In such cases, the ISF will include a site file note stating the location of the TPF.

In the case that a trial has not recruited a participant during the time it has been open to recruitment the research pharmacist should check exactly what documentation is required in the Pharmacy File. If the Sponsor is in agreement then site file notes listing the Summary of Product Characteristics (SmPC) and where they can be found electronically can be used and the paper copies destroyed to minimise storage requirements.



## 5.2.2 Clinical Samples

The wishes of the participants as documented on their consent forms will dictate whether clinical samples will be stored in accordance with the trial protocol, site agreement and the Human Tissue Act or disposed of.

## 5.3 Close down and essential documentation

It must be noted that not all 'essential documentation' may be in paper form (see Appendix 8). Electronic registers must also be 'archived' according to Trust IT Policies and Guidelines. (see appendix 9)

## 6. Related SOPs and Documents

R&D SOP TD01 Managing Trial Master File, Trial Site File and Trial Pharmacy File  
R&D SOP TD05 Archiving

### MHRA end of trial

End a trial:

<https://www.gov.uk/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#end-of-trial>

Suspend or terminate a trial:

<https://www.gov.uk/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#suspend-or-terminate-a-trial>

End of trial for medical devices

<https://www.gov.uk/notify-mhra-about-a-clinical-investigation-for-a-medical-device>

### NIHR clinical trials tool kit

<http://www.ct-toolkit.ac.uk/routemap/clinical-trial-summary-report>

### NHS HRA website REC end of trial reporting

<http://www.hra.nhs.uk/resources/during-and-after-your-study/end-of-study-notification-clinical-trials-of-investigational-medicinal-products-ctimps-eudract-form/>

### EudraCT website for 'declaration' proforma

<https://eudract.ema.europa.eu/document.html>

### HRA Notification of end of study to Confidentiality Advisory Group

<http://www.hra.nhs.uk/research-community/end-of-study-and-beyond/notifying-the-end-of-study/>

## Care of participants after the trial has stopped

<http://www.hra.nhs.uk/documents/2013/08/care-after-research.pdf>

## European Directive (2010/C 82/01)

Communication from the Commission — Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial (CT-1)

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2010:082:0001:0019:en:PDF>

**Appendix 1 - Declaration of the end of trial form**

<http://www.hra.nhs.uk/resources/during-and-after-your-study/end-of-study-notification-clinical-trials-of-investigational-medicinal-products-ctimps-eudract-form/>

**Declaration of the End of Trial Form (cf. Section 4.2.1 of the *Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of the trial*<sup>1</sup>)**

**NOTIFICATION OF THE END OF A CLINICAL TRIAL OF A MEDICINE FOR HUMAN USE TO THE COMPETENT AUTHORITY AND THE ETHICS COMMITTEE**

*For official use*

Date of receipt :	Competent authority registration number : Ethics committee registration number:
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**To be filled in by the applicant**

**A MEMBER STATE IN WHICH THE DECLARATION IS BEING MADE :**

**B TRIAL IDENTIFICATION**

<b>B.1 EudraCT number :</b>	(..)
<b>B.2 Sponsor's protocol code number:</b>	(..)
<b>B.3 Full title of the trial :</b>	

**C APPLICANT IDENTIFICATION (please tick the appropriate box)**

<b>C.1 DECLARATION FOR THE COMPETENT AUTHORITY</b>	<input type="checkbox"/>
C.1.1 Sponsor	<input type="checkbox"/>
C.1.2 Legal representative of the sponsor	<input type="checkbox"/>
C.1.3 Person or organisation authorised by the sponsor to make the application.	<input type="checkbox"/>
<b>C.1.4 Complete below:</b>	
C.1.4.1 Organisation :	
C.1.4.2 Name of person to contact :	
C.1.4.3 Address :	
C.1.4.4 Telephone number:	
C.1.4.5 Fax number :	
C.1.4.6 E-mail	

<sup>1</sup> OJ, C82, 30.3.2010, p. 1; hereinafter referred to as 'detailed guidance CT-1'.

<b>C.2</b>	<b>DECLARATION FOR THE ETHICS COMMITTEE</b>	<input type="checkbox"/>
C.2.1	Sponsor	<input type="checkbox"/>
C.2.2	Legal representative of the sponsor	<input type="checkbox"/>
C.2.3	Person or organisation authorised by the sponsor to make the application.	<input type="checkbox"/>
C.2.4	Investigator in charge of the application if applicable <sup>2</sup> :	
	• Co-ordinating investigator (for multicentre trial):	<input type="checkbox"/>
	• Principal investigator (for single centre trial):	<input type="checkbox"/>
C.2.5	<b>Complete below :</b>	
C.2.5.1	Organisation:	
C.2.5.2	Name :	
C.2.5.3	Address :	
C.2.5.4	Telephone number :	
C.2.5.5	Fax number :	
C.2.5.6	E-mail :	

## D END OF TRIAL

<b>D.1</b>	<b>Date of the end of the complete trial in all countries concerned by the trial?</b>
D.1.1	(YYYY/MM/DD):

<b>D.2</b>	<b>Is it an early termination?<sup>3</sup></b>	yes <input type="checkbox"/> no <input type="checkbox"/>
D.2.1	If yes, give date (YYYY/MM/DD):	
D.2.2	Briefly describe in an annex (free text):	
D.2.2.1	The justification for early termination of the trial;	
D.2.2.2	Number of patients still receiving treatment at time of early termination in the MS concerned by the declaration and their proposed management;	
D.2.2.3	The consequences of early termination for the evaluation of the results and for overall risk benefit assessment of the investigational medicinal product.	

## E SIGNATURE OF THE APPLICANT IN THE MEMBER STATE

<b>E.1</b>	I hereby confirm that/confirm on behalf of the sponsor that (delete which is not applicable):
	<ul style="list-style-type: none"> <li>• The above information given on this declaration is correct; and</li> <li>• That the clinical trial summary report will be submitted within the applicable deadlines in accordance with the applicable guidance by the Commission.<sup>4</sup></li> </ul>

<b>E.2</b>	<b>APPLICANT TO THE COMPETENT AUTHORITY</b> (as stated in C.1)	<input type="checkbox"/>
E.2.1	Date :	
E.2.2	Signature :	
E.2.3	Print name:	

<b>E.3</b>	<b>APPLICANT TO THE ETHICS COMMITTEE</b> (as stated in C.2) :	<input type="checkbox"/>
E.3.1	Date :	
E.3.2	Signature :	
E.3.3	Print name:	

<sup>2</sup> According to national legislation.

<sup>3</sup> Cf. Section 4.2. of the detailed guidance CT-1.

<sup>4</sup> Section 4.3. of the detailed guidance CT-1.

**Appendix 2 Health Research Authority end of study procedures for nonCTIMP studies**

<http://www.hra.nhs.uk/research-community/end-of-study-and-beyond/notifying-the-end-of-study/>

**DECLARATION OF THE END OF A STUDY**

(For all studies except clinical trials of investigational medicinal products)  
 To be completed in typescript by the Chief Investigator and submitted to the Research Ethics Committee (REC) that gave a favourable opinion of the research within 90 days of the conclusion of the study or within 15 days of early termination. For questions with Yes/No options please indicate answer in bold type.

**1. Details of Chief Investigator**

Name:	
Address:	
Telephone:	
Email:	
Fax:	

**2. Details of study**

Full title of study:	
Research sponsor:	
Name of REC:	
REC reference number:	

**3. Study duration**

Date study commenced:	
Date study ended:	
Did this study terminate prematurely?	<p style="text-align: center;"><b>Yes / No</b></p> <p><i>If yes, please complete sections 4, 5, 6, &amp; 7.                  If no, please go direct to section 8.</i></p>

**4. Recruitment**

Number of participants recruited	
Proposed number of	

participants to be recruited at the start of the study	
If different, please state the reason or this	

### 5. Circumstances of early termination

What is the justification for this early termination?	
---	--

### 6. Temporary halt

Is this a temporary halt to the study?	Yes / No
If yes, what is the justification for temporarily halting the study? When do you expect the study to re-start?	<i>e.g. Safety, difficulties recruiting participants, trial has not commenced, other reasons.</i>

### 7. Potential implications for research participants

Are there any potential implications for research participants as a result of terminating/halting the study prematurely? Please describe the steps taken to address them.	
--	--

### 8. Final report on the research

Is a summary of the final report on the research enclosed with this form?	Yes / No <i>If no, please forward within 12 months of the end of the study.</i>
---	--

### 9. Declaration

Signature of Chief Investigator:	
Print name:	
Date of submission:	

**Appendix 3 After Completion or Termination of the Trial - locality of documentation**

Title of Document	Purpose	Located in Files of	
		Investigator/ Institution	Sponsor
INVESTIGATIONAL PRODUCT(S) ACCOUNTABILITY AT SITE	To document that the investigational product(s) have been used according to the protocol. To documents the final accounting of investigational product(s) received at the site, dispensed to subjects, returned by the subjects, and returned to sponsor	X	X
DOCUMENTATION OF INVESTIGATIONAL PRODUCT DESTRUCTION	To document destruction of unused investigational products by sponsor or at site	X (if destroyed at site)	X
COMPLETED SUBJECT IDENTIFICATION CODE LIST	To permit identification of all subjects enrolled in the trial in case follow-up is required. List should be kept in a confidential manner and for agreed upon time	X	

Title of Document	Purpose	Located in files of	
		Investigator/ institution	Sponsor
TREATMENT ALLOCATION AND DECODING DOCUMENTATION	Returned to sponsor to document any decoding that may have occurred		X
FINAL REPORT BY INVESTIGATOR TO IRB/IEC WHERE REQUIRED, AND WHERE APPLICABLE, TO THE REGULATORY AUTHORITY(IES)	To document completion of the trial	X	
CLINICAL STUDY REPORT	To document results and interpretation of trial	X  (if applicable)	X
FINAL TRIAL CLOSE-OUT MONITORING REPORT	To document that all activities required for trial close-out are completed, and copies of essential documents are held in the appropriate files		X



## **Appendix 4**

Countywide IT policies

Information Governance policy

[http://glnt313/sites/ghnhsft\\_policy\\_library/NonClinPolicies/B0413.pdf](http://glnt313/sites/ghnhsft_policy_library/NonClinPolicies/B0413.pdf)

Clinical and non clinical information systems

[http://glnt313/sites/ghnhsft\\_policy\\_library/NonClinPolicies/B0259.pdf](http://glnt313/sites/ghnhsft_policy_library/NonClinPolicies/B0259.pdf)

IT Security

[http://glnt313/sites/ghnhsft\\_policy\\_library/NonClinPolicies/B0591.pdf](http://glnt313/sites/ghnhsft_policy_library/NonClinPolicies/B0591.pdf)

Portable IT equipment and removal media

[http://glnt313/sites/ghnhsft\\_policy\\_library/Procedures/B0692.pdf](http://glnt313/sites/ghnhsft_policy_library/Procedures/B0692.pdf)

Information Governance Forensic Readiness

[http://glnt313/sites/ghnhsft\\_policy\\_library/Procedures/B0693.pdf](http://glnt313/sites/ghnhsft_policy_library/Procedures/B0693.pdf)

Mont. O. of Health