South Eastern Health and Social Care Trust

Standard Operating Procedures (SOP) Research and Development Office

Title of SOP:	Notification of End of Study
SOP Number:	22
Version Number:	2.0
Supercedes:	1.0
Effective date:	August 2013
Review date:	August 2015

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Date:	01 August 2013

Version History:

Version No.	Date	Author	Reason for Change
1.0	Sept 2007	Katrina Hughes	N/A
2.0	Aug 2011	Alison Murphy	Updated to new SOP layout. Expanded guidance on early termination and suspension. Included requirement to submit final report to MHRA. Included documents in appendices

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1. INTRODUCTION

The Medicines for Human Use (Clinical Trial) Regulations (2004) and the National Research Ethics Service (NRES) states that for all Clinical Trials of Investigational Medicinal Products (CTIMPs) and for all other research (non-CTIMPs), written notification of the end of study should be provided within 90 days of the end of project, or within 15 days if the project is terminated early.

2. OBJECTIVE

The purpose of this Standard Operating Procedure (SOP) is to describe the procedure for notifying the Research Ethics Committee (REC), Sponsor and Medicines and Healthcare product Regulatory Agency (MHRA) of the end of a research study.

3. SCOPE

All non commercial research undertaken in South Eastern Health & Social Care Trust both Clinical Trials of Investigational Medicinal Products (CTIMPs) and all other research (non-CTIMPs).

4. PROCESS

The definition of the end of a study should be provided in the protocol and any changes to this should be notified as a substantial amendment. In most cases, it will be the date of the last visit of the last participant undergoing the study or the completion of any follow-up monitoring and data collection described in the protocol. The end of the recruitment period does not automatically signify the end of the trial.

Final analysis of the data (following 'lock' of the study database) and report writing is normally considered to occur after formal declaration of the end of the study.

4.1 Notification of End of Study for Clinical Trials of Investigational Medicinal Products (CTIMPs)

It is the responsibility of the sponsor (or the sponsor's representative) to notify the MHRA and main REC of the end of the trial, within 90 days of the trial conclusion, using the EudraCT Declaration of the End of a Clinical Trial Form (Appendix 1).

Submission of the form to the MHRA should be electronic. Applicants should submit electronic documents on disk, with one PDF file for each document. All disks should be sent to:
Information Processing Unit
Area 6
MHRA

151 Buckingham Palace Road
Victoria
SW1W 9SZ

The MHRA will acknowledge receipt of the End of Trial Declaration.

The form should also be submitted to the REC which gave a favourable opinion of the research (the 'main REC')

For South Eastern Health and Social Care Trust sponsored studies, this responsibility is delegated to the Chief Investigator (CI). The CI must provide a copy of this form to the Trust Research Office and a copy of the MHRA acknowledgement.

For CTIMPs not sponsored by the South Eastern Health and Social Care Trust the Trust PI should obtain a copy of the End of Trial Declaration from the study sponsor and submit to the Research Office.

Once the declaration of the end of a clinical trial form has been received only the end of trial study report will be accepted, it is not possible to submit any further amendments to the trial once the end of trial declaration has been received.

4.1.2 Early Termination

If a trial is prematurely terminated before the date for conclusion as specified in the protocol (or the event specified in the protocol as the event which indicates the end of the trial has not occurred) then the sponsor (or the sponsor's representative) should notify the MHRA and REC within 15 days of the date of termination and clearly explain the reasons for termination.

For South Eastern Health and Social Care Trust sponsored studies, this responsibility is delegated to the Chief Investigator (CI), however the CI must seek approval of the Trust Research Office BEFORE acting with delegated responsibility. If the early termination of the trial is approved, the CI must provide a copy of the form to the Trust Research Office and a copy of the MHRA acknowledgement.

4.1.2 Trial Temporarily Suspended

If the trial is to be halted temporarily, this should be notified to the MHRA and main REC by submitting a notice of substantial amendment within 15 days. The form should clearly explain the reasons for the halt and the scope, e.g. stopping recruitment and/or interrupting the treatment of participants already included.
To re-start a trial that has been temporarily halted the sponsor must make the request as a substantial amendment and provide evidence that it is safe to do so (such as a Data Monitoring Committee review). If a sponsor decides not to recommence a halted trial, the MHRA and REC must be notified within 15 days of it decision using the Declaration of End of Trial Notification Form and include a brief explanation for ending the trial.

For South Eastern Health and Social Care Trust sponsored trials, this responsibility is delegated to the Chief Investigator (CI), however the CI must seek approval of the

Trust Research Office BEFORE acting with delegated responsibility. If the suspension of the trial is approved, the CI must provide a copy of the substantial amendment form to the Trust Research Office.

4.1.3 Trial Does Not Commence

If the CI decides not to commence the trial, they should notify the MHRA, REC and Sponsor and clearly explain the reasons for not starting the trial.

4.1.4 Trials that Commenced before 1st May 2004

If the trial was commenced before 1st May 2004 as a Clinical Trial Exemption (CTX) and Doctors and Dentist Exemption (DDX) study, a CT Form UK 1 must also be completed by the CI with the Declaration of End of Trial Notification form. This is because limited information was required at the time of application for a CTX/DDX, the MHRA have been unable to process end of trial notifications electronically and resulted in delays. A CT form UK1 need only be completed once, therefore if it was already completed in order to submit a substantial amendment after 1st October 2007 it need not be submitted again, just the declaration of end of trial form.

4.2 Notification of End of Study for all Other Research (non-CTIMPs)

For all research studies other than CTIMPs, the chief investigator should notify the REC which gave a favourable opinion of the research (the 'main REC') and the Sponsor of the conclusion or early termination of a project using the NRES Declaration of the End of a Study form (Appendix 2).

For South Eastern Health and Social Care Trust sponsored studies, this responsibility is delegated to the Chief Investigator (CI). The CI must provide a copy of this form to the Trust Research Office and a copy of the REC acknowledgement.

For studies not sponsored by the South Eastern Health and Social Care Trust the Trust PI should obtain a copy of the Declaration of the End of a Study form from the study sponsor and submit to the Trust Research Office.

4.2.1 Study Temporarily Suspended for all Other Research (non-CTIMPs)

If a study is to be halted temporarily for safety reasons, this should be notified to the main REC by submitting a notice of substantial amendment. The form should clearly explain the reasons for the halt and the scope, e.g. stopping recruitment and/or interrupting the treatment of participants already included.

To restart the study, a further notice of substantial amendment should be submitted for ethical review. Evidence should be provided that it is safe to restart the trial. If the sponsor decides not to recommence the trial after a temporary halt, the end of the study should be declared.

For South Eastern Health and Social Care Trust sponsored studies, this responsibility is delegated to the Chief Investigator (CI), however the CI must seek

approval of the Trust Research Office BEFORE acting with delegated responsibility. If the suspension of the study is approved, the CI must provide a copy of the substantial amendment form to the Trust Research Office.

4.3 Final report on the research

The sponsor must submit the end of trial study report to the MHRA and main REC within one year of the end of the trial. Where this is a multi-national study this is the end of study in all participating countries and not just in the UK.

There is no standard format for final reports. As a minimum, the main REC and MHRA should receive information on whether the project achieved its objectives, the main findings and arrangements for publication or dissemination of the research, including any feedback to participants. A template for the final report is provided in appendix 3.

For South Eastern Health and Social Care Trust sponsored studies, this responsibility is delegated to the Chief Investigator (CI), the CI must provide a copy of this report to the Trust Research Office.

For studies not sponsored by the South Eastern Health and Social Care Trust, the Trust PI should obtain a copy of the final report from the study sponsor and submit to the Trust Research Office.

5. REGULATIONS, GUIDELINES, REFERENCES, SOP LINKS ETC

MRC Clinical Trial Toolkit

6. APPENDICES

6.1 Appendix 1: Declaration of the End of Trial (CTIMP)

6.2 Appendix 2: Declaration of the End of Study (non-CTIMP)

6.3 Appendix 3: Template for the Final Report

6.1 **Appendix 1: Notification of End of Trial (CTIMP)**

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*[1])

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:

To be filled in by the applicant

A MEMBER STATE IN WHICH THE DECLARATION IS BEING MADE :

B TRIAL IDENTIFICATION

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

C APPLICANT IDENTIFICATION (please tick the appropriate box)

C.1	**DECLARATION FOR THE COMPETENT AUTHORITY**	☐
C.1.1	Sponsor	☐
C.1.2	Legal representative of the sponsor	☐
C.1.3	Person or organisation authorised by the sponsor to make the application.	☐
C.1.4	**Complete below**:	
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	

C.2	**DECLARATION FOR THE ETHICS COMMITTEE**	☐
C.2.1	Sponsor	☐
C.2.2	Legal representative of the sponsor	☐
C.2.3	Person or organisation authorised by the sponsor to make the application.	☐
C.2.4	Investigator in charge of the application if applicable[2]:	
	• Co-ordinating investigator (for multicentre trial):	☐
	• Principal investigator (for single centre trial):	☐
C.2.5	**Complete below** :	
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

D.1	**Date of the end of the complete trial in all countries concerned by the trial**?

[1] OJ, C82, 30.3.2010, p. 1; hereinafter referred to as 'detailed guidance CT-1'.

[2] According to national legislation.

D.1.1	(YYYY/MM/DD):

D.2	**Is it an early termination?**[3]	yes ☐ no ☐
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

E.1 I hereby confirm that/confirm on behalf of the sponsor that (delete which is not applicable):

- The above information given on this declaration is correct; and
- That the clinical trial summary report will be submitted within the applicable deadlines in accordance with the applicable guidance by the Commission.[4]

E.2	**APPLICANT TO THE COMPETENT AUTHORITY** (as stated in C.1) ☐
E.2.1	Date :
E.2.2	Signature :
E.2.3	Print name:

E.3	**APPLICANT TO THE ETHICS COMMITTEE** (as stated in C.2) **:** ☐
E.3.1	Date :
E.3.2	Signature :
E.3.3	Print name:

[3] Cf. Section 4.2. of the detailed guidance CT-1.

[4] Section 4.3. of the detailed guidance CT-1.

6.2 Appendix 2: Declaration of the End of Study (non-CTIMP)

NHS
National Patient Safety Agency

National Research Ethics Service

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 that gave a favourable opinion of the research ("the main REC") 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 main REC:	
Main REC reference number:	

3. Study duration

Date study commenced:	
Date study ended:	
Did this study terminate prematurely?	*Yes / No* *If yes please complete sections 4, 5 & 6, if no please go direct to section 7.*

4. Circumstances of early termination

What is the justification for this early termination?	

5. 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?	*e.g. Safety, difficulties recruiting participants, trial has not commenced, other reasons.*

6. 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.	

7. Final report on the research

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

8. Declaration

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

6.3 Appendix 3: Template for the Final Report

1. TITLE PAGE

The title page could contain the following information:

- study title
- name of test drug/investigational product
- indication studied
- if not apparent from the title, a brief (1 to 2 sentences) description giving design
- (parallel, cross-over, blinding, randomised) comparison (placebo, active,
- dose/response), duration, dose, and patient population
- name of the sponsor and Sponsor contact
- protocol identification (code or number)
- development phase of study
- study initiation date (or date of first patient enrolled)
- study completion date (or date of last patient completed) (or date of early study termination, if applicable)
- name and affiliation of Chief Investigator
- date of the report (identify any earlier reports from the same study by title and date)

2. SYNOPSIS/ABSTRACT

A brief synopsis or abstract that summarises the study should be provided. The synopsis should include numerical data to illustrate results, not just text or p-values.

3. STUDY OBJECTIVES

A statement describing the overall purpose(s) of the study should be provided.

4. STUDY DESIGN AND DESCRIPTION

The overall study plan and design (configuration) of the study (e.g., parallel, cross-over) should be described briefly but clearly, using charts and diagrams as needed.
The information provided could include:

- treatments studied (specific drugs, doses and procedures)
- patient population studied and the number of patients to be included.
- level and method of blinding/masking (e.g., open, double-blind, single-blind, blinded
- evaluators and unblinded patients and/ or investigators)
- kind of control(s) (e.g., placebo, no treatment, active drug, dose-response, historical)
- and study configuration (parallel, cross-over)
- method of assignment to treatment (randomisation, stratification)
- Selection of Study Population (inclusion and exclsuion criteria)
- sequence and duration of all study periods, including pre-randomisation and posttreatment periods, therapy withdrawal periods and single- and double-blind treatment periods. It is usually helpful to display the design graphically with a flow chart which includes timing of assessments (for example the CONSORT flow diagram http://www.consort-statement.org/index.aspx?o=1077)
- Removal of patients from therapy or assessment
- any safety, data monitoring or special steering or evaluation committees
- any interim analyses
- Changes in the Conduct of the Study or Planned Analyses
- Sample size
- Statistical and analytical plans

5. STUDY RESULTS
   - Information could include:
   - Description of study population (e.g. demographics, disease status)
   - Details of treatment received
   - Measurements of Treatment Compliance
   - Protocol deviations

6. SAFETY EVALUATION
   - Brief summary of adverse events
   - Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

7. DISCUSSION AND CONCLUSION