

**Document Title: Reporting Serious Breaches of Protocol or GCP**

**Document Number: 033**

Version:	2
Ratified by:	R&D Committee
Date ratified:	30/11/2017
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Date issued:	04/12/2017
Review date:	04/12/2020
Target audience:	All research staff
Intranet:	NA
Key related documents:	SOP006 Roles and Responsibilities for the Conduct of Research Studies SOP031 Adverse Event Reporting SOP032 Handling of Non-Compliance
This document supports: <i>Standards and legislation</i>	Medicines for Human Use (Clinical Trials) Regulations 2004 and all associated amendments. UK Policy Framework for Health and Social Care (2017) Guidance for the Notification of Serious Breaches of GCP or the Trial Protocol (MHRA) (updated in January 2014)
Date equality analysis completed.	30/11/2017
<b><u>This is a controlled document</u></b>	
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**Version Control**

Version	Date	Author	Status	Comment
1	01/07/2017	Heidi Saunders	Final	New Document
1.1	03/10/2017	Lucy Parker	Final	SOP Review Date Time Extension
2	26/09/2017	Lucy Parker	Final	New SOP Template. Update from Research Governance Framework for Health and Social care (2005) to UK Policy Framework for Health and Social Care (2017)

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## 1. INTRODUCTION

This document sets out the standardised process to be followed by all RF Staff who are involved in clinical research within the Trust. It aims to provide clear guidance on how serious breaches of the trial protocol or GCP should be reported.

This SOP ensures compliance with Medicines for Human Use (Clinical Trials) Regulations 2004 and Research Governance Framework (2005).

## 2. OBJECTIVE

This document defines the Trust's procedures for identifying and reporting serious breaches in research studies taking place at the Royal Free London Hospital NHS Foundation Trust.

This SOP states the procedures to be followed to protect patients, maintain the integrity of the trial and comply with legal requirements and Good Clinical Practice guidelines (GCP).

## 3. DEFINITIONS

**Serious Breach** - is a breach which is likely to effect to a significant degree:

- a) the safety or physical or mental integrity of the subjects of the trial; or
- b) the scientific value of the trial.

**RFL or RF** - Royal Free London Hospital NHS Foundation Trust

**RM&G** - Research Management & Governance

**R&D** - Research & Development

**Clinical Trial of Investigational Medicinal Product (CTIMP)** - Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamics effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal products(s) and/or Study absorption, distribution, metabolism and excretion of one or more investigational product(s) with the object of ascertaining its (their) safety and/or efficacy.

**Sponsor** - Individual, organisation or group taking on responsibility for securing the arrangements to initiate, manage and finance a study. A group of individuals and/or organisations may take on sponsorship responsibilities and distribute them by agreement among the members of the group, provided that, collectively, they make arrangements to allocate all the responsibilities in this research governance framework that are relevant to the study.

**CI** - Chief Investigator (CI) is the authorised health care professional who takes primary responsibility for the conduct of the trial. There is only one Chief Investigator per Member State.

**PI** - Principal Investigator (PI) is the person who takes responsibility for the initiation and conduct of the study at site. There is one Principal Investigator at each site participating in a research study. For a single site study the Chief investigator may also take on the role of Principal investigator

**GCP** - Good Clinical Practice (GCP) is an international ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

**TMF** - The Trial Master File (TMF) contains all essential documents held by the sponsor/Chief Investigator which individually and collectively permits the evaluation of the conduct of a trial and the quality of the data produced.

**ISF** - The Investigator Site File (ISF) contains all essential documents held by Principal Investigator(s) conducting a trial which individually and collectively permit the evaluation of the conduct of a trial and the quality of the data produced.

**CRF** – Case Report Form (CRF) is a printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject.

#### **4. SCOPE**

This SOP applies to all studies sponsored or hosted by Royal Free London Hospital NHS Foundation Trust.

#### **5. EQUALITY STATEMENT**

The Royal Free London NHS Foundation Trust is committed to creating a positive culture of respect for all individuals, including job applicants, employees, patients, their families and carers as well as community partners. The intention is, as required by the Equality Act 2010, to identify, remove or minimise discriminatory practice in the nine named protected characteristics of age, disability (including HIV status), gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex or sexual orientation. It is also intended to use the Human Rights Act 1998 to treat fairly and value equality of opportunity regardless of socio-economic status, domestic circumstances, employment status, political affiliation or trade union membership, and to promote positive practice and value the diversity of all individuals and communities.

This document forms part of the trust's commitment. You are responsible for ensuring that the trust's policies, procedures and obligation in respect of promoting equality and diversity are adhered to in relation to both staff and service delivery.

The equality analysis for this SOP is attached at Appendix (2).

#### **6. DUTIES**

The Trust is committed to the delivery of world class care and expertise to both staff and patients, and our values of positively welcoming, actively respectful, visibly reassuring and clearly communicating are fundamental to the delivery of this. This policy has been developed with our values in mind, and is intended to be implemented within the spirit of these values.

This SOP applies to all personnel that are conducting research at the Trust including: staff that are full or part-time employees of the Trust, those working at the Trust with employment contracts funded partially or wholly by third parties, those working at the trust under honorary contract or under the remit of a valid research passport, those seconded to and providing consultancy to the Trust, and to students undertaking training at the Trust.

It is the responsibility of all staff involved in a study to identify and report potential serious breaches occurring during the day to day running of a research study.

The PI is responsible for notifying the Sponsor immediately of becoming aware of potential serious breaches.

The study Sponsor is responsible for notifying the MHRA and REC of serious breaches of GCP or the trial protocol within 7 days of becoming aware of that breach.

## 7. DETAILS OF THE PROCEDURE

Person Responsible	Task
<p>Anyone working on a research study hosted at RF or Sponsored by RF</p>	<p><b>7.1 Identification of a Serious Breach</b></p> <p>Deviations from study protocols and GCP occur commonly in clinical trials. The majority of these instances are technical deviations that do not result in harm to the trial subjects or significantly affect the scientific value of the reported results of the trial. These cases should be documented, for example in the Case Report Form (CRF), for the Investigator Site File (ISF) and Trial Master File (TMF) in order for appropriate corrective and preventative actions to be taken.</p> <p>Breaches can be identified by anyone involved in the conduct, management or monitoring of the trial. The PI should be informed if a breach is identified. The PI is responsible for notifying the Sponsor immediately. The initial notification should be followed by written notification of a potential serious breach within 24 hours of the PI becoming aware of the breach.</p> <p>All suspected serious breaches are classed as reportable trial-related Trust incidents. All suspected serious breaches must be notified to the R&amp;D Office (if different from the Sponsor) within 24 hours of the breach being identified. This notification should be done via Trust incident reporting system Datix and via email <a href="mailto:rf.randd@nhs.net">rf.randd@nhs.net</a>.</p>
<p>CI and PI at site</p>	<p><b>7.2 Process for RF Sponsored Studies</b></p> <p>The PI is responsible for notifying the Sponsor immediately of being made aware of the breach. The notification of the breach should be done via Trust incident reporting system, Datix and sent to the R&amp;D Office via email (<a href="mailto:rf.randd@nhs.net">rf.randd@nhs.net</a>).</p> <p>The initial notification should include:</p> <ul style="list-style-type: none"> <li>• Name of Chief Investigator and Principal Investigator at the site where the breach occurred.</li> <li>• Full title of the study</li> </ul>

	<ul style="list-style-type: none"> <li>• An explanation of how the breach was identified</li> <li>• Details of the breach</li> <li>• Details of any initial corrective actions</li> <li>• Assessment of the impact the breach will have on the trial subjects/patients and/or scientific integrity</li> </ul> <p>Following receipt of the initial report, the R&amp;D Office will take the following actions:</p> <ul style="list-style-type: none"> <li>• Promptly discuss the episode with relevant research staff to confirm the seriousness of the breach</li> <li>• Log the information in the study file on the R&amp;D database</li> <li>• Gather further information and supporting evidence</li> </ul> <p>Once all necessary information has been received, the R&amp;D Office will decide if the incident or event is a serious breach.</p> <p>If the incident/event is determined to be a serious breach, the PI should be asked to document and describe the event, including both corrective and preventative action taken or planned.</p> <p>If there is disagreement between the PI and the R&amp;D Office on whether the incident/event is a serious breach, it should be discussed, but the Sponsor is ultimately responsible for making this decision. Evidence and reasons behind the decision made should be carefully documented and filed appropriately.</p> <p>The notification of the serious breach will be submitted to the approving REC by the Sponsor. The REC will acknowledge in writing and further information or clarification may be requested until the incident is closed.</p> <p>The PI must ensure all required actions are completed and that the breach is then closed.</p>
<p>PI at RF site</p>	<p><b>7.3 Non CTIMP Study- Externally Sponsored Studies</b></p> <p>The PI is responsible for notifying the sponsor immediately of being made aware of the breach. The initial notification should be followed by written notification of a potential serious breach within 24 hours of the PI becoming aware of the breach.</p> <p>All suspected serious breaches are classed as reportable trial related incidents. All suspected serious breaches must be notified to the R&amp;D Office</p>

	<p>within 24 hours of the breach being identified. This notification should be done via Trust incident reporting system Datix and via email <a href="mailto:rfh.randd@nhs.net">rfh.randd@nhs.net</a>.</p> <p>The R&amp;D Manager will escalate to the R&amp;D committee for review. All breaches related to the Human Tissue will be related to the Trust HTA Committee.</p> <p>As it is the Sponsor's responsibility to assess the breach, report it to the REC and ensure resolution, the R&amp;D Office will assist only where requested or where necessary.</p>
<p>PI at RF</p>	<p><b>7.4 CTIMP Study - Externally Sponsored Studies</b></p> <p>The PI is responsible for notifying the Sponsor immediately of being made aware of a breach. The initial notification should be followed by written notification of a potential serious breach within 24 hours of the PI becoming aware of the breach. This may be done using the MHRA Notification of Serious Breach of Good Clinical Practice or Trial Protocol Form. The trial Sponsor will use this form to inform the MHRA of the serious breach.</p> <p>All suspected serious breaches are classed as reportable trial related incidents. All suspected serious breaches must be notified to the R&amp;D Office within 24 hours of the breach being identified. This notification should be done via Trust incident reporting system Datix and via email <a href="mailto:rf.randd@nhs.net">rf.randd@nhs.net</a>.</p> <p>When the R&amp;D Office is notified of a potential serious breach, the information will be reviewed in a timely manner and logged appropriately in the study file on the R&amp;D database. Any additional information required will be requested. The R&amp;D Manager will escalate to the R&amp;D committee for review. All breaches related to the Human Tissue will be related to the Trust HTA Committee.</p> <p>As it is the Sponsor's responsibility to assess the breach, report it to the relevant regulatory agencies and ensure resolution, the R&amp;D Office will assist only where requested or where necessary.</p> <p>The PI should retain all correspondence and documentation that relates to the breach and copies should be filed in the Investigator Site File (ISF).</p>



## 8. POLICY

This SOP is mandatory and non-compliance with it may result in disciplinary procedures.

## 9. RISK MANAGEMENT/ LIABILITY/MONITORING & AUDIT

- The SOP Working Group will ensure that this SOP and any future changes to this document are adequately disseminated.
- The R&D Office will monitor adherence to this SOP via the routine audit and monitoring of individual clinical trials and the Trust's auditors will monitor this SOP as part of their audit of Research Governance. From time to time, the SOP may also be inspected by external regulatory agencies (e.g. Care Quality Commission, Medicines and Healthcare Regulatory Agency).
- In exceptional circumstances it might be necessary to deviate from this SOP for which written approval of the RM&G Manager/Deputy R&D Director should be gained before any action is taken.
- SOP deviations should be recorded including details of alternative procedures followed and filed in the Investigator and Sponsor Master File.
- The R&D Office is responsible for the ratification of this procedure.

## 10. FORMS/TEMPLATES TO BE USED

MHRA Notification of Serious Breach of Good Clinical Practice or Trial Protocol Form

<https://www.gov.uk/guidance/good-clinical-practice-for-clinical-trials>

is used by the Sponsor of a CTIMP to notify the MHRA of a serious breach.

## 11. FLOWCHART

None applicable

**APPENDIX 1**  
**SOP Reading Log**

READ BY			
NAME	TITLE	SIGNATURE	DATE

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**APPENDIX 2**

**Royal Free London NHS Foundation Trust Equality Analysis guide and Tool**

An equality analysis is a review of a policy, practice, function, business case, project or service change which establishes whether there is a negative effect or impact on particular social groups. This In turn enables the organisation to demonstrate it does not discriminate and, where possible, it promotes equality to meet the needs of the diverse patients and communities we serve.

This check list is a way to help you think carefully about the likely impact on equality groups and take action to improve services. This is also an opportunity to evidence positive practices in our services and demonstrate strategic integrity to ensure that our services and employment practices are fair, accessible and appropriate for all patients, visitors and carers, as well as our talented and diverse workforce.

Name of the policy / function / service development being assessed				
Briefly describe its aims and objectives:				
Directorate and Lead:				
Evidence sources: DH, legislation. JSNA, audits, patient and staff feedback				
Is the Trust Equality Statement present?	<table border="0"> <tr> <td style="text-align: center;">Yes</td> <td style="text-align: center;">No</td> <td style="text-align: center;">if no do not proceed with Equality Analysis (EA)</td> </tr> </table>	Yes	No	if no do not proceed with Equality Analysis (EA)
Yes	No	if no do not proceed with Equality Analysis (EA)		

If you are conducting an EA on a procedural document please identify evidence sources and references, who has been involved in the development of the document, process or strategy, and identify positive or negative impacts. It is the discussion regarding the equality impact of the document that is important.

**Equality Analysis Checklist**

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Go through each protected characteristic below and consider whether the policy, practice, function, business case, project or service change could have any impact on groups from the identified protected characteristic, involve service users where possible and get their opinion, use demographic / census data (available from public health and other sources), surveys (past or maybe carry one out), talk to staff in PALS and Complaints and Patient Experience.

Please ensure any remedial actions are Specific, Measureable, Achievable, Realistic, and Timely ( SMART).

Equality Group	Identify negative impacts	What evidence, engagement or audit has been used?	How will you address the issues identified?	Identifies who will lead the work for the changes required and when?	Please list positive impacts and existing support structures
<b>Age</b>	None identified	R&D administrative document	N/A	N/A	This SOP on the handling of serious breaches of protocol or GCP introduces a requirement to include the Trust Equality Statement in all SOPs that describe the standard activities used in Research Studies and Clinical Trials at the Royal Free London Hospital NHS Foundation Trust.  It also introduces a
<b>Disability</b>	None identified	R&D administrative document	N/A	N/A	
<b>Gender Reassignment</b>	None identified	R&D administrative document	N/A	N/A	
<b>Marriage and Civil Partnership</b>	None identified	R&D administrative document	N/A	N/A	
<b>Pregnancy and maternity</b>	None identified	R&D administrative document	N/A	N/A	
<b>Race</b>	None identified	R&D administrative document	N/A	N/A	
		R&D	N/A	N/A	

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Equality Group	Identify negative impacts	What evidence, engagement or audit has been used?	How will you address the issues identified?	Identifies who will lead the work for the changes required and when?	Please list positive impacts and existing support structures
Religion or Belief	None identified	administrative document			new Equality Analysis Template for the SOPs, that requires the presence of the Equality statement.  These actions are designed to embed the equality agenda and promote equality compliance within the Trust.
Sex	None identified	R&D administrative document	N/A	N/A	
Sexual Orientation	None identified	R&D administrative document	N/A	N/A	
Carers	None identified	R&D administrative document	N/A	N/A	

It is important to record the names of everyone who has contributed to the policy, practice, function, business case, project or service change.

Equality Analysis completed by: (please include every person who has read or commented and approval committee(s). Add more lines if necessary)	Organisation	Date
SOP Working Group	Royal Free London NHS Foundation Trust	20/10/2017
R&D Committee	Royal Free London NHS Foundation Trust	30/11/2017

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