NHS Humber Health Partnership

Serious Breach SOP

Document control use only	
Reference	R&D SOP 17
Directorate / Care Group	Research & Development
Version	Version 4
Result of last review	Regulatory Changes
Issue date	27/04/2026

Author / Owner Use Only	
Group or Trust specific document	HHP (Group) – Hull University Teaching Hospitals NHS Trust, Northern Lincolnshire and Goole NHS Foundation Trust
Date approved by owner (for minor changes only outside committee)	N/A
Date approved	13/5/2026
Approving body	R&D Sponsor Oversight Group / RDI Committee
Next full review date	12/05/2029
Lead Director	Professor Sathyapalan – R&D Director James Illingworth – R&D Manager
Document type	Standard Operating Procedure
Author / Contact	Leanne Cox – R&D QA Manager
Key words	GCP, SOPs, R&D, Research & Development, Serious Breach

Distribution:	HHP R&D internet Click on GCP SOPs for HHP-sponsored CTIMPs https://www.hey.nhs.uk/research/researchers/gcp-sops-for-hey-sponsored-ctimps/

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AI update statement: This Standard Operating Procedure (SOP) was reviewed and updated with the assistance of an Artificial Intelligence (AI) tool. The AI output was used to support drafting and editing only; all content was verified, amended where required, and approved by the document owner/author in accordance with the Trust's document control and governance requirements.

Authorized by		Sign	Date
R&D Director	Professor Thozhukat Sathyapalan	DocuSigned by: 4C017C4E6DDA4B...	13/5/2026
R&D Manager	James Illingworth	DocuSigned by: James Illingworth 3DDA0F90873F430...	13/5/2026

Working in partnership:
Hull University Teaching Hospitals NHS Trust
Northern Lincolnshire and Goole NHS Foundation Trust

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This page details the version history and the main changes made for each new version.

Version Log		
Version number and date	**Author**	**Details of significant changes**
Version 1, 27.10.10		Original SOP approved by R&D Committee on 27.10.10.
Version 2, 26.01.15	J Pacynko	Web links up-dated. Page 5 and 6 in red type – recording of protocol deviations in CRFs, file notes and the protocol deviation form for the trial.
Version 3, 03.01.23	S Moffat	SOP changed to new format. Web links updated. Page 7, Section 3.6, Temporary halt of a trial. Addition of " For trials not submitted through the Combined Review process: Substantial amendments relating to a temporary halt must be submitted using MHRA Submissions via the Human Medicines Tile. Please select 'Clinical Trial' as the Regulatory Activity and 'CT – Amendment' from the Regulatory sub activity dropdown list. Instructions to gain access to the MHRA Submissions Portal can be found via the link below: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/983080/URG_Gaining_Access_to_MHRA_Submissions.pdf If the trial has been submitted via the Combined Review process then the substantial amendment should be submitted via IRAS." Page 7, Section 3.7, Initial Notification of Breach to MHRA Removal of Appendix 3, Notification of Serious Breach Form, replaced with web link to the current form. Updated email address for submission of form. Page 8, 3.8 Provision of follow-up investigation report to the MHRA Additional information from the MHRA Inspectorate Blog regarding information required in any follow-up reports. Timeframe added in which the serious breach investigation panel should meet to review the breach in full. Page 9, Section 5, References Addition of MHRA GCP Guide 2012 Addition of MHRA Blog – GCP Serious Breaches update Page 15, Appendix 3 Trust name updated and re-formatted.
Version 4, 27.04.2026	L Cox	Purpose and Scope now reference ICH E6(R3) directly, confirming that the SOP supports quality-by-design, risk-based approaches, and prevention of recurrence of non-compliance. Introduction and Background has been expanded to link UK Regulation 29A requirements with ICH E6(R3) Principles 1–9, emphasising participant safety, ethical conduct, and the need for proactive management of serious non-compliance. (Section 3.1) Responsibilities and Timelines now require a risk-based and proportionate assessment of deviations and breaches, ensure that individuals involved are appropriately qualified, and link serious breach management to the sponsor's wider quality management system.

		(Section 3.2) Deviation vs Serious Breach includes new wording requiring assessment of deviations using ICH E6(R3) critical-to-quality factors such as participant safety, rights, and data reliability. (Section 3.3) Monitoring has been strengthened to require risk-based, proportionate monitoring focused on processes and data critical to quality. (Section 3.4) Information Required by Sponsor now includes the need to assess and document the impact of the suspected breach on critical-to-quality factors. (Section 3.5) Sponsor Assessment has been expanded to require structured, risk-based evaluation of suspected breaches, integration of findings into the quality management system, and explicit prevention of recurrence in line with ICH E6(R3). (Section 3.6) Temporary Halt now references ICH E6(R3) Principle 1.1, reinforcing that participant safety must always take precedence. (Section 3.7) Initial Notification to MHRA includes a requirement that the notification reflects the risk-based assessment and immediate mitigation actions. (Section 3.8) Follow-Up Investigation Report has been updated to require documentation of methodology, assessment of critical-to-quality impact, and compliance with ICH E6(R3) data governance expectations (audit trails, metadata, secure storage). (Section 3.9) CAPA Planning now requires corrective and preventative actions to be designed using quality-by-design and risk-based principles, with outcomes feeding into ongoing quality management, training, and monitoring. (Section 4) Dissemination and Implementation includes wording linking learning from serious breaches to continuous improvement under ICH E6(R3). (Section 5)References now include the ICH E6(R3) Guideline for Good Clinical Practice (2025). Update from HUTH to HPP incorporating both HUTH and NLaG.

Please note for definitions of acronyms refer to Appendix 1 of Management of SOPs. Refer to Appendix 2 of Management of SOPs for the standards to which clinical trials that investigate the safety and/or efficacy of a medicinal product are conducted.

All the HHP R&D GCP SOPs are available at:
https://www.hey.nhs.uk/research/researchers/gcp-sops-for-hey-sponsored-ctimps/

1. PURPOSE, SCOPE and WHO SHOULD USE THIS SOP

- This SOP describes the process for declaration and notification of serious breaches of Good Clinical Practice (GCP) or the approved trial protocol.

- This SOP applies to all clinical trials using investigational medicinal products (CTIMPs) sponsored by Humber Health Partnership (HHP).

- This SOP should be used by all staff involved with HHP sponsored CTIMPs for example, R&D staff, chief/principal investigators, co-investigators or sub-investigators, research nurses, trial managers, trial co-ordinators, data managers, research staff, pharmacy staff, laboratory staff (list not exhaustive).

- This SOP is aligned with the principles of ICH GCP (R3), which emphasise protection of participants, reliability of trial results, and a proportionate, risk-based approach to managing non-compliance. In accordance with ICH GCP (R3) processes described in this SOP are designed to support quality by design, ensure timely detection of issues critical to participant safety or data integrity, and prevent recurrence of serious non-compliance.

2. INTRODUCTION AND BACKGROUND

The EU GCP Directive 2005/28/EC was transposed into UK law as the Medicines for Human Use (Clinical Trials) Amendment Regulations 2006 on the 29th August 2006.

Under the amendment it is now a requirement that serious breaches of GCP or the trial protocol are reported to the Medicines and Healthcare products Regulatory Agency (MHRA). The amended regulation 29A states that:

Regulation 29A: Notification of serious breaches

(1) The sponsor of a clinical trial shall notify the licensing authority in writing of any serious breach of –

(a) the conditions and principles of GCP in connection with that trial; or
(b) the protocol relating to that trial, as amended from time to time in accordance with regulations 22 to 25, **within 7 days of becoming aware of that breach.**

(2) For the purposes of this regulation, a "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.

In addition to UK regulatory requirements, the sponsor must ensure that management of serious breaches is consistent with ICH E6(R3) Principles 1–9, including participant protection, scientific soundness, qualified oversight, and proportionate quality management. ICH E6(R3) requires that 'strategies should be implemented to avoid, detect, address and prevent recurrence of serious noncompliance with GCP, the trial protocol and applicable regulatory requirements.' These principles underpin the processes described in this SOP.

These stipulations were incorporated into regulation in order to:

1. Enhance the safety of trial subjects/patients by seeking to ensure that the licensing authority is promptly informed of such serious breaches, in order to take appropriate action in response to the breach and/or,
2. To take the information regarding serious breaches into account when assessing future applications for clinical trial authorisation, and applications for marketing authorisation, which include data from trials affected by serious breaches.

3. PROCEDURES

3.1 Responsibilities and timelines

3.1.1 Any major deviations or breaches of the study should be notified by telephone or in person to the HHP R&D Manager, QA Manager, Monitor or Office **within 24 hours** of the deviation or breach being identified. If you are unsure whether a serious breach has occurred please discuss with the R&D Manager, QA Manager or Monitor by telephone or in person. Assessment of deviations and potential serious breaches must be undertaken using a risk-based and proportionate approach, consistent with ICH E6(R3) Principle 7. This includes evaluating the impact of the event on critical-to-quality factors, participant safety, and the reliability of trial results.

3.1.2 It is the responsibility of the trial sponsor to assess whether a deviation or breach of the study is serious and therefore should be reported to the MHRA. Individuals involved in assessing and managing serious breaches must be appropriately qualified by education, training and experience. The sponsor must ensure that oversight of serious breaches forms part of the broader quality management system.

3.1.3 It is the responsibility of the trial sponsor or a person legally authorised by the sponsor to notify the MHRA **within 7 days** of becoming aware of the serious breach.

3.1.4 It is the responsibility of the sponsor to assess the impact of the breach on the scientific value of the trial.

3.1.5 It is the investigators responsibility to notify R&D of protocol deviations and to record deviations in patients case report forms (CRFs) if applicable. At the end of each study visit in the CRF, there is a reminder to record any protocol deviations in the Protocol Deviations Log at the end of the CRF.

3.1.6 The R&D monitor will ensure that the Protocol Deviations Form for the study is up-dated after monitoring visits.

3.1.7 It is the responsibility of the investigator to include and consider any protocol deviations or breaches in the clinical study report at the end of the study, as they may have an impact on the analysis of the data.

3.2 Deviation or serious breach?

3.2.1 Deviations from clinical trial protocols and GCP can occur in clinical trials. Most of these deviations do not result in harm to the trial subjects or significantly affect the scientific value of the results of the trial.

3.2.2 Protocol deviations, and actions taken, will be documented in patients CRFs (if applicable) and in the Protocol Deviation Form for the study and explained in File Notes kept in the Trial Master File. The actions taken should be corrective and preventative.

3.2.3 The decision on whether a breach is likely to have a significant impact on the scientific value of the trial depends on a variety of factors including the design of the trial, the type and extent of the data affected by the breach, the overall contribution of the data to key analysis parameters, the impact of excluding the data from the analysis etc (list not exhaustive).

3.2.4 When determining whether a deviation constitutes a serious breach, the sponsor should consider the event's impact on factors critical to quality, as described in (R3) Principle 6. These include participant safety, rights and well-being, and the reliability and interpretability of trial results. This assessment should be documented in the Initial Review of Serious Breach form.

3.3 Monitoring

3.3.1 Humber Health Partnership will monitor and may audit clinical trials as part of its Quality Assurance procedures.

3.3.2 The R&D clinical trial monitor will review all deviations during monitoring visits. The monitor will assess whether each deviation has been adequately identified and documented and will make an independent assessment of the severity of the deviation. If the trial monitor notes a pattern of repetition of deviations this may become a serious breach and reportable for that reason. The monitor will assess individual deviations and also the overall quality of their management within the trial. Monitoring activities should be proportionate to the risks associated with the trial and should focus on processes and data critical to quality. Patterns of repeated deviations should be evaluated as potential indicators of systemic non-compliance requiring escalation.

3.3.3 All deviations and serious breaches will be recorded on the Protocol Deviations Form for the study and will be recorded in the monitoring visit report. Frequently the monitor will be involved in preparing File Notes to fully document protocol deviations.

3.4 Information required by sponsor

3.4.1 The following information is required from the person reporting the suspected breach:

- Name of Chief/Principal Investigator
- R&D number
- Title of the clinical trial
- An explanation of how the breach was identified
- Details of the breach
- Date and time of breach
- Number of study patients in the trial at the time of the breach
- Which patients were affected by the breach.
- Details of any initial corrective and preventative actions
- Assessment of the impact the breach will have on the safety of trial study patients and scientific integrity of the trial.

- Where applicable, information should also include any potential impact on critical-to-quality factors, including participant safety, rights, well-being, and the reliability of key trial endpoints.

3.4.2 With this information, the R&D manager, QA manager or monitor will complete the R&D form: Initial Review of Serious Breach of GCP or Trial Protocol in ***Appendix 1.***

3.5 Sponsor assessment of a Serious Breach

3.5.1 An investigation panel will be convened usually to include the R&D Director, R&D Manager, QA Manager and R&D Monitor. The investigation panel must assess the suspected breach using a structured, risk-based approach. This includes evaluating the event's impact on participant safety, scientific validity, and critical-to-quality factors, and determining whether additional risk mitigation or monitoring adjustments are required.

3.5.2 The R&D Manager will discuss the issues with the Chief/Principal Investigator to identify which section of GCP or the protocol has been breached and how the breach impacts on subject safety and/or the scientific integrity of the trial.

3.5.3 The investigation panel will decide whether a breach is serious.

3.5.4 Examples of serious breaches can be found in the MHRA's Guidance for the Notification of Serious Breaches of GCP or the Trial Protocol – Appendix II https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/905577/Guidance_for_the_Notification_of_Serious_Breaches_of_GCP_or_the_Trial_Protocol_Version_6__08_Jul_2020.pdf

3.5.5 The decision may require telephoning the MHRA to speak to an MHRA inspector for advice. The telephone conversation and outcome will be recorded on the R&D form: Initial Review of Serious Breach of GCP or Trial Protocol.

3.5.6 The investigation panel will decide if the trial should be temporarily halted. If this is so a letter will be sent from the R&D Director to the Chief/Principal Investigator. See ***Appendix 2*** for the letter template. The sponsor must ensure that strategies are implemented to avoid, detect, address and prevent recurrence of serious non-compliance. Findings from the assessment should be fed back into the sponsor's quality management system.

3.5.7 As per the letter, the investigation panel will meet with the Chief/Principal Investigator and the study team to discuss the serious breach and compile the facts for notification to the MHRA. The panel will work with the Chief/Principal Investigator to identify the extent of the serious breach and to initiate any safety measures that may be required.

3.5.8 The R&D Manager, QA Manager or Monitor will notify the Ethics Committee, who gave the favourable opinion for the trial, of the serious breach.

3.6 Temporary halt of a trial

3.6.1 Should the decision be to suspend the study until the breach has been investigated, the IRAS Modification Tool will be completed by the R&D Manager (or nominated deputy) according to the instructions on the MHRA website at the link below.
https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#suspend-or-terminate-a-trial

3.6.2 Instructions taken from the MHRA link:
When a sponsor halts a trial temporarily, he should notify the MHRA and Ethics Committees immediately and at least within 15 days from when the trial is temporarily halted. The notification should be made as a substantial modification using the IRAS Modification Tool and clearly explain what has been halted (for example stopping recruitment and/or interrupting treatment of subjects already included) and the reasons for the temporary halt. Decisions to temporarily halt a trial must consider (R3) Principle 1.1, which states that 'the rights, safety and well-being of the participants are the most important considerations and should prevail over interests of science and society.

3.6.3 For trials not submitted through the Combined Review process: Substantial modifications relating to a temporary halt must be submitted using MHRA Submissions via the Human Medicines Tile. Please select 'Clinical Trial' as the Regulatory Activity and 'CT – Amendment' from the Regulatory sub activity dropdown list. Instructions to gain access to the MHRA Submissions Portal can be found via the link below:
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/983080/URG_Gaining_Access_to_MHRA_Submissions.pdf

3.6.4 If the trial has been submitted via the Combined Review process then the substantial modification should be submitted via IRAS.

3.6.5 To restart a trial that has been temporarily halted, the sponsor should make the request as a substantial modification using the IRAS Modification Tool and providing evidence that it is safe to restart (risk assessment update + CAPA implementation status + monitoring/verification plan) the trial.

3.6.6 If a sponsor decides not to recommence a temporarily halted trial, the MHRA and Ethics Committees should be notified within 15 days of his decision, using the End of Trial Declaration form and including a brief explanation of the reasons for ending the trial.
The Chief/Principal Investigator will complete the End of Trial Declaration form on behalf of the sponsor. Please follow R&D GCP SOP 12 End of Trial.

3.7 Initial Notification of Breach to MHRA

3.7.1 The R&D Manager (or nominated deputy) will complete the Notification of Serious Breach of GCP or Trial Protocol form. The form can be found via the link below:
https://www.gov.uk/guidance/good-clinical-practice-for-clinical-trials#report-a-serious-breach

3.7.2 The form will be submitted via e-mail to the MHRA within the 7 day reporting period defined in the regulation. The form will be sent to: GCP.SeriousBreaches@mhra.gov.uk

3.7.3 The R&D Manager (or nominated deputy) will be the contact person for all correspondence with the MHRA.

3.7.4 A copy of the Notification of Serious Breach form will also be sent to the Ethics Committee who approved the trial.

3.7.5 The sponsor should ensure that the initial notification reflects the risk-based assessment undertaken, including any immediate actions taken to protect participants or preserve data integrity. Before submission, the Sponsor must perform a documented accuracy check to ensure information provided to the MHRA/REC is complete and not false or misleading (with evidence retained in TMF).

3.8 Provision of follow-up investigation report to the MHRA

3.8.1 As the initial notification must be submitted within 7 days of first awareness, details and information may be incomplete at that point. However, follow-up reports should strive to provide the complete information. The follow-up investigation report must document the methodology used to assess the impact on critical-to-quality factors.This includes evaluating the reliability of affected data, the adequacy of corrective and preventative actions, and any implications for ongoing risk management. Please see below examples listed by the MHRA in their MHRA Inspectorate Blog – GCP Serious Breaches Update https://mhrainspectorate.blog.gov.uk/2020/08/03/gcp-serious-breaches-update/

- What impact assessment has been done, what methodology was used and what was the outcome?
- If applicable, has this issue happened at other sites/on other trials? How do you know this is an issue only at one particular site if you have not checked across sites?
- What root cause assessments have been undertaken, how was this done, what was found and how does this link to the CAPA provided?
- How has the issue been documented in the Trial Master File/s (TMF/s) across all organisations involved?
- Have you ensured this incident is transparently reported in the Clinical Study Report/s?

3.8.2 If relevant, the initial report should indicate that the investigation or corrective and preventative action is ongoing at the time of reporting the serious breach and give predicted timelines for this to be completed and when follow-up reports will be provided to the MHRA.

3.8.3 Once the initial Notification of Serious Breach form has been submitted to the MHRA, the serious breach investigation panel will review the breach in full to identify the extent of the breach. This review should take place no later than 5 days after submission of the initial notification to the MHRA.

3.8.4 In conjunction with the Chief/Principal Investigator, the serious breach investigation panel will compile an investigation report for submission to the MHRA. (***see Appendix 4 for report template***).

3.8.5 The R&D Director and R&D Manager (or Medical Director) will review the investigation report and submit to the MHRA after confirmation by the Chief/Principal Investigator (signed and dated) that the content is accurate and true. A copy of this report will be sent to the Ethics Committee who approved the trial.

3.8.6 The MHRA may request additional information such as a copy of the protocol, ethics application, drug stability data, SOPs etc. The R&D Manager will liaise with the study team to obtain additional documents and submit them to the MHRA.

All documentation generated as part of the investigation must comply with GCP data governance expectations, including appropriate metadata, audit trails, secure storage, and retention within the Trial Master File.

3.9 Planning and Implementing Corrective and Preventative Action

3.9.1 Corrective and preventative actions must be designed using a quality-by-design and risk-based approach. CAPA should address root causes, prevent recurrence, and strengthen processes critical to quality.

3.9.2 The serious breach investigation panel will work with the study team to devise a formal plan of corrective and preventative actions to address the breach. The corrective action plan will be submitted to the MHRA as part of the investigation report. Monitoring of the action plan will be undertaken by the R&D Department and most likely by the MHRA during any future GCP inspections.

3.9.3 Depending on the initial assessment of seriousness and impact, the R&D Department may carry out a full audit of the trial and general trial management systems and procedures.

3.9.4 The sponsor should ensure that CAPA outcomes are incorporated into ongoing quality management activities, including training, monitoring strategy, and risk assessment updates.

4. DISSEMINATION AND IMPLEMENTATION

4.1 As part of the dissemination process, the R&D Department may send anonymised information regarding the breach to:

- Heads of appropriate departments for circulation amongst staff
- HHP staff that have signed up to receive R&D corporate emails.
- The appropriate internal research governance forum/committee.

4.2 Dissemination of learning from serious breaches should support continuous improvement ensuring that staff understand the impact of non-compliance on participant safety and data reliability.

4.3 Dissemination and implementation of this SOP will conform to the process outlined in R&D SOP 01 Management of SOPs.

5. REFERENCES

Statutory instrument 2004/1031: The Medicines for Human Use (Clinical Trials) Regulations 2004.

Statutory Instrument 2006/1928: The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006.

MHRA Good Clinical Practice Guide 2012

Guidance for the Notification of Serious Breaches of GCP or the Trial Protocol, MHRA.
https://www.gov.uk/guidance/good-clinical-practice-for-clinical-trials#report-a-serious-breach

MHRA Blog – GCP Serious Breaches update, 3 August 2020
https://mhrainspectorate.blog.gov.uk/2020/08/03/gcp-serious-breaches-upda

ICH E6(R3) Guideline for Good Clinical Practice (2026).

NHS Humber Health Partnership

Appendix 1: Initial Review of Serious Breach of GCP or trial protocol

R&D Number:	**Short Study Title:**				
Principal Investigator (PI) at HHP:			**Sponsor:**	**Funding Organisation:**	
Has the PI assessed the seriousness of the breach?	☐ Yes	☐ No	Has recruitment at this site ceased immediately?	☐ Yes	☐ No
Date of suspected GCP/ trial protocol breach : / /			Time of suspected GCP/ trial protocol breach : :		
Does the suspected breach relate to: ☐ Patient/participant safety ☐ Scientific validity of the data			Estimated number of participants affected by the breach:		

Details of how suspected breach was identified and overview of the GCP or trial protocol breach:

Details of decision of whether breach is serious: *details of telephone call to MHRA, date trial suspended (if applicable) etc*

Corrective and Preventative actions undertaken to date:

R&D Staff member completing this form.			
Name:	**Signature:**	**Date:** / /	**Time:** :

Appendix 2: Letter to the Chief/Principal Investigator

(*please put completed letter on the Trust Letter Template*)

Research & Development
Office 12
Castle Hill Hospital
Castle Road
Cottingham
HU16 5JQ

Email: james.illingworth3@nhs.net

[Insert date]
[Insert recipient address]

Dear [Insert name(s)]

Study title			
Sponsor R&D ref:	**IRAS Project ID:**	**EudraCT:** (*if applicable*)	**REC ref:**
Chief investigator:		**Principal investigator:**	
Sponsor: [Insert Sponsor]		**Participating site(s):**	

As a result of an issue relating to the above trial being brought to my attention, I have to inform you that, effective from today, recruitment into this trial is suspended pending the result of our investigations. Patients already recruited should continue as per protocol.

The issues of concern are:

1. [Insert list of known issues at time of writing the letter]

A serious breach investigation panel has been convened to include the following members:

- [Insert name] Research & Development Manager
- [Insert name] QA Manager
- [Insert name] Director of R&D
- [Insert name] R&D Clinical Trials Monitor
- [Insert other members as appropriate]

The initial Terms of Reference of the Investigation Panel are:

- To establish the events leading to the incident and identify the root cause(s).
- To review the overall current trial management to ensure compliance with the study protocol and Good Clinical Practice (GCP).
- To consider other events which may be relevant to the investigation.
- To identify educational/training requirements in relation to the incident.
- To make recommendations and form an action plan outlining corrective and preventative actions that have been, and will be, implemented.
- [Amend as appropriate]

A member of the panel will be in contact shortly to arrange an initial meeting to discuss the issues. I would hope that the concerns raised can be resolved quickly to ensure

minimal disruption to the research. The incident has been given the unique identifier [insert reference number].

Please don't hesitate to contact any of the panel members for further information at this time. Thank you for your continued co-operation.

Yours sincerely
[Insert name]

Director of Research & Development
Humber Health Partnership

Appendix 3: Serious Breach Internal Investigation Report Template

Hull University Teaching Hospitals NHS Trust

R&D Department

Serious Breaches of GCP or the Trial Protocol: Internal Investigation Report Template

When this document is viewed as a paper copy, the reader is responsible for checking that it is the most recent version.

This page should detail the version history for this Template and the main changes corresponding to the versions.

Version Log		
Version number and date	**Author**	**Details of significant changes**
Version 1, (add approved date)		Original template approved by R&D Committee on (add date)
Version 2, (add approved date)		Trust name updated. Front page reformatted.

RESEARCH & DEVELOPMENT NOTIFICATION OF SERIOUS BREACH REPORT (TRIAL insert identifier)

[INSERT MONTH AND YEAR]

SERIOUS BREACH REPORT [INSERT MONTH AND YEAR]
Humber Health Partnership Internal Investigation Report

CONTENTS **PAGE**

SUMMARY OF TRIAL (insert trial identifier)

Title:	
MREC:	
Eudract number	
IRAS ID	
Chief Investigator	
Funder:	
Sponsor:	
Date ReDA number assigned:	
Date of Ethics Approval:	
Date of Trust Approval:	
Method:	
Pre-study monitoring visit:	
Additional study monitoring visit:	
First patient recruited:	
Total number of patients recruited to date:	
Pharmacy issues:	
Outcome:	
Trial Design issues:	
Outcome:	
Version control/management issues: **[add issues rows as applicable]**	

1. PURPOSE OF THE REPORT

To summarise and present the findings established by the Humber Health Partnership Research and Development Department following an investigation by the serious breach investigation panel into [insert one sentence summary of issue].

2. INVESTIGATION (incident/investigation/findings/recommendations)

Terms of Reference [amend as appropriate]

- To establish the events leading to the incident and identify the root cause(s).
- To review the overall current trial management to ensure compliance with the study protocol and Good Clinical Practice (GCP).
- To consider other events which may be relevant to the investigation.
- To identify educational/training requirements in relation to the incident.
- To make recommendations and form an action plan outlining corrective and preventative actions that have been, and will be, implemented.

Investigation Panel [others co-opted as necessary]

- [Insert name] Research & Development Manager
- [Insert name] QA Manager
- [Insert name] Director of R&D
- [Insert name] R&D Clinical Trials Monitor
- [Insert other members as appropriate]

Sources of data [examples below – amend as applicable]

- Incident reports (Datix)
- Interviews with key staff
- Initial stability data from the manufacturer
- Ethics correspondence including protocol versions approved
- Pharmacy records (*See Appendix 1 for table of supply information*)
- Drug accountability forms.

3. TIMELINE

[Insert brief overview of timelines and key milestones from initial notification to submission to MHRA]

The Trust has gathered sources of information and held discussions with key personnel involved in order to establish the facts surrounding the incident and to ensure that corrective and preventative actions can be put in place immediately.

(See Appendix 2 for detailed chronology of events and actions taken in the Trust).

4. KEY ISSUES

[Insert number] key issues were identified in need of further investigation as part of the Trusts declaration of a serious breach:

- [insert each issue heading]:

[Insert summary paragraph for each key issue identified]

(See Appendix 4 for table documenting protocol version history [add as applicable]).

5. KEY CONTRIBUTING FACTORS

- [insert each contributing factor heading – should be one heading for each key issue above]:

  [Insert summary paragraph (or bullet points) for each contributing factor identified]

6. ROOT CAUSES

The investigation identified the following root causes precipitating this declaration of a serious breach to the MHRA:

- The failure of [list each identified root cause – there will usually be 2 or 3 root causes]

7. IMPACT ON PATIENT SAFETY & SCIENTIFIC VALIDITY

[Insert summary sentence of why there may be impact on patient safety and or scientific validity].The investigation has ascertained the following impact of this in relation to patient outcome:

- [list each impact]

As part of establishing the impact on outcome, in terms of patient safety the Trust [insert what action taken in this regard]

The Trust acknowledges its duty of care to inform the patients [insert details if applicable]. Patients will be notified following consultation with the Trust Communications Department [insert details if applicable].

It may be that the unauthorised shift in methodology away from the approved protocol, further compounded by the [insert details if applicable], limits the use of the data collected. The [insert details if applicable] significantly affects the scientific validity of the data preventing true comparison in the treatments.

8. RECOMMENDATIONS

As a matter of priority, the Trust Pharmacy Department [if applicable] should:

- [list all agreed actions]
- Implement and monitor all corrective and preventative actions taken to date and ongoing. (*See Appendix 3 for details of corrective and preventative actions taken by [insert]*).

As a matter of priority, the Trust Research and Development Department [if applicable] should:

- [list all agreed actions]
- Implement and monitor all corrective and preventative actions taken to date and ongoing. (*See Appendix 3 for details of corrective and preventative actions taken by [insert]*).

9. RISK ASSESSMENT

It should be noted that, [insert details of risk assessment]

10. LIKELIHOOD OF RECURRENCE

The recommendations and the associated corrective and preventative measures should minimise the risk of recurrence.

11. SHARING LESSONS

An anonymous case-study pulling out the lessons that can be learnt will be disseminated to all known researchers, the Research and Development Committee and the Trust Patient Quality, Safety Experience Committee (PQSE). The key issues will also be anonymised and included in the bi-monthly R&D Newsletter.

12. DISSEMINATION

The report will be disseminated to the following:[add others as applicable]

- MHRA
- Local Ethics Committee
- Chief Pharmacist
- Chief Investigator
- Medical Director
- General Manager – Clinical Governance

13. DECLARATION

Chief Investigator/Principal Investigator:

I declare that the content of the serious breach investigation report is, to the best of my knowledge, a true and accurate account.

Signed..... Date.....

Director of R&D (or nominated investigation panel lead):

I declare that the content of the serious breach investigation report is, to the best of my knowledge, a true and accurate account.

Signed..... Date.....

Appendices 1 – 5

[amend as applicable]

Appendix 1

Clinical Trial (insert identifier)[insert trial title]

Table of patients [Example only - amend as applicable]

Study no.	Initials	Hospital Site	Treatment	Date dispensed	Results (outcome)	Comments

CHH = Castle Hill Hospital HRI = Hull Royal Infirmary

Table completed [insert date].

Appendix 2

NOTIFICATION OF SERIOUS BREACH TIMELINE AND ACTIONS TAKEN BY R&D (insert trial identifier)		
Date	**Action taken**	**Comments/ongoing corrective and preventative actions.**

Appendix 3

CORRECTIVE AND PREVENTATIVE ACTIONS TAKEN /TO BE TAKEN [example – amend as applicable]

Trust R&D Department:		
	Action	**Date/Evidence**
1		
2		
3		
4		
5		
Trust Pharmacy		
	Action	**Date/Evidence**
1		
2		
3		
4		
5		
Chief Investigator		
	Action	**Date/Evidence**
1		
2		
3		
4		
5		

Appendix 4

Clinical Trial [insert title] (insert identifier)
Protocol versions [amend as applicable]

Version	Date of EC favourable opinion	Comments

Appendix 5

Stability Data

[Insert manufacturer stability data as applicable]