Standard Operating Procedure

MANAGEMENT OF BREACHES IN RESEARCH

SETTING Trust-wide for research sponsored by UHBW

AUDIENCE All research staff involved in UHBW sponsored research

ISSUE This SOP relates to the identification and management of breaches in research sponsored by UHBW.

QUERIES Contact R&D department via research@uhbw.nhs.uk

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Review date	Version number	Version date	Effective date	Author/ Reviewer	Authorised by
-	V1.0	12/JAN/2017	14/FEB/2017	Jess Bisset	Diana Benton
05/JAN/2018	V1.1	05/JAN/2018	22/FEB/2018	Jess Bisset	Katharine Wale
29/JUL/2019	V2.0	29/JUL/2019	09/AUG/2019	Katharine Wale	Diana Benton
OCT/2020	V2.1	09/NOV/2020	09/NOV/2020	Katharine Wale Sarah Bishop	Jess Bisset
26/JUL/2021	V2.2	26/JUL/2021	27/JUL/2021	Katharine Wale	Jess Bisset
FEB/2023	V2.3	20/FEB/2023	01/APR/2023	Lucy Riddolls	Nicola Manning
OCT/2023	V2.4	17/OCT/2023	18/OCT/2023	Sara Bishop	Jess Bisset
AUG/2025	V2.5	08/SEP/2025	08/SEP/2025	Sonia Athanatou	Jess Bisset
NOV/2025	V3.0	15/JAN/2026	28/APR/2026	Sonia Athanatou Jess Bisset Sarah Bishop	Diana Benton (on behalf of TRG)

Document History

Version Number	Reason for change
Original V1.0	N/A
V1.1	Annual review and minor updates.
V2.0	Additional text in section 6 (Procedure) about completion of database.
V2.1	Biennial review with several minor updates and clarifications.
V2.2	Clarification on reporting timelines and guidance on completing CAPAs.
V2.3	Departmental name change from Research & Innovation to Research & Development. Updated throughout SOP as a minor amendment.
V2.4	Biennial review with minor clarifications on R&D responsibilities and update to preferred form used in 6.3 for reporting serious breaches.
V2.5	Biennial review with several clarifications on processes including monthly sponsor breaches review meeting, who within R&D processes breaches and expectations for reporting breaches occurring in externally sponsored research.
V3.0	Major update to include information related to the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 and addition of reporting requirements for protocol deviations for Clinical Investigation of Medical Device trials.

1. Introduction

All research must be conducted in compliance with the Medicines for Human Use (Clinical Trials) Regulations 2004 (and subsequent amendments, including the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025) and Medical Devices Regulations 2002 (SI 2002 No 618, as amended) (UK MDR 2002) , Good Clinical Practice (GCP), participant consent, and the approved research related documentation including the protocol and participant information sheets. Any non-compliance must be captured, assessed and managed appropriately by the research team delivering the research and the Sponsor.

There are many types of breaches and with differing degrees of severity which may be identified during the course of a study. The terminology to describe those breaches is often used interchangeably (e.g. protocol non-compliance can also be referred to as a protocol deviation or violation). There is no definitive guidance regarding the meaning of the term protocol violation and therefore it is not used in this document. Any unintended departure from the protocol is therefore referred to as a protocol deviation or a breach. Both terms are used interchangeably in this SOP.

A risk proportionate approach must be adopted for each study to determine how best to report breaches to the Sponsor to allow pragmatic and effective assessment in compliance with GCP and applicable regulations.

Protocol waivers are prospective deviations or waivers to the protocol. **These types of non-compliances are not acceptable.** They constitute an intentional breach of GCP and in the case of CTIMPs, also a breach of regulation 29 of SI 2025/538:

'*Subject to regulation 30, no person shall conduct a clinical trial otherwise than in accordance with – (a) the protocol relating to that trial, as may be modified from time to time in accordance with regulations 20 to 22C'*

An example of a protocol waiver is to allow participants entry into a trial when the participants do not meet one or more eligibility criteria of the approved protocol. Instead, if the eligibility criteria require updating, a substantial modification must be submitted to the REC, HRA and MHRA (if applicable).

2. Purpose

The purpose of this SOP is to describe the procedure for identifying and managing all types of breaches (serious and non-serious) of an approved research protocol and/or deviation of GCP. It describes the roles of:

- research personnel in identifying the breach and notifying UHBW as sponsor
- UHBW as sponsor in appropriate management of the breach.

3. Scope

In Scope:

UHBW sponsored research.

Out of scope:

- Research sponsored by other organisations whose own procedures should be followed.
- Breaches which are not related to research.

To note, whilst research sponsored by other organisations is out of scope it is encouraged that research teams at UHBW share serious breaches with R&D in order to maintain governance oversight across the trust. R&D will not log these on the database but will file applicable correspondence in the study folder and a member of the senior team will review for any required actions above what has been captured in the CAPA or equivalent by the sponsor.

4. Responsibilities

All research staff delivering UHBW sponsored research have a responsibility to ensure that any identified breaches are processed in accordance with this SOP. This should include maintaining clear and comprehensive documentation of the breach, implementing corrective and preventative actions where appropriate and reporting to UHBW as Sponsor where required.

All Research & Development (R&D) staff managing UHBW sponsored research have a responsibility to ensure that any reported breaches are documented, reviewed for seriousness, have appropriate corrective and preventative actions in place (including any onward reporting to ethics and the regulatory authorities), and are managed in accordance with this SOP.

5. Abbreviations and Definitions

Abbreviations	
CAPA	Corrective and Preventative Action
CI	Chief Investigator
CIMD	Clinical Investigation of a Medical Device
CTIMP	Clinical Trial of an Investigational Medicinal Product
GCP	Good Clinical Practice
HRA	Health Research Authority
ISF	Investigator Site File
MHRA	Medicines and Healthcare Products Regulatory Agency
R&D	Research & Development Department
REC	Research Ethics Committee
RMF	Research Management Facilitator
SMT	Senior Management Team
TMF	Trial Master File

Definitions	
Breach	Any departure from the applicable regulations (e.g. Clinical Trials Regulations, Data Protection Legislation etc.), Good Clinical Practice, the approved protocol and any other applicable research documents e.g. SOPs. All deviations and non-compliances are breaches.
Protocol non-compliance	Any departure from the approved research protocol which is identified retrospectively. This can also be referred to as a *protocol deviation*.
Deviation of the Protocol or GCP	Any unintended departure from the research protocol/GCP. Examples include but are not limited to: -Missed visit window (if patient did not attend) -Malfunctioning equipment -An incorrectly consented participant

6. Procedure

6.1 Potential breaches log

Some types of breach which occur during the conduct of a research study may not necessarily require immediate reporting to the Sponsor, if they have been identified at study set up and the process described below has been put in place. For UHBW sponsored CTIMPs and sponsored complex interventional studies (other than Clinical Investigation of a Medical Device (CIMD) trials) managed by the R&D Research Projects Manager, an assessment may be undertaken at study set up with relevant study staff (including where applicable the statistician) of types of potential breaches which may not need immediate reporting to the Sponsor and what triggers should be put in place (e.g. if exceeds a certain threshold) for reporting to the Sponsor.

The *Potential Breaches reporting log (TMPL_055)* will be used to document any breaches that do not require immediate reporting to the sponsor. This should be prepared by the study team and reviewed and signed off by the Sponsor and the CI. The Sponsor and the research team should agree at study set up how Sponsor oversight will be maintained e.g. a six-monthly review of unreported breaches. The potential breaches reporting log may be amended during the conduct of the trial.

All breaches which do not fall under the above, must be reported to the Sponsor as soon as the breach has been identified (unless otherwise agreed).

6.2 CAPA submission

- The Principal Investigator or delegated personnel must assess a breach as soon as it is identified and report to the central study team within **24 hours** of becoming aware of the event (unless it is the central study team or the Sponsor who have identified the breach). The central study team should onward report the breach to the Sponsor within **24 hours** (unless it does not require immediate reporting because it is captured in *The Potential Breaches reporting log* as described in 6.1 above). This should be reported in writing to research@uhbwnhs.uk.
- Where the breach is considered to have an impact on patient safety, the Investigator must also call 0117 342 0233 immediately and speak to either the Research Projects Manager or the Research Governance and Quality Officer.
- An initial *Corrective and Preventative Action (CAPA) form (TMPL_057)* must be submitted by the study team within **3 calendar days** of the initial notification to the Sponsor and sent to research@uhbw.nhs.uk for review, unless the Sponsor confirms a CAPA is not required. The CAPA should include as much information as is available at the time of reporting. It should also be as specific as possible i.e. who (job role) did what, when (date) and how and why activities were undertaken and set out in chronological order.
- Where a CAPA is not required, the decision should be fully documented in the Trial Master File (TMF) and, if applicable, Investigator Site File (ISF).
- The Research Governance and Quality Officer should review the notified breaches and the submitted CAPAs for UHBW sponsored studies and will discuss for approval with the Research Projects Manager / Research Operations Manager as applicable. If the RGQO is on leave, the allocated sponsor representative should review the breach and discuss with senior staff as applicable.
- The review of the breach by R&D will involve assessing whether the breach is considered serious (as defined in section 6.3 below). This decision should be made with reference to the definitions as provided in 6.3, and determining whether onward reporting to the REC and the MHRA is required.
- The Sponsor will assess the CAPA for completeness and should also assess the adequacy of the corrective and preventative actions, and the timeliness of the completion dates. The relevant personnel in R&D should liaise with the study team if any changes are required. Once

agreed, the Sponsor and Investigator (and representatives from any support departments where applicable) must sign the CAPA form. This should be carried out within the required timelines if the breach is assessed as serious as described in section 6.3. For non-serious breaches, every effort must be made to complete and sign off the CAPA in a timely manner.

- Every signature on a CAPA should either be a wet ink signature, or an electronic signature via a recognised e-signature platform which guarantees the security of the e-signature i.e. so that it can only be applied by the 'owner' of that signature . Typewritten or scanned images of handwritten signatures are only permitted if they are accompanied by the original email of the signatory from their professional email address.
- The Research Governance and Quality Officer must document all correspondence relating to the breach, complete the R&D breach database (RedCap) and, where relevant, discuss with the R&D monitors whether any triggered monitoring is required.

  For those studies where an external trials unit has been given delegated responsibility for management of breaches (see section 6.4 below), the delegated trials unit should maintain its own database and routinely provide the Sponsor with cumulative reports of breaches at regular intervals. It is not necessary for R&D staff to record breaches on the R&D database- the reports received from the delegated trials unit will be saved within the electronic study folder.

- The Chief Investigator or delegated personnel must keep a log of all breaches identified throughout the trial which can be shared with the study statistician to ensure data integrity has not been affected. *TMPL_058 Study breaches log* may be used for this purpose.
- R&D staff conduct ad hoc reviews of CAPA action completion, for UHBW sponsored CTIMPs and sponsored complex interventional studies.

6.3 Serious breaches

The Sponsor of a clinical trial is obliged to notify the licensing authority in writing of any ***serious breach* of:**

  - the conditions and principles of GCP in connection with that trial; or
  - the protocol relating to that trial, as amended from time to time in accordance with regulations 20 to 22C, within 7 calendar days of becoming aware of that breach.

- For the purposes of this regulation, a "serious breach" is a breach which is likely to affect to a significant degree:
  - the safety or physical or mental integrity of the subjects of the trial; and/or
  - the scientific value of the trial.
- For the purposes of this regulation, the timeline for reporting a serious breach applies from the date that the trials unit with the delegated function to manage the trial on behalf of the Sponsor is notified of the breach.
- It is the Sponsor's responsibility to review a breach and decide whether it fulfils the criteria set out above. Further details can be found on the MHRA website.
- While non-CTIMP studies are not subject to Clinical Trials Regulations, the same principles and definitions for serious breaches apply, and any serious breaches of GCP or the protocol should be reported to the relevant ethics committee in accordance with the Research Ethics Committee Standard Operating Procedures.

- For serious breaches, the MHRA (if applicable) and Ethics committee **must be notified within 7 calendar days of the breach being identified**. Where UHBW is the Sponsor, either the Research Projects Manager or the Research Governance and Quality Officer in R&D should liaise with the research team in order to make the required notification. A template form for notifications of serious breaches to the MHRA is available on the MHRA GCP webpage (https://www.gov.uk/guidance/good-clinical-practice-for-clinical-trials#report-a-serious-breach) and this will be used.
- Where the serious breach has a potential impact on patient safety, an assessment should be made by the Sponsor and the Chief Investigator whether any immediate actions are required, for example: halting the trial; withdrawing a participant; closing study location(s).

  Where there is an urgent safety concern, the Chief Investigator and Principal Investigators should follow the required action as described in the *SOP_009 Research Safety Reporting on urgent safety measures* (or other applicable documentation if it has been agreed to follow an external trial unit's urgent safety reporting procedures). Where there is no urgent safety concern the proposed action may be discussed with the MHRA prior to implementation (applicable to CTIMP clinical trials only).

- All documentation relating to breaches must be stored in both the ISF where the breach was identified, and in the TMF.

6.4 Reporting deviations for CIMDs

- Sponsors must notify the MHRA of all deviations as soon as they are aware of them. The notification should include details about the nature of the deviation, when it occurred, where it occurred, and any proposed corrective and preventative actions.
- Deviations occurring in CIMD trials should be reported to sponsor as described in Section 6.2 above and using the following MHRA protocol deviation tracker Excel template.
- The MHRA protocol deviation tracker must be kept as a 'live' document so that new deviations can be added. This enables both the sponsor and the MHRA to have a complete overview each time it is submitted.
- The deviation will be recorded and reviewed following the procedure detailed in section 6.2.
- The Research Projects Manager or the Research Governance and Quality Officer in R&D should send the completed spreadsheet by email to info@mhra.gov.uk.

6.5 Sponsor management of breaches

- Monthly meetings are held with applicable representatives from R&D to review breaches reported in the previous month, identify any new systemic issues, and review previous systemic issues to ensure required actions have been implemented satisfactorily. Identification of a random sampling of studies and CAPAs to review implementation of preventative actions will also be carried out during this meeting in line with 6.2 above.

6.6 External trials units' SOPs

- If the study is managed by an external trials unit and if it has been agreed with Sponsor to follow the breaches SOP of the trials unit, then it is the responsibility of the trials unit to

classify the types of breaches identifying which breaches need immediate reporting to the Sponsor, and to record the breaches.

6.7 SOP related breaches

- Any planned or unplanned/accidental non-compliance with *study specific SOPs* (i.e. breaches) should be recorded and reported to the Sponsor or delegated other as agreed. Any non-compliance should be reviewed, and appropriate corrective and preventative actions should be put in place as applicable. These must be documented in the ISF and TMF.
- Any breaches relating to R&D SOPs should be reviewed by a member of the R&D Senior Management Team (SMT) and corrective and preventative actions put in place (which may involve updating the SOPs).

7. Dissemination and training in the SOP

This SOP should be disseminated to applicable research staff (including R&D) and will be available on the R&D website.

Plan Elements	**Plan Details**
The Dissemination Lead is:	Research Operations Manager
Is this document: A – replacing the same titled, expired SOP, B – replacing an alternative SOP, C – a new SOP:	A – replacing the same titled, expired SOP
If answer above is B: Alternative documentation this SOP will replace (if applicable):	N/A
This document is to be disseminated to:	All applicable research staff (including R&D)
Method of dissemination:	For major updates to the SOP dissemination will be: 1. To Chief Investigators of UHBW Sponsored CTIMPs 2. Research Unit leads across UHBW 3. Head of Research Governance at UoB (where SOP is applicable) All updates (major and minor to the SOP) will be: 1. Updated on the trust MyStaff App 2. Updated on the R&D website 3. Cascaded in R&D communications
Is Training required:	All staff whose activities are subject to this SOP should ensure that they read and understand the content of the SOP. The personal training log of the individual (and the

	Investigator Site File/Trial Master File if required) should be completed to document that the content of this SOP has been read and understood as described in *SOP_007 Research Training UHBW*

REFERENCES	Medicines for Human Use Clinical Trials Regulations 2004 (and any amendments) Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 Medical Devices Regulations 2002 (SI 2002 No 618, as amended) (UK MDR 2002)
RELATED DOCUMENTS AND PAGES	• SOP_007 Research Training • SOP_009 Research Safety Reporting • TMPL_055 Potential breaches reporting log • TMPL_056 File Notes • TMPL_057 Corrective and Preventative Actions (CAPA) Form • TMPL_058 Study breaches log Latest versions can all be found on the Research & Development section of UHBW's website: http://www.uhbristol.nhs.uk/research-innovation/
AUTHORISING BODY	Trust Research Group
SAFETY	N/A
QUERIES AND CONTACT	Research & Development via research@uhbw.nhs.uk
AUDIT REQUIREMENTS	R&D departmental Quality Management System audits are undertaken annually.