Pharmacovigilance and Safety Reporting Policy

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Contents

1. BACKGROUND AND PURPOSE

This Operational Policy sets out the KHP-CTO's approach to managing pharmacovigilance and safety reporting for CTIMPs sponsored by KHP.

2. SCOPE

This Operational Policy applies to all Clinical Trials sponsored by KHP.

The following safety event classifications are in scope:

- Adverse Events (AEs)
- Adverse Reactions (ARs)
- Serious Adverse Events (SAEs)
- Serious Adverse Reactions (SARs)
- Suspected Unexpected Serious Adverse Reactions (SUSARs)
- Important Medical Event (IME)

Each safety event is defined in Section 7: Glossary (below).

Please note safety event classifications are not mutually exclusive i.e. an AE can also be an SAE, a SAR and a SUSAR.

This Operational Policy applies to the following Clinical Trial staff:

- Chief Investigators (who can also be Medical Assessors)
- Sponsor Teams
- Principal Investigators (who can also be Medical Assessors)
- Trial Location Teams
- Medical Assessors (with no other role in the Clinical Trial)
- KHP-CTO staff, including the:
    - Non-Commercial Trials Manager (NCTM)
    - Clinical Research Associates (CRAs)

Please note this Operational Policy is not an exhaustive list of the policies and procedures that must be followed by Clinical Trial staff, with respect to safety events. Clinical Trial staff may also have to comply with safety event-related policies and procedures operated by:

- The Trial Locations (including the sole Sponsor/NHS Co-Sponsor R&D Dept.)
- The Funder
- The IMP manufacturer
- The NIMP manufacturer if applicable

The Chief Investigator is responsible for identifying the safety event-related policies and procedures, operated outside of the KHP-CTO, that need to be followed, and to ensure they're adhered to.

3. PROCEDURES

3.1 General Roles and Responsibilities

Chief Investigator (CI)

The Chief Investigator has overall responsibility for the conduct of the Clinical Trial in accordance with the approved protocol, applicable legislation, and GCP.

Where the Chief Investigator is a GMC-registered medical practitioner, they may also act as the **Sponsor-level** Medical Assessor for the Clinical Trial, subject to 1) approval from the Sole Sponsor/NHS Co-Sponsor R&D Dept., 2) the role being explicitly delegated to the CI, and 3) conflicts of interest being appropriately managed.

The Chief Investigator is responsible for:

- Formally establishing the Data Monitoring and Ethics Committee (DMEC), including proposing suitable independent members and ensuring it's constituted and ready to commence its oversight role in accordance with the DMEC Charter.
- Ensuring that any Serious Adverse Events (SAEs), that are **excluded** from routine SAE reporting, are:
    - Clearly justified
    - Explicitly described in the protocol
    - Subject to an alternative reporting mechanism to the Sponsor
- Ensuring that the Reference Safety Information (RSI) is clearly identified in the protocol and that updates to the RSI are implemented and communicated in accordance with Sponsor procedures and regulatory requirements
- Reviewing emerging safety information and, where necessary, recommending Modifications, risk mitigation measures, or Clinical Trial suspension/termination in response to safety concerns
- Ensuring appropriate engagement with the Sponsor and DMEC regarding safety issues, trends, and recommendations

Principal Investigator (PI)

For single-centre trials, the Chief Investigator and Principal Investigator may be the same individual.

Where the Principal Investigator is a GMC-registered medical practitioner, they may also act as the **Trial Location-level** Medical Assessor for the Trial Location, subject to 1) the role being explicitly delegated to the PI, and 2) conflicts of interest being appropriately managed.

In accordance with ICH GCP E6 (R3), the Principal Investigator is responsible for ensuring that safety reporting requirements are met at the Trial Location. This includes ensuring that delegated staff are appropriately trained, resourced, and supervised to meet pharmacovigilance obligations.

Medical Assessors

A Medical Assessor is a GMC-registered medically practitioner responsible for providing clinical judgement on individual safety reports arising during a Clinical Trial.

The assessor may be involved in the Clinical Trial in another role (i.e. as a CI, PI, Sponsor Team member or Trial Location Team member), or their sole involvement may be as the assessor.

Sponsor-level Medical Assessor (typically the Chief Investigator) responsibilities:

- Classifying SARs as Suspected Unexpected Serious Adverse Reactions (SUSARs) depending on **expectedness** by reference to the Reference Safety Information (RSI)
- Provide timely medical judgement to support regulatory reporting, risk assessment, and escalation decisions
- Documenting assessments in accordance with Sponsor pharmacovigilance procedures

Trial Location-level Medical Assessor (typically the Principal Investigator) responsibilities:

- Assessing AEs for **seriousness** and classifying as SAEs where appropriate
- Assessing AEs for IMP **causality** and classifying as ARs where appropriate
- Assessing SAEs for IMP **causality** and classifying as SARs where appropriate
- Assessing AEs for IME status according to the **IME definition in the protocol**, and/or **the assessor's medical judgement**
- Provide relevant clinical context and follow-up information to support Sponsor safety review

Non-Commercial Trials Manager (NCTM)

On behalf of the Sponsor, the Non-Commercial Trials Manager (NCTM) is responsible for operational oversight of pharmacovigilance and safety reporting.

The Non-Commercial Trials Manager is responsible for:

- Ensuring that safety reports are submitted to the MHRA in accordance with applicable legislation and regulatory timelines
- Ensuring that events assessed as SUSARs are reported in accordance with statutory requirements and SOPs
- Overseeing the preparation and submission of periodic safety reports (e.g. DSURs)
- Ensuring that, for Double-Blinded Trials, procedures are in place to prevent the Chief Investigator from having access to information that could result in Unblinding, in line with ICH GCP E6 (R3)
- Where Unblinding is required, maintaining Unblinded safety records

- Ensuring timely MedDRA coding of all SAEs
- Coordinating responses to MHRA or REC safety queries, inspections, and follow-up actions

Data Monitoring and Ethics Committee (DMEC) Members

Prior to the DMEC commencing its activities, proposed DMEC members must:

- Provide a current Curriculum Vitae (CV) for filing in the Trial Master File (TMF)
- Complete and sign conflict of interest declarations
- Review and formally agree to the DMEC Charter and any other agreements defining the committee's remit, responsibilities, independence, and operating procedures

Completion of these steps enables the DMEC to be formally constituted and ready to undertake its independent oversight role for the Clinical Trial.

Sole Sponsor/NHS Co-Sponsor R&D Dept.

Confirm the Sponsor-level Medical Assessor.

3.2 Assessing the relatedness of AEs and SAEs to the IMP

The following categories are determined by Trial Location-level Medical Assessor:

- Assessing AEs for IMP **causality** and classifying as ARs where appropriate
- Assessing SAEs for IMP **causality** and classifying as SARs where appropriate

Definition	Category
There is no evidence of any causal relationship	Unrelated
There is little evidence to suggest there is a causal relationship (e.g. the AE/SAE did not occur within a reasonable time after the administration of the IMP); or There is another reasonable explanation for the AE/SAE (e.g. the participant's clinical condition, other concomitant treatment).	Unlikely
There is some evidence to suggest a causal relationship (e.g. because the AE/SAE occurs within a reasonable time after administration of IMP); or The influence of other factors may have contributed to the AE/SAE (e.g. the participant's clinical condition, other concomitant treatments).	Possibly

There is evidence to suggest a causal relationship and the influence of other factors is unlikely.	Likely
There is clear evidence to suggest a causal relationship	Definitely
There is insufficient or incomplete evidence to make a clinical judgement of the causal relationship; or A judgement of the causal relationship has not yet been completed.	No assessment

3.3 Adverse Event process

Task	Responsibility	Activity
1	Clinical Research Associate	Ensure that protocol-defined AE reporting requirements are clearly communicated to the Trial Location Team during the Site Initiation Visit (SIV), including expectations for documentation, reporting pathways, and timelines. This activity must be conducted in accordance with **SOP 13.0 Study Set-Up and Initiation of an Investigator Site**
2	Principal Investigator	The Principal Investigator must ensure that any Clinical Trial-specific requirements for AE recording and reporting (including whether and how non-serious AEs are reported to the Sponsor, and applicable timelines) are followed.
3	Principal Investigator or delegate	Any untoward medical occurrence in a participant administered an IMP must be identified and recorded as an AE, irrespective of causal relationship. All AEs that are required to be recorded or reported under the protocol must be accurately documented in Source Records and made available for verification. Source Records relating to AEs must be complete, contemporaneous, and accessible for monitoring.
4	Trial Location-level Medical Assessor	Assessing the AE for **seriousness** and classifying as an SAE where appropriate • If the AE is an SAE, report it to the Sponsor via the KHP-CTO. See Section 3.4 Serious Adverse Event process (below) Assessing the AE for IME status according to the **IME definition in the protocol**, and/or **the assessor's medical judgement** • If the AE is an IME, report it to the Sponsor via the KHP-CTO. See Section 3.7 Important Medical Events process (below)

		Assessing the AE for IMP **causality** and classifying as an AR where appropriate
5	Principal Investigator or delegate	Where the AE is not an SAE, ensure that all recorded AE data is consistent, complete, and in compliance with protocol requirements.
6	Clinical Research Associate	In accordance with the Monitoring Plan, review Source Records and reported AE data to verify consistency, completeness, and compliance with protocol requirements. Record activities per **SOP 3.0 Clinical Trial Monitoring**.

3.4 Serious Adverse Event process

Task	Responsibility	Activity
1	Trial Location-level Medical Assessor	Where an AE is classified as an SAE depending on **seriousness**, the Trial Location-level Medical Assessor must ensure that the SAE is reported to the Sponsor via the KHP-CTO without undue delay, in accordance with protocol and Sponsor timelines. The SAE must be assessed for IMP **causality** and classified as an SAR where appropriate The SAE must be recorded using the Sponsor-approved SAE reporting form and emailed to the KHP-CTO pharmacovigilance inbox. The SAE report must include sufficient clinical detail to enable the Sponsor, via the KHP-CTO, to review and follow-up.
2	Clinical Trials Administrator	Upon receipt of an SAE report in the KHP-CTO pharmacovigilance inbox: • Acknowledge receipt of the SAE report to the sender and retain a copy of the acknowledgement in the TMF • Record Sponsor awareness (which is KHP-CTO awareness) of the SAE in the TMF, including the date and time the SAE was first received by the Sponsor via the KHP-CTO ○ Where the SAE report is initially sent to the CI or CRA, and subsequently forwarded to the KHP-CTO pharmacovigilance inbox, the date of the original receipt constitutes the date of Sponsor awareness (which is KHP-CTO awareness) • Make sure the relevant CRA is aware of the SAE report if a) they weren't Cc'd when the SAE report was emailed to the KHP-CTO pharmacovigilance inbox, or b) they didn't

		forward the SAE report to the KHP-CTO pharmacovigilance inbox
3	Clinical Research Associate	Notify the Chief Investigator (and the Sponsor-level Medical Assessor if the Chief Investigator isn't undertaking this role) that an SAE has been received. Undertake MedDRA coding for the reported event, including the following meta-data: • System Organ Class (SOC) • Preferred Term (PT) • Version • Lower-Level Term (LLT) Record the information in the TMF Update MedDRA coding as further clinical information becomes available.
4	Clinical Research Associate	If the SAE is a SAR, notify the Sponsor-level Medical Assessor and confirm the version and date of the RSI to be used for the **expectedness** assessment. Retain evidence of notification (e.g. email correspondence) in the TMF
5	Sponsor-level Medical Assessor	Assess whether the SAR should be classified as a SUSAR depending on **expectedness** by reference to the Reference Safety Information (RSI). If the SAR is a SUSAR, follow Section 3.5 Suspected Unexpected Serious Adverse Reaction process (below). Document the assessment and file in the TMF
6	Trial Location-level Medical Assessor	Any follow-up information about the SAE must continue to be recorded using the Sponsor-approved SAE reporting form and emailed to the KHP-CTO pharmacovigilance inbox. The follow-up information must include sufficient clinical detail to enable the Sponsor, via the KHP-CTO, to review and follow-up.
7	Clinical Research Associate	Throughout the conduct of the Clinical Trial, ensure that ongoing safety reporting obligations (including annual safety reporting) are fulfilled in accordance with **SOP 17.0 Preparation and Submission of Development Safety Update Reports (DSURs)**, and that required submissions are made to the MHRA within applicable timelines.
8	Sponsor-level Medical Assessor	Throughout the Clinical Trial, ensure that safety information is reviewed proportionately and in consideration of risk, in accordance with **SOP 22.0 Proportionality and Risk**

		Assessment for Clinical Trials of Investigational Medicinal Products Document reviews in the TMF
9	Clinical Research Associate	At End of Trial (EoT), and at interim points where required by the Statistical Analysis Plan (SAP), generate a listing of all reported SAEs for: • Reconciliation with the main Clinical Trial database • Provision to the statistician for analysis and reporting Retain the SAE listings in the TMF

3.5 Suspected Unexpected Serious Adverse Reaction process

Task	Responsibility	Activity
1	Trial Location-level Medical Assessor	Any follow-up information about the SAE must continue to be recorded using the Sponsor-approved SAE reporting form and emailed to the KHP-CTO pharmacovigilance inbox. The follow-up information must include sufficient clinical detail to enable the Sponsor, via the KHP-CTO, to review and follow-up.
2	Sponsor-level Medical Assessor	When a SAR is assessed as a SUSAR, the Sponsor-level Medical Assessor must confirm the **seriousness**, **causality** and **expectedness** assessments (the rationale) that support the SUSAR assessment. This confirmation must be documented in the TMF. Ask the CRA to procure any outstanding **seriousness**, **causality** or **expectedness** assessments. Ask the Trial Location-level Medical Assessor for any clinical information necessary to support the SUSAR assessment.
3	Clinical Research Associate	Make reasonable efforts to obtain any outstanding **seriousness**, **causality** or **expectedness** assessments to support SUSAR reporting, within the requested timelines. Document all attempts to obtain outstanding assessments in the TMF.
4	Trial Location-level Medical Assessor	Make reasonable efforts to provide any clinical information requested by the Sponsor-level Medical Assessor necessary to support the SUSAR assessment and reporting, within requested timelines.

5	Clinical Research Associate	For placebo-controlled, Blinded Trials, perform Sponsor-level Unblinding of the affected participant only where required to confirm whether the participant received the IMP. Unblinding must be conducted in accordance with **SOP 14.0 Emergency Code Break In Clinical Trials** Treatment allocation must not be disclosed to the Chief Investigator, Sponsor Team, Principal Investigator, nor Trial Location team, unless explicitly required for participant safety. Record the Unblinding outcome in the TMF, clearly labelling documents as containing potentially Unblinding information. Where the participant is confirmed to have received placebo only, no SUSAR submission is required. Where the participant is confirmed to have received the active IMP, proceed with SUSAR submission in accordance with the steps below.
6	Non-Commercial Trials Manager or delegate	Required regulatory timelines are calculated from the date of Sponsor awareness (which is KHP-CTO awareness): • Fatal or life-threatening SUSARs: **Initial Report** within 7 calendar days, with the **Follow-up Report** submitted within a further 8 calendar days (i.e. by day 15). • All other SUSARs: **Full Report** within 15 calendar days. Ensure the applicable SUSAR reports are submitted to the MHRA by the CRA within the required regulatory timelines, calculated from the date of Sponsor awareness (which is KHP-CTO awareness). Note: Where the protocol specifies more stringent reporting timelines, these must be followed.
7	Clinical Research Associate	For SUSARs that are fatal or life-threatening, submit the **Initial Report** to the MHRA. Retain evidence of submission in the TMF. Collate the required information and submit the **Follow-up Report** to the MHRA. Retain evidence of submission in the TMF. Note: The MHRA may share SUSAR information with the REC where appropriate. Separate routine SUSAR submission to the REC is not required unless otherwise specified.
8	Clinical Research Associate	For SUSARs that <u>are not</u> fatal nor life-threatening, submit the **Full Report** to the MHRA.

		Retain evidence of submission in the TMF. Note: The MHRA may share SUSAR information with the REC where appropriate. Separate routine SUSAR submission to the REC is not required unless otherwise specified.
9	Clinical Research Associate	For Blinded Trials, to preserve the Blinding, if the Chief Investigator is not the Sponsor-level Medical Assessor, do not tell the Chief Investigator which SAE resulted in a SUSAR
10	Clinical Research Associate	For Open-Label Trials, if the Chief Investigator is not the Sponsor-level Medical Assessor, inform the Chief Investigator that a SUSAR has been reported to the MHRA in accordance with regulatory requirements. Retain confirmation correspondence in the TMF.
11	Non-Commercial Trials Manager or delegate	As new information becomes available, send **Follow-up Reports** to the MHRA as necessary. Respond promptly to any requests for information from the MHRA or REC, coordinating input from the following individuals as necessary: • Chief Investigator • Sponsor-level Medical Assessor • Principal Investigator • Trial Location-level Medical Assessor • Clinical Research Associate File all correspondence and submissions in the TMF.

3.6 Contraception process and pregnancy reporting process

Task	Responsibility	Activity
1	Chief Investigator	Ensure that appropriate contraceptive requirements for the following participants are defined in the protocol: • Female participants of child-bearing potential • Fertile male participants (where relevant) Where the definition of 'female of child-bearing potential' and/or 'fertile male' differs from that set out in the Clinical Trials Facilitation and Coordination Group (CTFG) guidance (See Section 5 Related Documents below), ensure the protocol states the alternative definition. Refer to **SOP 9.0 Writing a Good Clinical Practice (GCP) Compliant Clinical Trial Protocol**

2	Principal Investigator or delegate	Promptly notify the Sponsor via the KHP-CTO of any suspected or confirmed pregnancy involving: • A female participant; or • The female partner of a male participant (where exposure is relevant) Pregnancy reports must be submitted using the Sponsor-approved SAE reporting form and emailed to the KHP-CTO pharmacovigilance inbox.
3	Clinical Research Associate	Upon receipt of a pregnancy report: • Confirm receipt to the reporting Trial Location by email and save correspondence in the TMF • Inform the Chief Investigator of the suspected or confirmed pregnancy, including all available relevant information, and save correspondence in the TMF
4	Chief Investigator or delegate	Where appropriate, assess whether the protocol should be modified to enable relevant pregnancy and outcome data to be collected and included in Clinical Trial reports and listings. If it's decided that the protocol should be modified to enable relevant pregnancy and outcome data to be collected and included in Clinical Trial reports and listings, submit a Modification. The Modification submission package may require updated versions of Clinical Trial documents, including but not limited to, the: • Protocol • Case Report Form template • ICF • PIS Refer to: • SOP 8.0 Case Record Form Design • SOP 12.0 Application & Maintenance of a Clinical Trial Authorisation • SOP 22.0 Proportionality and Risk Assessment for Clinical Trials of Investigational Medicinal Products
5	Principal Investigator or delegate	Where applicable, seek informed consent from the female participant, or from the female partner of a male participant (where exposure is relevant), for the collection of follow-up data relating to: • The pregnancy • Its outcome The following supporting documents should be used, as appropriate: • Pregnancy Notification Form template • Pregnant Partner Consent Form template • Pregnant Partner GP Letter template • Pregnant Partner Information Sheet template

		Refer to: • SOP 7.0 Obtaining Informed Consent for Clinical Trials
6	Principal Investigator or delegate	Where consent has been obtained, ensure that the relevant pregnancy and outcome data are accurately recorded in the Case Report Form in accordance with the protocol.

3.7 Important Medical Events process

Task	Responsibility	Activity
1	Chief Investigator	Where AEs that do not meet the standard seriousness criteria are nonetheless required to be subject to expedited reporting, ensure that these AEs are clearly defined as Important Medical Events (IMEs) in the protocol.
2	Trial Location-level Medical Assessor	Promptly report to the Sponsor via the KHP-CTO: • Any IMEs specified in the protocol • Any other AEs which, in the Trial Location-level Medical' Assessor's judgement, warrant expedited reporting Reports should be submitted by completing n Sponsor-approved SAE reporting form and emailing it to the KHP-CTO pharmacovigilance inbox.
3	Clinical Trials Administrator	On receipt of an IME report, follow the standard SAE receipt process, including: • Acknowledging receipt of the IME report to the sender and retaining a copy of the acknowledgement in the TMF • Recording Sponsor awareness (which is KHP-CTO awareness) of the IME in the TMF, including the date and time the IME was first received by the Sponsor via the KHP-CTO ○ Where the IME report is initially sent to the CI or CRA, and subsequently forwarded to the KHP-CTO pharmacovigilance inbox, the date of the original receipt constitutes the date of Sponsor awareness (which is KHP-CTO awareness) • Make sure the relevant CRA is aware of the IME report if a) they weren't Cc'd when the IME report was emailed to the KHP-CTO pharmacovigilance inbox, or b) they didn't forward the IME report to the KHP-CTO pharmacovigilance inbox
4	Clinical Research Associate	On receipt of an IME report, send notification of the IME to the Chief Investigator. Record correspondence in the TMF.

5	Chief Investigator	Complete the **CI Pharmacovigilance Oversight Supplementary Form** and send it to the CRA. Record the form and the correspondence in the TMF.
6	Chief Investigator	Undertake follow-up of the IME with the Trial Location-level Medical Assessor, as appropriate, based on the nature of the AE and any emerging safety concerns. Ensure that all correspondence is retained in the TMF.

4. RELATED TEMPLATES

- Pregnancy Notification Form template.docx
- Pregnant Partner Consent Form template.docx
- Pregnant Partner GP Letter template.docx
- Pregnant Partner Information Sheet template.docx
- SAE Reporting Form Guide.docx
- Serious Adverse Event Report Form template.docx

5. RELATED DOCUMENTS

SOPs

SOP 3.0 Clinical Trial Monitoring
SOP 7.0 Obtaining Informed Consent for Clinical Trials
SOP 8.0 Case Record Form Design
SOP 9.0 Writing a Good Clinical Practice (GCP) Compliant Clinical Trial Protocol
SOP 12.0 Application & Maintenance of a Clinical Trial Authorisation
SOP 13.0 Study Set-Up and Initiation of an Investigator Site
SOP 14.0 Emergency Code Break In Clinical Trials
SOP 17.0 Preparation and Submission of Development Safety Update Reports (DSURs)
SOP 22.0 Proportionality and Risk Assessment for Clinical Trials of Investigational Medicinal Products

Other Documents

ICH GCP E6 (R3)
ICH_E6(R3)_Step4_FinalGuideline_2025_0106.pdf

MHRA Guidance for Managing CTAs and Reporting Safety Issues
Clinical trials for medicines: manage your authorisation, report safety issues - GOV.UK (www.gov.uk)

MHRA Decision Tree to Determine Unblinding Following a SAR
https://assets.publishing.service.gov.uk/media/68dac869ef1c2f72bc1e4bc1/Fig3._Unblinding_after_SARs.pdf

Clinical Trials Facilitation and Coordination Group (CTFG) (a UK-wide strategic coordination body) guidance related to contraception and pregnancy testing in Clinical Trials
2020_09_HMA_CTFG_Contraception_guidance_Version_1.1_updated.pdf

The Medicines for Human Use (Clinical Trials) Regulations 2004 (as amended)
The Medicines for Human Use (Clinical Trials) Regulations 2004 (legislation.gov.uk)

Trial Steering Committee (TSC) and Data Monitoring and Ethics Committee (DMEC) Guidance for NIHR portfolio trials:
Research Governance Guidelines | NIHR

6. CHANGE HISTORY

CHANGE HISTORY			
Date	Version Number	Change details	Approved by
01/02/2008	1.0	Original version	Jackie Powell
12/02/2009	2.0	Addition of Pregnancy Safety Reporting	Jackie Powell
31/08/2010	3.0	Updated with respect to change in MHRA policy re eSUSAR reporting. Clarification of Unblinding & downgrading of PI reports by CI. Transfer to King's Health Partner Livery.	Jackie Powell
14/09/2011	4.0	Amendment of ASR to DSUR as per ICH E2 guidance	Jackie Powell
19/10/2012	5.0	Change of branding to KHP-CTO and update to include reporting of Important Medical Events	Jackie Powell
11/11/2013	6.0	Minor clarifications to reporting procedure	Jackie Powell
08/12/2016	7.0	Updates of Glossary. Updates to MHRA contact information for Urgent Safety Measures. Clarification that follow-up safety data may be collected from Unblinded participants.	Jackie Pullen
16/04/2018	8.0	Update to clarify reporting process for eSUSARs. Update so Important Medical Event correlates to "Other Medically Important Condition" for eSUSAR reporting. Update to ensure use of MedDRA terminology when coding eSUSAR events. Inclusion of MedDRA in the glossary.	Jackie Pullen
26/09/2018	8.1	Minor amendment to include Clinical Trials managed by the KHP-CTO.	Jackie Pullen
30/11/2021	8.2	Minor amendment to update reporting procedures.	Jackie Pullen

22/09/2023	8.3	Update to align with current MHRA SUSAR reporting requirements	Kirsty Hough
29/01/2024	9.0	Updated as part of MHRA Inspection findings. Updated to include details of expectedness assessments and responsibilities, MedDRA coding, RSI information, SUSAR processing for Blinded Trials, causality gradings and management, pregnancy of partners of Clinical Trial participants. Removed statement regarding Sponsor withdrawing Unblinded participants.	Ann-Marie Murtagh
23/04/2026	10.0	• Operational Policy template updated • Updated to align with The Medicines for Human Use (Clinical Trials) Regulations 2004 (as amended) and ICH GCP E6 (R3) • Addition of Medical Assessor duties where the CI is not a GMC licensed doctor • Addition of reference to reconciling reported SAEs with main Clinical Trial database	Ann-Marie Murtagh

7. GLOSSARY

Adverse Event (AE) - Any untoward medical occurrence in a participant who has been administered an IMP, which does not necessarily have a causal relationship with that IMP.

Adverse Reaction (AR) - An Adverse Event that is suspected to be causally related to the administration of an IMP, regardless of dose, and includes reactions resulting from authorised use, off-label use, misuse, medication error, overdose, or interactions where applicable.

Blinded Trial - A Clinical Trial in which treatment allocation is concealed from one or more parties involved in the Clinical Trial (e.g. participant, investigator, Sponsor staff), in accordance with the protocol and randomisation procedures.

Blinding - A procedure used in a Clinical Trial to withhold information about treatment allocation from one or more parties (e.g. participants, investigators, Sponsor staff) in order to minimise bias in Clinical Trial conduct, assessment, and reporting. 'Blind' and 'Blinded' to be construed accordingly.

Case Report Form - A printed, optical or electronic document designed to record all of the protocol-required information for each trial participant, to be reported to the Sponsor.

Chief Investigator (CI) – The overall lead researcher for a Clinical Trial (Outside the UK the term 'Coordinating Investigator', 'Principal Investigator' or 'Investigator' may be used for the overall lead researcher for a Clinical Trial). Chief Investigators are responsible for the overall conduct of a Clinical Trial.

Clinical Research Associate (CRA) – A staff member employed by the KHP-CTO who conducts monitoring activities for a Clinical Trial, including but not limited to the initiation phase, routine phase, and close down phase.

Clinical Trial of an Investigational Medicinal Product (CTIMP) - Any investigation in human participants (other than a non-interventional trial) intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more medicinal products and/or to identify any adverse reactions to one or more such products and to study absorption, distribution, metabolism and excretion of one or more such products with the object of ascertaining the safety and/or efficacy of those products. Includes clinical trials of ATMPs.

Clinical Trials Administrator - A staff member employed by the KHP-CTO who conducts administrative activities for a Clinical Trial.

Code Break – The controlled process by which the treatment allocation for an individual participant is Unblinded, typically in the event of a medical emergency, where the identity of the Clinical Trial treatment has been withheld as part of the Clinical Trial's Blinding procedures.

Co-Sponsors – Two organisations that take responsibility for the initiation, management and financing (or arranging of the financing) in relation to a Clinical Trial. The Co-Sponsors agree how the Sponsor functions for the Clinical Trial are divided between themselves and document this accordingly.

Curriculum Vitae (CV) - A summary of a person's education, professional history and job qualifications.

Data Monitoring and Ethics Committee (DMEC) – An independent committee, convened prior to the commencement of a Clinical Trial, that periodically reviews accumulating safety and Clinical Trial data at predefined intervals, or when specified Clinical Trial milestones are met. The DMEC provides independent advice to the Chief Investigator and Sponsor on whether the Clinical Trial should continue, be modified, or be terminated, taking into account participant safety, ethical considerations, and the overall risk–benefit balance.

Development Safety Update Report (DSUR) - A common standard for periodic reporting on drugs under development (including marketed drugs that are under further study).

Double-Blinded Trial - A Clinical Trial design in which both the participants, and the investigators responsible for their care and assessment, are unaware of the treatment allocation for the duration of the Clinical Trial.

End of Trial (EoT) – The end of the trial as defined in the protocol. The end of the trial is typically expressed as a condition-based event, not a predetermined date.

eSUSAR – A SUSAR that's submitted by the Sponsor through an electronic pharmacovigilance reporting system, rather than by paper or email. The term eSUSAR is not defined in the Regulations, it's an informal term.

Good Clinical Practice (GCP) - An international ethical and scientific quality standard for designing, conducting, recording, and reporting Clinical Trials that involve human participants. It ensures the safety, well-being, and rights of participants are protected while

maintaining the credibility and accuracy of trial data. GCP is crucial for safeguarding participants and ensuring Clinical Trials produce reliable, scientifically valid results.

ICH GCP E6 (R3) – The International Council for Harmonisation – Good Clinical Practice, Guideline E6 (Revision 3). This is an internationally recognised ethical and scientific quality standard for the design, conduct, oversight, recording, and reporting of Clinical Trials.

Important Medical Event (IME) - An Adverse Event or Adverse Reaction that may not immediately result in death, be life-threatening, or require hospitalisation, but which, in the judgement of a medically qualified individual, may jeopardise the participant or require medical or surgical intervention to prevent one of those serious outcomes.

Investigator's Brochure (IB) - A Sponsor-prepared reference document that compiles the clinical and non-clinical data on an IMP that are relevant to its use in a Clinical Trial. It's intended to provide Clinical Trial staff with sufficient information to understand the rationale for the Clinical Trial, the known and potential risks and benefits of the IMP, including Adverse Reactions, and the appropriate management of participants. Where the IMP has a Marketing Authorisation, an SmPC will be available and it will supersede the IB as the RSI.

Investigational Medicinal Product (IMP) – A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a Clinical Trial. This includes products with marketing authorisation when used in a way different from the approved form, for an unapproved indication, or to gain further information about an approved use.

Investigator Site File (ISF) – The Trial Location-specific set of essential documents held at the Trial Location by the Principal Investigator, demonstrating how the trial was conducted at that particular location and that the investigator complied with the protocol, Sponsor instructions, and GCP.

KHP-CTO Non-Commercial Team - Comprises the Non-Commercial Trials Manager, CRA(s), Clinical Trial Administrator(s), and Training Executive(s).

King's Health Partners (KHP) - King's College London, Guy's and St Thomas' NHS Foundation Trust, King's College Hospital NHS Foundation Trust, and South London and Maudsley NHS Foundation Trust.

King's Health Partners Clinical Trials Office (KHP-CTO) – The department established by King's College London, Guy's and St Thomas' NHS Foundation Trust, King's College Hospital NHS Foundation Trust, and South London and Maudsley NHS Foundation Trust to 1) undertake the set up and financial management for commercial research hosted by one or more of the KHP Partners, and 2) undertake the regulatory submissions and oversight, as well as monitoring activity for non-commercial research studies sponsored by one of the KHP Partners.

Marketing Authorisation – A regulatory approval granted by the competent authority that permits a medicinal product to be placed on the market, confirming that its quality, safety, and efficacy have been adequately demonstrated.

Medical Assessor - A medically qualified individual responsible for providing clinical judgement on individual safety reports arising during a Clinical Trial. The assessor may be involved in the Clinical Trial in another role (i.e. as a CI, PI, Sponsor Team member or Trial Location Team member), or their sole involvement may be as the assessor. At Trial Location-level, assessment of safety events involves initial clinical evaluation and causality

assessment for participants at the Trial Location. At Sponsor-level, assessment involves reviewing serious safety events across all Trial Locations, confirming seriousness, causality, and expectedness, and supporting regulatory determinations such as SAR and SUSAR reporting.

Medical Dictionary for Regulatory Activities (MedDRA) - A clinically validated international medical terminology dictionary (and thesaurus) used by regulatory authorities for the purposes of Adverse Event classification.

Medicines & Healthcare products Regulatory Agency (MHRA) – The UK government agency responsible for regulating medicines, medical devices, and Clinical Trials. In the context of Clinical Trials, the MHRA i) acts as the licensing authority for Clinical Trials, ii) reviews the scientific, quality, and safety aspects of a Clinical Trial application, iii) issues CTAs, iv) oversees GCP and GMP inspections, v) monitors pharmacovigilance and safety reporting, and vi) enforces compliance with UK medicines legislation.

Modification - Any change to a Clinical Trial after initial approval that affects the information or conditions on which the Clinical Trial was authorised. Includes minor modifications, Modifications of an Important Detail (MOIDs), Route A and Route B substantial modifications.

Monitoring Plan - A Sponsor-approved document that sets out how Clinical Trial monitoring will be conducted, managed, and documented, using a risk-based approach to ensure participant safety, data integrity, and compliance with the approved protocol and applicable regulations.

Non-Commercial Trials Manager (NCTM) – The most senior member of the KHP-CTO Non-Commercial Team.

Open-Label Trial - a Clinical Trial that is not designed to be Blinded, meaning that the participant, investigator, and trial staff are aware of the treatment being administered.

Operational Policy - A formal governance document that sets out the principles, roles, responsibilities, and high-level requirements for how an aspect of Clinical Trial oversight is managed by the KHP-CTO, ensuring compliance with applicable legislation, regulatory guidance, and GCP.

Partner Trusts – Guy's and St Thomas' NHS Foundation Trust, King's College Hospital NHS Foundation Trust, and South London and Maudsley NHS Foundation Trust.

Principal Investigator (PI) – The individual at a Trial Location who has primary responsibility for the conduct of the Clinical Trial at that Trial Location.

Reference Safety Information (RSI) – The authoritative document used to determine the expectedness of SARs occurring during a Clinical Trial. It defines which SARs are considered expected for the IMP, based on the safety information available at the time, and is used by the Sponsor to assess whether a SAR qualifies as a SUSAR. If the IMP has a Marketing Authorisation, the SmPC will be used as the RSI. If the IMP does not have a Marketing Authorisation, the IB will be used as the RSI.

Regulations – The Medicines for Human Use (Clinical Trials) Regulations 2004 (as amended including the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025).

Research & Development Department (R&D Dept.) – The department at a Trial Location that's responsible for research and development at that Trial Location.

Research Ethics Committee (REC) – A national independent body consisting of healthcare professionals and non-medical members, whose responsibility is to protect the rights, safety and well-being of human subjects involved in a Clinical Trial, and to provide public assurance of that protection by, among other things, expressing an opinion on the Clinical Trial protocol, the suitability of the investigators and the adequacy of facilities, and on the methods and documents to be used to inform Clinical Trial participants and obtain their informed consent.

Serious Adverse Event (SAE) - An Adverse Event that results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or consists of a congenital anomaly or birth defect.

Serious Adverse Reaction (SAR) - An Adverse Reaction that is both serious and suspected to be causally related to an IMP. In other words, it is an untoward and unintended response to the IMP that results in death, is life-threatening, requires or prolongs hospitalisation, results in persistent or significant disability or incapacity, involves a congenital anomaly or birth defect, or is otherwise judged to be a medically important event.

Site Initiation Visit (SIV) - A formal visit conducted by the Sponsor or their representative before a Trial Location begins participant recruitment, to confirm that the Trial Location is fully prepared to conduct the Clinical Trial in accordance with the approved protocol, regulatory requirements, and GCP.

Source Records - The original documents, data, and records in which information about a participant is first recorded.

Sponsor Team – The team selected by the CI to undertake the sponsorship functions of the Clinical Trial.

Standard Operating Procedures (SOPs) - Detailed, written instructions to achieve uniformity of the performance of a specific function. SOPs are the basis upon which Quality Systems and Processes are conducted and monitored against.

Statistical Analysis Plan (SAP) - A detailed, pre-specified document that describes the planned statistical methods and analyses to be applied to a Clinical Trial's data.

Summary of Product Characteristics (SmPC) - A regulatory document approved by the MHRA that provides authoritative information for healthcare professionals on the safe and effective use of a medicinal product. It includes details on the product's composition, indications, dosing, contraindications, warnings and precautions, interactions, pharmacological properties, and known Adverse Reactions, and forms part of the product's Marketing Authorisation. Where a medicinal product does not have a Marketing Authorisation (i.e. an unlicensed IMP), an SmPC will not be available, and the equivalent safety information is provided through the IB, which serves as the RSI for pharmacovigilance and safety reporting.

Suspected Unexpected Serious Adverse Reaction (SUSAR) - A Serious Adverse Reaction to an IMP that is unexpected, meaning that the nature or severity of the reaction is not consistent with the applicable product information according to the RSI.

Trial Location - Means a hospital, health centre, surgery or other establishment, or facility or premises at or from which a Clinical Trial, or any part of such a Clinical Trial, is conducted.

Trial Location Team - The team selected by the PI to undertake the Trial Location functions of the Clinical Trial.

Trial Master File (TMF) - A standard filing system which contains all essential documents which individually and collectively permits the evaluation of the conduct of a Clinical Trial and the quality of the data produced. The filing system can be in the form of a single project file or a number of files/filing cabinets, depending on what is deemed most appropriate for a particular Clinical Trial given its size and complexity. The regulatory documents and approvals within the TMF will be maintained alongside Case Report Forms and Source Records.

Unblinding - A procedure used in a Clinical Trial in which treatment allocation is revealed for an individual participant or, in rare cases, for the Clinical Trial as a whole. Unblinding may occur in accordance with the protocol (e.g. at EoT), or prematurely, where necessary to protect participant safety or to meet regulatory reporting requirements. 'Unblind' and 'Unblinded' to be construed accordingly.