Standard Operating Procedures (SOP) for:			
Pharmacovigilance and Safety Reporting for Sponsored non-CTIMPs			
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Purpose and Objective:
To identify and standardise the process for reporting Adverse Events (AEs), Serious Adverse Events, Serious Adverse Reactions (SARs - in this case reactions to the Medical Device or study procedure being investigated), and Urgent Safety Measures (USM). To ensure that systems are in place for the management of AEs for all studies, not just clinical trials of medicinal products (CTIMPs) to ensure that during the course of a study the participants' involvement in the research is recorded and reported to ensure their continued safety. To be compliant with Good Clinical Practice (GCP), Research Governance Framework (RGF), Medical Devices Regulations 2002, Sponsors of Non-CTIMP clinical studies have a responsibility to record and report SAEs.
Scope:
This SOP covers procedures primarily for Barts Health NHS Trust [BH] and Queen Mary University of London [QMUL] sponsored Non - CTIMPs. (See SOP 26a for Pharmacovigilance for CTIMPs) Reporting mechanisms for SAEs in Non-CTIMPs are determined by the sponsor. The PI informs the sponsor of SAEs that occur in all study participants according to the sponsor Pharmacovigilance SOP and/ or the process outlined in the protocol. For all studies sponsored by an external sponsor, the sponsor procedure should be followed.
Abbreviations:
AE Adverse Event APR Annual Progress Report BH Barts Health NHS Trust CI Chief Investigator CRF Case Report Form CTIMP Clinical Trial of an Investigational Medicinal Product(s)

DSUR	Development Safety Update Report
EOT	End of Trial
GCP	Good Clinical Practice
IMP	Investigational Medicinal Product
IRAS	Integrated Research Application System
JRMO	Joint Research Management Office
MHRA	Medicines and Healthcare Regulatory Agency
PI	Principal Investigator
QMUL	Queen Mary University of London
REC	Research Ethics Committee
ReDA	JRMO Research Database
SAE	Serious Adverse Event
SOP	Standard Operating Procedures
SUSAR	Suspected Unexpected Serious Adverse Reaction

Definitions (if needed):

Non-CTIMP: Non- Clinical Trial of an Investigational Medicinal Product(s) [non-drug trial]

Delegation of Responsibilities
For multi-site studies, the Chief Investigator (CI) has overall responsibility for Pharmacovigilance and Safety Reporting for Sponsored non-CTIMPs at all the sites.

Each Principal Investigator is delegated responsibilities for Pharmacovigilance and Safety Reporting for Sponsored non-CTIMPs at their site.

Assessment of An Adverse event is a medical decision and as such MUST be performed by a Medically qualified team member. This may not be the PI if they are not medically qualified.

If there is only one site in the study, the CI usually is also the PI.

Relevant SOPs

SOP 26a - Phamacovigilance reporting for CTIMPs

- Associated document 1; AE flow chart
- Associated document 2: SAE form
- Associated document 3: NRES report
- Associated document 4: DSUR template

SOP Text

	Responsibility	Activity
1.	All	**Identify adverse events within studies** An adverse <u>event</u> [AE] is commonly defined as an untoward medical occurrence in a patient or clinical investigation subject who has been administered any research procedure. An adverse <u>reaction</u> [AR] can further be described as an untoward medical occurrence in a patient or clinical

		investigation subject who has been administered any research procedure, that can have a causal relationship with this treatment or procedure. An adverse reaction [AR] can, therefore, be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporarily associated with the use of a medical device product or taking part in research procedures, whether or not related to the clinical study.
2.	Principal Investigator / medically qualified delegated team member	**The PI assesses if the AE is serious** The Principal Investigator (PI) / medically qualified delegated team member for the study assesses the AE or AR to establish if it should be classified as a Serious Adverse Event (SAE). An Adverse Event is classed as SERIOUS (SAE) if it : • results in death, • is life threatening, • requires hospitalisation or prolongation of hospitalisation, • Results in persistent or significant disability or incapacity • Is a congenital anomaly or birth defect. • Or the event is deemed by the PI to be medically significant.
3.	Principal Investigator / medically qualified delegated team member	**If the AE is NOT serious the PI should record, document and follow-up** If the AE is **not** defined as serious as per the list above the PI must: • **Record** the AE in the case report form (CRF) • **Document it** in the participant's source data/ medical notes (e.g. electronic medical notes/hard-copy medical notes, as appropriate). This recording should include a description of the event, the date/time that it started and stopped, the severity of the event and details of any actions taken in response to the event. • **Follow-up** the AE with the participant until resolution. This should be also recorded in the participant's medical notes (where appropriate) and the participant followed up until the event abates. **For BH and QMUL sponsored studies do not report AEs that are NOT serious to the JRMO.**
4.	Principal Investigator / medically qualified delegated team member	**If the AE is serious the PI should, record, document, and follow-up** **The PI is responsible for recording, assessing and reporting events to the sponsor.** If the AE is deemed to be serious the PI must: • **Record** (as above)

		• **Document** (as above) • **Follow-up** (as above) • **Report** the SAE to the CI and sponsor using their SOP and following the protocol. Before reporting check against the protocol to identify whether there are any SAEs that do not need to be reported to the sponsor (proceed to point 5). **For BH and QMUL sponsored studies only serious, related and unexpected events should be reported to the JRMO.**
5.	Chief Investigator/ Principal Investigator	**The PI is responsible for assessing adverse events.** Prior to reporting the SAE to the CI or sponsor the PI must make an assessment of: **Relatedness and Expectedness.** To make this assessment the PI should review the protocol where all expected reactions should be listed. The PI makes the assessment of related and expectedness on the SAE form and sends the form to the CI. PLEASE NOTE: upon receipt of the SAE form the CI can upgrade the SAE's expectedness and relatedness, i.e. changing the event the PI's has reported to become 'related' or 'unexpected.' However, the CI cannot downgrade the reported event to become 'unrelated' or 'expected'. Should a difference of opinion arise the CI and PI should discuss the event but the PI at site will make the final decision.
6.		**If the SAE is NOT related to the study, the PI should record, document and follow-up.** If the SAE report is assessed by the PI and CI as **not** being related to any study procedures, the SAE must be recorded in the case report form (CRF) and the participant followed-up by the research team. The SAE must be documented in the participant's medical notes (where appropriate). If the SAE is classified as being **likely** to be related to a study procedure and expected, **proceed to 7**. If the SAE is not related proceed to section 8. **For BH and QMUL sponsored studies do not report unrelated SAEs to the JRMO.**
7.	Principal Investigator / medically qualified delegated team member	**The PI is responsible for reporting related and/or unexpected SAEs to the sponsor.** The PI must report to the JRMO within 1-working day of the PI/Research team becoming aware of the SAE A safety reporting form must be completed for each SAR that requires reporting. Once completed the SAE form should be signed by the PI or appropriate delegated person. A scanned signed copy should be emailed to: research.safety@bartshealth.nhs.uk

		If the research team does not have a scanner the SAE form should be faxed to: 0207 882 7276 and an email research.safety@bartshealth.nhs.uk to alert the GCP team. If the study is NOT SPONSORED by BH/QM, the PI/CI should use the sponsor's SAE form and the sponsor's SOP. Do not send SAEs / AEs for studies not sponsored by BH or QMUL to the JRMO.
8.	Chief Investigator	**If an SAE is related and/or unexpected the CI must report it to the JRMO and Research Ethics Committee (REC) who approved the study.** See the HRA website for details of submitting non-CTIMP SAE forms. http://www.hra.nhs.uk/research-community/during-your-research-project/safety-reporting/ If the SAE relates to any of the following it should also be submitted to REC: it is a new event, related to the conduct of the study or the development of the investigational medical device, that is likely to affect the safety of subjects an SAE associated with the study procedures and which could modify the conduct of the study Upon submission to REC assess whether the SAE impacts of trial design i.e. whether there are new risks to be included in Patient information sheet or whether the protocol needs to be amendment.
9.	JRMO Study Monitor	**When an SAE form is received by the JRMO, the form is checked for completeness.** • Upon receipt of an SAE the JRMO will send an acknowledgement of receipt email to the PI/research team. • The JRMO may request further information from the CI/PI or research team. • The JRMO will update their database as per the ReDa manual. • File the SAE in the sponsor's study file(as per SOP 10 JRMO Filning). • Any follow-up information about the SAE received from the study will be saved in the study file. .
10.	Chief Investigator	**CI must submit Annual Progress Reports (APRs) to REC** As sponsor, BH/QMUL delegates to the CI the responsibility of creating and submitting all annual reports to the regulators. Annual progress reports should be submitted to the approving REC twelve months after the date of the "favourable ethical opinion" letter was granted and annually thereafter. Details of how to submit an APR can be found on the HRA website. http://www.hra.nhs.uk/research-community/during-your-research-project/progress-reporting/

		The CI should create the report and submit to the REC when completed. A copy must also be sent to the sponsor via research.safety@bartshealth.nhs.uk for sponsor file. Evidence of submission should be retained in the Study Master File (and site files). PLEASE NOTE: Non-CTIMP annual progress reports to do not to be approved by the JRMO before they are submitted to REC.
11.	Chief Investigator/ Principal Investigator/ Sponsor	**Urgent Safety Measures** **The sponsor and investigator may take appropriate urgent safety measures to protect clinical study subjects from any immediate hazard to their health and safety.** On becoming aware of a potential hazard the CI or delegate should contact the sponsor immediately. If the CI is unable to contact the sponsor or REC, an Urgent Safety Measure (USM) can be implemented to protect the subject. The CI must then notify (in the form of a substantial amendment) the sponsor within one working day. The CI must then ensure the REC is notified within three days, in writing, of the measures taken and the reason for the measures using the 'Non- CTIMP safety report to REC' form (see HRA website to download the form). This notification should include a covering letter detailing the measures taken, the reason for them, and any supporting documentation. The REC will acknowledge receipt within 30 days. Details of reporting Urgent Safety Measures can be found on the HRA website: http://www.hra.nhs.uk/research-community/during-your-research-project/safety-reporting/
12.	Site Principal Investigator	Ensure any incident that falls within the Barts Health NHS trust incident policy is appropriately reported. Please see the BH NHS trust intranet for the adverse incident policy for details of events to be reported.
13.	External Sponsor	Where possible, provide the annual progress reports to the JRMO on an annual basis. JRMO does not require SAE reports from external sponsors to be submitted.

List of Associated Documents

Document	Document Name
1.	Safety Reporting (Research other than CTIMPs)
2.	JRMO Non CTIMP reporting form

NON-CTIMP SAFETY FLOW CHART