Joint Research Management Office Standard Operating Procedure for:			
Site Level Pharmacovigilance and safety reporting for sponsored CTIMPs and ATIMPs			
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Purpose:

This standard operating procedure (SOP) outlines the Principal Investigator's (PI) responsibilities to ensure management and oversight of pharmacovigilance of Barts Health NHS Trust (Barts Health) and Queen Mary University of London (Queen Mary) sponsored clinical trials of investigational medicinal products (CTIMPs) and advanced therapy investigational medicinal products (ATIMPs).

See *SOP 26d for guidance on Safety Reporting for Clinical Investigations of Medical Devices*.

This SOP will identify and standardise the process for recording and managing reportable safety events This SOP also describes the procedure for updating reference safety information (RSI), and the management of pregnancy.

Scope:

This SOP is primarily applicable to the safety reporting procedures for all CTIMPs and ATIMPs sponsored by Barts Health and Queen Mary and defines the standard procedure for these studies.
In some cases, the procedure may be adapted to meet the requirements of specific studies; any such adaptation must be agreed with the Joint Research Management Office (JRMO). For study specific arrangements see the study specific Sponsor-Chief Investigator (CI) agreement.

For all studies sponsored by external organisations i.e. NHS Trusts other than Barts Health, universities other than Queen Mary, or commercial companies, the principles of this SOP apply but the sponsor's pharmacovigilance procedure must be followed.

Responsibilities:
For multi-site studies, the CI has overall responsibility for pharmacovigilance and safety reporting for all the sites. The CI delegates responsibility for pharmacovigilance to the PI of each site. The PI is responsible for informing the CI of all Serious Adverse Events (SAE)/ Suspected Unexpected Serious Adverse Reactions (SUSAR) that occur at their site in accordance with the guidance below. Where the CI is also a site PI (for example in single-centre studies), they are responsible for their site's pharmacovigilance.

The CI is delegated by the sponsor to be the pharmacovigilance medical assessor.

Unless formally delegated, the sponsor is responsible for ensuring that all relevant information about UK relevant SUSARs are reported to the UK competent authority, the Medicines and Healthcare products Regulatory Agency (MHRA). The MHRA's definition of 'UK-relevant' includes:

- SUSARs originating in the UK
- SUSARs originating outside the UK where the sponsor has an ongoing study in the UK involving the same medicinal product.

Abbreviations:	
AE	Adverse Event
AESI	Adverse Event of Special Interest
ATIMP	Advanced Therapy of Investigational Medicinal Product
Barts Health	Barts Health NHS Trust
CI	Chief Investigator
CRF	Case Report Form
CTIMP	Clinical Trial of an Investigational Medicinal Product
IMP	Investigational Medicinal Product
JRMO	Joint Research Management Office
MedDRA	Medical Dictionary for Regulatory Activities
MHRA	Medicines and Healthcare products Regulatory Agency
nIMP	Non-IMP
PI	Principal Investigator
Queen Mary	Queen Mary, University of London
RSI	Reference Safety Information
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction
USM	Urgent Safety Measure

Definitions:

See Associated Document 1 Pharmacovigilane Definitions.

Relevant SOPs:	
• SOP 26b	Pharmacovigilance and safety reporting for sponsored Interventional and Research Studies
• SOP 26c	Pharmacovigilance - (Process for Sponsor and CI)
• SOP 26d	Safety Reporting for Clinical Investigations of Medical Devices
• SOP 17a	Amendments for sponsored studies (including halting studies) - Process for JRMO

SOP Text:		
	Responsibility	**Activity**
		Site set-up
1.	PI	**Confirm that all procedures are in place in order to record, assess and send SAE reports to the coordinating team.** Before opening to recruitment, ensure that the site is ready to record, assess and report safety data. This should include ensuring that: • The study team are aware of the pharmacovigilance procedures detailed in the study protocol and are able to comply with them. • The study team will use secure email addresses when transferring identifiable data (i.e., NHS.net to NHS.net). • There is at least one other medic available to act as a back-up and provide medical assessment of events if the primary medical assessor is unavailable. • The delegation log has been completed by all study team members and countersigned by the PI to indicate who can perform each specific role. • All staff are trained on their specific roles and this is documented on the training log. • All staff can access the current forms and study documents necessary for their role.
		Recording and reporting of events for Barts Health & Queen Mary sponsored studies
2.	PI	**Record Advers Events (AE) in patients' notes and assess whether AEs are serious (i.e.SAEs) and whether they need to be reported to the sponsor.** Each event must be identified and reported separately. Care must be taken to avoid reporting/recoding the symptoms of the event, rather than the event itself. The PI or the medically qualified delegate for the study site must assess the AE to establish if it must be classified as an SAE. This assessment must occur within a timely manner to allow the event to be reported within 24 hours if necessary. For definition of an SAE see *Associated Document 1 Pharmacovigilance Definitions.* If the AE **is** defined as SERIOUS as per the criteria above, **proceed to section 4**.

		If the AE is **not** defined as SERIOUS, the AE is recorded in the case report form (CRF) and the participant is followed up by the research team until resolution. The AE must be documented in the participant's medical notes (paper or electronic medical notes as appropriate). For some studies the Investigational Medicinal Product (IMP) manufacturer/funder may identify Adverse Event of Special Interest (AESI). An AESI (serious or non-serious) is one of scientific and medical concern specific to the IMP or study, for which ongoing monitoring and rapid communication by the investigator to the sponsor/IMP manufacturer maybe appropriate. Such an event might warrant further investigation in order to characterise and understand it. Depending on the nature of the event, rapid communication by the study sponsor to other parties (e.g. regulators) might also be warranted. **Please see section 8** for more details.
3.	PI	**Assess whether an AE is related to the studies IMP or non-IMP (nIMP) to establish whether or not it is a Serious Adverse Reaction (SAR).** Prior to submitting the SAE, the PI or a medically qualified delegate responsible for the treatment of the participant must make an assessment of relatedness of the event to the study IMPs and nIMPs. If the SAE is classified as being **possibly** a reaction to the medicinal product, the event is classified as a SAR, **proceed to section 5**. If the SAE is assessed as **not** being a reaction to the medicinal product, **proceed to section 6**.
4.	PI	**If requested by Sponsor assess whether a SAR is expected or unexpected i.e. is this a SUSAR?** Once it has been established that the event is a SAR, the PI must assess the expectedness. To make the expectedness assessment the PI must review the study specific RSI together with the protocol. The RSI is normally listed in the IB or the SmPC. • If the SAR is **EXPECTED** (i.e. in the RSI), **proceed to section 6** for reporting process. • If the SAR is **UNEXPECTED**, it should be classified as a SUSAR. A SUSAR is an SAE which is suspected to be a reaction to the medicinal product and is **unexpected** i.e. it is not listed in the RSI. For SUSAR reporting process, **proceed to section 7.**
5.	PI	**Report the SAE/expected SAR to the sponsor or delegate as defined in the protocol.** Details of the SAE/expected SAR must be recorded in the participant's source data, and the participant must be followed up by the research team to the resolution of the event. The PI must report all SAEs/expected SARs to the sponsor according to the protocol and any study specific SOPs. The Barts Health/Queen Mary SAE form (see Associated Document 2) **must be used unless a formal written waiver is issued and logged by the JRMO GCP team.** A separate SAE form should be completed for each SAE/expected SAR that requires reporting. **The PI's team must complete the Barts Health/Queen Mary SAE reporting form**. **Once completed/partially completed, the SAE**

		form must be signed by the PI or appropriate delegated medically qualified person at the site. SAE forms which have not been signed by PI or delegated medical representative will not be accepted by the sponsor and will be returned to the PI to be completed. A scanned signed copy of the form should be emailed to: research.safety@qmul.ac.uk.
6.	PI	**Report the unexpected SARs (SUSAR) to the sponsor within 24 hours.** SARs that are UNEXPECTED and therefore fulfil the criteria of a SUSAR require "immediate" reporting to the sponsor. The PI reports the SUSAR (using the same form as SAEs). The form must be signed by the PI or appropriate delegated medically qualified person at the site. The sponsor will acknowledge receipt of the SUSAR in writing to the PI or coordinating team (depending on submitting party and agreements). If the PI does not receive an acknowledgement of receipt the PI must contact the sponsor and request written acknowledgment. Should follow-up information for a SUSAR be received by the sponsor before the reportable deadline i.e. it has been downgraded to an SAE/SAR, the event will not be reported to the competent authority by the sponsor. However, the sponsor must be provided with the reasons given for the downgrade by the PI and confirmation that the CI is in agreement.
7.	PI	**Agree the MedDRA term for the SAE.** If the SAE is not reported with a Medical Dictionary for Regulatory Activities (MedDRA) event term, the sponsor will code the event using a MedDRA term and inform the site of the coding. If the PI disagrees with this coding then they must provide an alternative MedDRA term.
8.	PI	**Inform the sponsor about AESIs.** If the event is not classed as serious, but is specified as an n AESI in the protocol, the PI must inform the sponsor within same time lines as a SAE. AESIs may be: 1. An increase in the rate of occurrence of an expected serious adverse event, which is judged to be clinically important 2. Post-study SUSARs that occur after the patient has completed a study 3. A new event related to the conduct of the study or the development of the IMP, that is likely to affect the safety of subjects, such as: • A serious adverse event that could be associated with the study procedures and which could modify the conduct of the study; • A significant hazard to the subject's population such as lack of efficacy of an IMP used for the treatment of a life-threatening disease; a major safety finding (for example, carcinogenicity) from a newly completed animal study; • Any anticipated end to a study or temporary halt for safety reasons where the study is conducted by the same sponsor with the same IMP in another country; • The conclusions or recommendations of a data monitoring committee, where relevant for the safety of subjects.

Pregnancy within an ATIMP/CTIMP		
9.	PI	**PI notifies sponsor of all pregnancies and follows them up to conclusion.** Within 24 hours of becoming aware of a participant or spouse pregnancy, the PI at site is responsible for notifying the sponsor (as per protocol) using the sponsor's pregnancy form. The PI is responsible for collecting all information and following up the pregnancy to outcome and according to the protocol's specified follow-up period (See Associated Document 3)
10.	GCP team	**Obtain independent medical advice for any pregnancy reports received.** When receiving a pregnancy report, the GCP team will request medical advice from a suitable expert e.g. a consultant obstetrician as agreed with The JRMO Clinical Director (see SOP 26c Pharmacovigilance and Device Safety Reporting (Process for the Sponsor and Chief Investigator))
Urgent Safety Measures		
11.	PI	**Implement USM** Upon receiving notification of an USM, implement it immediately. Do not await regulatory or ethics approval. Please see *SOP 17a Amendments for sponsored studies (including halting): Process for researchers* for guidance on the sponsor's process for managing USM.
For externally sponsored (hosted) studies		
12.	Site PI	**Use external sponsor's forms and SOPs, report incidents via Queen Mary and Barts Health systems.** Report SAEs and SUSARs as per external sponsor's procedures using the external sponsor's forms. Ensure that research team is trained and complies with the study specific pharmacovigilance reporting requirements. If any SAE or SUSAR meets Barts Health or Queen Mary incident reporting standards, ensure that appropriate procedures are followed. Please see Barts Health trust intranet for the Adverse Incident Policy for details of how to report these events/incidents.
13.	Externally sponsored studies	**There is no need to send the JRMO reports and SAEs for externally sponsored studies, i.e. sponsored by pharmaceutical company or another university or Trust.** The JRMO does not require SAE reports or SUSAR reports for externally sponsored CTIMPs. These documents need to be processed according to the external sponsor's SOP. The JRMO does not review nor is it obliged to keep copies of these documents. However any direct unexpected patient harm meeting the Barts Health serious incident definition must be reported on the Barts Health Trust Datix system

Change control

This section outlines changes from version **13.0** to version **14.0**

Section changed	Summary and description of changes
All	Rename and reformat

List of associated documents

Document ref.	Document name
Associated document 1	Pharmacovogilance definitions
Associated document 2	Bart Health/Queen Mary SAE form
Associated document 3	Pregnancy reporting form