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Recording, Managing and Reporting Adverse Events in the UK

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Version	Date	Reason for Change
Version 1.0	03 Jul 2006	Non-IMP SAE clarification and updated instructions from NRES and MHRA
Version 2.0	25 Jun 2007	Annual review
Version 3.0	26 Jun 2008	Formation of Joint Research Office. Recommended additions following MHRA inspection.
Version 4.0	08 Feb 2010	Content review and addition of controlled document statement
Version 5.0	14 Jul 2011	Annual Review and addition of e-SUSAR reporting process
Version 6.0	29 Nov 2012	Annual Review
Version 7.0	18 Feb 2015	Scheduled Review
Version 8.0	25 Oct 2017	Scheduled Review

Version 9.0	29 Aug 2018	Updated to address the MHRA inspection findings
Version 10.0	19 Oct 2020	Scheduled Review Templates removed and administrative changes to SOP. JRCO name change to RGIT.
Version 11.0	03 Nov 2020	Safety reporting update
Version 12.0	13 Jan 2021	Amendments due to leaving the European Union from 1st January 2021.
Version 13.0	06 Feb 2024	Scheduled Review

Table of Contents

1.2 PURPOSE

This SOP describes the process for recording, managing and reporting adverse events for Imperial College sponsored studies of both Investigational Medicinal Products (IMPs) and non-IMPs in the UK, but the principles are relevant for all clinical trials.

1.3 INTRODUCTION

It is essential that all adverse events which occur during study participants' involvement in a research project are recorded and reported in order to ensure their continuing safety.

The Medicines for Human Use (Clinical Trials) Regulations 2004 and the Department of Health's Research Governance Framework for Health and Social Care set out specific requirements for the managing of adverse events (AE). Of importance is the assessment of any event for *causality* and *expectedness*.

Consequently, AEs can be classified into different categories (further explanations are given in section 2.1.)

1. Adverse Event
2. Adverse Reaction
3. Serious Adverse Event/Reaction
4. Suspected Serious Adverse Reaction
5. Suspected Unexpected Serious Adverse Reaction (SUSAR)

Each type of AE is subject to different reporting requirements.

It is important that this SOP is followed as failure to report incidents, or deal with incidents adequately, can result in regulatory approval being withdrawn from an individual project, or, in extreme cases, from all research carried out by the Chief Investigator (CI) or Principal Investigator (PI).

1.1 DEFINITIONS

2.1.1. Adverse Event (AE)

Any untoward medical occurrence in a patient or clinical trial subject administered a medicinal product, and which does not necessarily have a causal relationship with this treatment.

Comment: An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an investigational medicinal product (IMP), whether or not considered related to the IMP.

2.1.2. Adverse Reaction (AR)

All untoward and unintended responses to an IMP related to any dose administered.

Comment: All adverse events judged by either the reporting investigator or the Sponsor as having a reasonable causal relationship to the IMP qualify as adverse reactions.

2.1.3. Serious Adverse Event/ Reaction (SAE/SAR)

Any adverse event or adverse reaction that at any dose:

- results in death
- is life-threatening
- requires hospitalisation, or prolongation of existing inpatients' hospitalisation.
- results in persistent or significant disability or incapacity
- is a congenital anomaly or birth defect
- other important medical event

Comments: Life-threatening, in the definition of an SAE or SAR, refers to an event in which the subject was at risk of death at the time of event; it does not refer to an event which hypothetically might have caused death if it were more severe.

Should a study participant become pregnant whilst undertaking a clinical trial of an investigational medicinal product (CTIMP), or aid in the conception of a child whilst they are participating in a CTIMP, the pregnancy and resulting child should be followed up for a period of no less than 18 months to verify whether a congenital anomaly or birth defect is present. This will be subject to guidance from the relevant pharmaceutical company. Pregnancies and outcome will be included in the Annual Safety Reports. The Chief Investigator (CI) will report any pregnancy occurring on a Clinical trial via the SAE form to the RGIT.

Medical judgement should be exercised in deciding whether an adverse event/reaction is serious in other situations. Important adverse events/reactions that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

Severity: The term "severe" is often used to describe the intensity (severity) of a specific event. This is not the same as "serious", which is based on patient/event outcome or action criteria.

2.1.4. Suspected Serious Adverse Reaction (SSAR)

Any adverse reaction that is classed as serious and which is consistent with the information about the IMP listed in the Summary of Product Characteristics (SmPC) or Investigator Brochure (IB). For IMPs used within their Marketing Authorisation (MA), the SmPC must be in the Trial Master File (TMF) and provided to the clinical trial pharmacist. The CI is responsible for ensuring the SmPC or IB is reviewed at least annually and any changes to the Reference Safety information (RSI) should be notified to the clinical trial pharmacist. Current SmPCs can be accessed at Electronic Medicines Compendium (EMC) (*cited on 03 Dec 2023*)

2.1.5. Suspected Unexpected Serious Adverse Reaction (SUSAR)

Any adverse reaction that is classed as serious and is suspected to be caused by the IMP that is ***not*** consistent with the information about the IMP in either the SmPC or IB, i.e. it is suspected and unexpected. The RSI includes a list of medical events defining which reactions are expected for the IMP being administered to clinical trial subjects, and therefore do not require expedited reporting to the Competent Authority. For reactions to be excluded from expedited regulatory reporting they must be listed in the RSI or clearly defined in the current approved version of the protocol. Any change to the RSI is a change to the Risk/Benefit and requires a substantial amendment be submitted and approved by the MHRA before it is implemented in the trial. It is the CI's responsibility to ensure the amendment is submitted to the MHRA. Only then an updated SmPC/IB should be added to the TMF and used by the CI/PI as reference for safety reporting (SUSARs).

The trial protocol should include a list of known side effects for each drug in the study. This should be checked with each serious adverse event that occurs in terms of expectedness. If the event is not listed as expected or has occurred in a more serious form than anticipated, this should be considered a SUSAR.

1.2 RESPONSIBILITIES

There are several responsibilities when managing adverse events. Below is a list of responsibilities for both the Investigator and the Sponsor (for Imperial College sponsored studies.

The CI has overall responsibility for the conduct of the study. In a multi-site study, the CI has co-ordinating responsibility for reporting adverse events to the Medicines and Healthcare products Regulatory Agency (MHRA) and to the relevant Research Ethics Committee (REC).

The Principal Investigator (PI) has responsibility for the research at a local site where the study involves specified procedures requiring site-specific assessment. There should be one PI for each research site. In the case of a single-site study, the CI and the PI should be the same person. The PI is responsible for informing the CI, or the coordinating research team, of all adverse events that occur at their site following the guidelines below.

Any CI/PI who has agreed to undertake duties for pharmacovigilance delegated by the Sponsor must undertake both Investigator's and Sponsor's responsibilities as described throughout this document.

1.2.1 Investigator's Responsibilities

1. PI to report all SAEs and SUSARs within agreed timelines to the CI (see section 3.3)
2. CI to report all SAEs within agreed timelines to Sponsor
3. CI to report SUSARs within agreed timelines to Sponsor, MHRA, REC and relevant NHS Trust Research and Development Office (R&D) (see section 3.3)

4. Provide the Sponsor with details of all AEs identified in the protocol as critical to the evaluation of safety within the agreed timeframes specified in the protocol.
5. Assess each event for causality and seriousness between the IMP and/or concomitant therapy and the adverse event.
6. Supply the Sponsor, MHRA, REC and relevant NHS Trust R&D with any supplementary information they request.

1.2.2 Sponsor's Responsibilities

1. *****Ongoing safety evaluation of any IMP(s), including trend analyses.
2. *****Promptly notify all Investigators, REC(s) and MHRA, of any findings that may affect the health of subjects. This may include informing investigators using the same IMP in different studies.
3. *****Keep detailed written reports of all AEs reported by PIs and performing an evaluation with respect to seriousness, causality and expectedness.
4. *****Report all relevant safety information to the relevant REC and MHRA.
5. *****Report all SUSARs to the MHRA, REC and relevant NHS Trust R&D in concerned Member States associated with comparator product(s) and Marketing Authorisation (MA) holder(s), within given timelines.
6. *****Break treatment codes before submitting expedited reports to MHRA and REC for specific subjects, even if the Investigator has not broken the code. (Note: A system for maintaining blinding for the CI/PI and trial staff may need to be agreed in advance).
7. *****Submit the annual safety report to Sponsor, MHRA and REC.
8. Encourage the setup of Independent Data Monitoring Committees (IDMC) for phase III clinical trials that have high morbidity/mortality and describe their function in the protocol.
9. Ensure written SOPs and systems are in place to ensure quality standards and contractual agreements are met.
10. Register users for pharmacovigilance data entry with the European Medicines Evaluation Agency (EMEA) if required.

***Note: Where Imperial College AHSC is Sponsor for a study, responsibilities 1-7 are delegated to the Chief Investigator. Correspondence for Imperial College AHSC sponsored studies should be sent to the Research Governance and Integrity Team (RGIT).**

1.3 PROCEDURES

1.1 STUDY PLANNING

All protocols should list known side effects and adverse reactions contained within the manufacturer's product information. This should be written in agreement with the relevant drug/device company where applicable. Rare/very rare events may or may not be included depending on individual study requirements.
A detailed explanation of SAE reporting procedures should also be included in the protocol.

A generic SAE reporting form is available in Appendix 1 RGIT_TEMP_003, please refer to the SOP, Associated Documents & Templates page (*cited on 04 Dec 2023*).

This form can be amended to create a study specific form following consultation with the RGIT.

1.1.1 Which AE to Record?

The CI can decide how to record and report adverse events, whether expected or not. Adverse events are usually described on case report forms (CRFs), unless they are classified as serious, in which case, these should be reported on a specific SAE form (see Appendix 1 RGIT_TEMP_003 for an example). It should be clearly stated in the study protocol and the local SOP what will be recorded and how the reporting is to be managed.

It may be decided that all, or only some, non-serious AEs are to be recorded. Whatever option is chosen, it must be consistent with the purpose of the trial and any toxicity and efficacy end points.

1.1.2 Which SAE to Report?

The management and reporting arrangements for SAEs should be in place for all trials. Agreements at the beginning of the trial should be made for such SAEs that can be defined as disease-related and therefore not subject to expedited reporting. The procedures for managing and reporting SAEs must be clearly defined in the protocol.

It is recommended that an Independent Data Monitoring Committee (IDMC) is appointed in order to review safety data regularly throughout the trial and when necessary, recommend to the Sponsor whether to continue, modify or terminate the trial. Again, this procedure must be defined in the protocol.

As with all recording and reporting, subject confidentiality and adherence to the Data Protection Act (2018) must be maintained on all reports.

1.2 DURING THE TRIAL

Each AE must be evaluated for **seriousness** (2.1.3)**, causality, and expectedness**. The responsibility for this evaluation can be shared between the CI and PIs. It may be most appropriate for the treating PI at each local site to evaluate each event, before reporting it to the CI. It must be stated in the clinical trial protocol and the local SOP who will take responsibility for the assessment and reporting of such events to the Sponsor and CI simultaneously. As expedited reporting may be required, this SOP assumes that responsibility of initial assessment and reporting to the CI lies with the PI.

Flowcharts in Appendix 2 RGIT_TEMP_004 are designed to enable Investigators/research personnel to assess AEs and SAEs should they occur during the trial and decide if the event requires further expedited reporting by the CI.

1.1 CAUSALITY

Adverse reactions should be assessed for causality. The definitions below can be used.

Relationship	Description
Unrelated	There is no evidence of any causal relationship
Unlikely	There is little evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after administration of the trial medication). There is another reasonable explanation for the event (e.g. the patient's clinical condition, other concomitant treatment).
Possible*	There is some evidence to suggest a causal relationship (e.g. because the event occurs within a reasonable time after administration of the trial medication). However, the influence of other factors may have contributed to the event (e.g. the patient's clinical condition, other concomitant treatments).
Probable*	There is evidence to suggest a causal relationship and the influence of other factors is unlikely.
Definitely*	There is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out.
Not assessable	There is insufficient or incomplete evidence to make a clinical judgement of the causal relationship.

*For AEs that are considered serious and unexpected; if the relationship is defined as possible, probable or definitely related, these AEs should be notified to the MHRA, the relevant REC and the Sponsor as SUSARS.

If different causality definitions are specified in the protocol, it must be clear which definitions constitute a 'related' event.

1.2 REPORTING GUIDELINES –CLINICAL TRIALS OF INVESTIGATIONAL MEDICINAL PRODUCTS (CTIMPS)

Once the CI/PI has evaluated the AE in terms of seriousness, causality and expectedness, the following guidelines should be followed.

1.2.1 AEs

AEs that are not considered serious should be included in the patient notes and on the relevant case report forms (CRFs). The completed form should be filed along with the other CRFs for the study and a copy provided to the Sponsor as agreed.

1.3 SAES

If the AE is assessed as serious, the PI **must** report the event to the CI **immediately or within 24 hours** of being made aware of the event (other than those SAEs identified in the protocol as not requiring immediate reporting). The initial report can be made verbally but must be promptly followed with a detailed, written report. The PI must record the event with his assessment of seriousness, (along with causality, expectedness and severity) on a trial SAE form provided by the CI (see Appendix 1). The PI should ensure that follow-up information is provided when available. Where supporting documents are sent with this form, these must be anonymised/psuedonymised. Where the information available is incomplete at that time, as much information as can be ascertained should be sent to ensure timely

reporting, with additional information provided as soon as it is known. Additional information received for an event (follow-up or corrections to the original event data) needs to be detailed on a new **Serious Adverse Event Reporting Form**.

1.4 FOLLOW-UP OF ADVERSE EVENTS

All adverse events must be followed-up until symptoms cease or the condition becomes stable. The **Adverse Event Record Sheet** requires a judgement on outcome, rating the adverse event as resolved (1), resolved with sequelae (2), persisting (3), worsened (4), fatal (5), or not assessable (6).

1.1 PROVIDING CONTACT DETAILS FOR ADVERSE EVENT REPORTING

Participants should be advised to contact the PI to report any unexpected occurrence or effect that they think might be related to the study medication. In addition to the participants themselves, pharmacy staff and other healthcare professionals responsible for the clinical care of the participant may notice suspected adverse events/reactions. It is essential that contact details for the study team are provided to anyone who may be in a position to recognise any change in the participant's behaviour or functioning, abnormal test results or untoward medical occurrences that may be related to the study medication. The most appropriate local contact details for a member of the study team must be included on the ethically approved **GP Letter**.

The CI should include all SSAR's and SUSAR's in the annual safety report (see section 3.5).

The PI/CI must send all SAE reports to the Research Governance and Integrity Team, Imperial College AHSC immediately or within 24 hours after becoming aware of the event at the below address: RGIT.CTIMP.TEAM@imperial.ac.uk

Local research governance procedures at each site, e.g. NHS Trust, should also be followed.

1.2 SUSARS

Any AE that the PI evaluates as serious, is suspected of having a causal relationship to the trial medication and is unexpected, will require **expedited** reporting to the RGIT, MHRA, REC and to other organisations as required under the terms of the individual contracts (e.g.: relevant pharmaceutical companies, NHS Trusts).

If the CI, or Trial Management Group if appropriate, is not in agreement with the "expectedness" decision of the PI, the CI cannot overrule the PI's decision. Both opinions should be recorded on the SAE form.

SUSARs should be reported following the timelines in section 1.1. via the e-SUSAR electronic reporting system outlined in section 1.3. Appendix 4 RGIT_TEMP_006 contains the covering document required for the main REC (CTIMPs Safety Report form).

The minimum data required for reporting SUSARs to the MHRA and REC are:

i) The suspected Investigational Medicinal Product (IMP)
ii) Subject trial Identification
iii) An adverse event assessed as serious and unexpected, and for which there is a reasonable suspected causal relationship
iv) An identifiable reporting source

1.1 TIMEFRAMES FOR EXPEDITED REPORTING

Fatal/life threatening SUSARs

The CI must inform the RGIT, MHRA, REC, and relevant pharmaceutical companies (if required under the terms of the contract) of fatal or life threatening SUSARs as soon as possible, but no later than **7 calendar days** after the CI has first knowledge of the minimum criteria for expedited reporting. In each case, relevant follow-up information should be sought and a report completed as soon as possible. This should be sent within an **additional 8 calendar days.**

Non- fatal and non-life threatening SUSARs

The CI must report all other SUSARs and safety issues to the RGIT, MHRA, REC, and relevant pharmaceutical companies (if required under the terms of the contract) as soon as possible, but no later than **15 calendar days** after the CI has first knowledge of the minimum criteria for expedited reporting. Further relevant information should be given as soon as possible.

1.2 URGENT SAFETY MEASURES

The Chief and Principal Investigators have the authority to deviate from the protocol if doing so relates to the immediate safety of a participant, where continuing to follow protocol would put that participant at risk. This is classed as an urgent safety measure and must be reported to the RGIT, MHRA and REC within **3 calendar days** of the occurrence. This may be reported verbally in the first instance but must be supported by a written report as soon as information is available. Please refer to RGIT_SOP_037

1.3 E-SUSAR REPORTING

Once a trial has received MHRA approval the RGIT will generate an e-SUSAR account which will be identified by trial title, CI and EudraCT number.

The RGIT will require the contact details of the person(s) responsible for entering the data onto the e-SUSAR system so that user accounts can be generated. Each user will only be given permission to access those trials they have responsibility for.

The Trial details are automatically populated in the report by first selecting the trial for which the report is to be made. The form guides the user through a series of steps collecting information on the Trial Subject, the Reaction and the IMP (Suspect Drug). The user's details are also automatically populated into the report and are defined by their account information.

Prior to submission, a summary of the data collected is presented and the user has the option to amend any details. The user also has the option to download a full report in either PDF format or as XML. Institutions may find these reports useful for informing Ethics Committees.

As well as creating and submitting new reports, users can submit follow-up reports, edit previously created but as yet not submitted reports and create and submit copy reports based on previous reports.

Once a report has been submitted it cannot be altered and any amendments will need to be included in follow-up reports.

For trials where the AHSC is acting as Legal Representative for a non-EU organisation, the sponsor has the option to register their organisation as an administrator for the e-SUSAR system or access the system via the AHSC account if the data are being entered by an AHSC staff member.

Sponsors of clinical trials, marketing authorisation holders and national competent authorities in the European Economic Area (EEA) must report SUSARs via safety reports (ICSRs/ Acknowledgements) and Information on Investigational Medicinal products via product reports (XEVPRMs/acknowledgements) through their organisations EudraVigilance account.

In accordance with the European Union legislation (article 17 of Directive 2001/20/EC) the sponsor of clinical trials authorised in the European Economic Area shall ensure that all relevant information about reports of SUSARs is recorded and reported to the competent authorities in all concerned member states individually.

For trials ongoing in both the UK and in European member states dual reporting is needed. You will need to report each SUSAR to both the MHRA and to the European Medicines Agency's (EMA's) Eudravigilance Clinical Trial Module (EVCTM).

For more information please visit the EudraVigilance website: EMA - EudraVigilance: electronic reporting (*cited on 04 Dec 2023*)..

1.4 UNBLINDING

Systems for SUSAR and SAR reporting should, as far as possible, maintain blinding of individual clinicians and of trials staff involved in the day-to-day running of the trial. It is important that the details of the unblinding process are included in the trial protocol.

For blinded trials involving a placebo and an active drug, seriousness, causality and expectedness should be evaluated as though the patient was on active drug. Cases that are considered serious, unexpected and possibly, probably or definitely related (i.e. possible SUSARs) would have to be unblinded. Only those events occurring among patients on the active drug (unless thought to be due to the excipient in the placebo) should be considered to be SUSARs requiring reporting to the MHRA, RECs and RGIT. It may be that individuals who are not directly involved in the management of the trial could perform unblinding.

For blinded trials involving two active drugs, the person responsible for the evaluation for causality and expectedness might be able to state that if the patient were on drug A the event would be causal and/or unexpected, but if on drug B it would be expected. If the event were unexpected for either of the active drugs, the case should be unblinded by the individual charged with unblinding, who would then classify the event accordingly. An IDMC has access to semi-blinded or unblinded data and can oversee the assessment of emerging risks, such as an increase in frequency or severity of adverse events. The committee's assessments are carried out without disclosure to the trial team. They may recommend protocol amendments, or termination of the study, if they detect serious safety issues. In addition, the chairman of an IDMC might be able to play a role in unblinding individual reports of SUSARs for expedited reporting (if this could be managed within the requisite timeframes) and SSARs for annual reports.

1.5 REPORTING TO PIS' INVOLVED IN STUDY

All PIs within the trial at other sites concerned must also be informed of the SUSAR, although this does not have to be within the 7/15-day deadline. All PIs should be sent a summary of SUSARs approximately every 3 months. This timeframe may vary between trials depending on the rates of recruitment and/or SUSARs.

If the CI is informed of SUSARs from other trials using the IMP by a pharmaceutical company, the CI should inform PIs as above.

1.6 REPORTING GUIDELINES – NON-IMP STUDIES

If a research participant experiences a SAE you should report this to the relevant Research Ethics Committee and the Research Governance and Integrity Team, Imperial College AHSC, wherein the opinion of the Chief Investigator the event was:

- '**related**': that is, it resulted from administration of any of the research procedures; and
- '**unexpected**': that is, the type of event is not listed in the protocol as an expected occurrence.

Reports of related and unexpected SAEs should be submitted within 15 days of the CI becoming aware of the event, using the HRA's Non-CTIMP safety report to REC form. The form should be completed in typescript and signed by the chief investigator.

For SAE reporting guidelines for ICREC/SETREC studies refer to RGIT_SOP_045_ICREC Safety Reporting (*cited on 04 Dec 2023*).

Reports of double-blind studies should be unblinded.

1.7 ANNUAL REPORTS

For IMP clinical trials please refer to RGIT_SOP_035 – Developmental Safety Update Reports. These replace the previous Annual Safety Report system for MHRA regulated trials.

1.8 ADVERSE EVENT REPORTING FOR INTERNATIONAL TRIALS

Clinical trials that involve sites outside of the UK must follow the requirements of the countries in which the trial is taking place.

The procedures for reporting relevant events onwards to regulatory and ethics committees should be included in any agreements between international groups performing the trial. The protocol and/ or study specific SOP should specify procedures for both the timing and format of reports of SUSARs in sites outside the EU.

1.9 REPORTING SUSARS TO THE ETHICS COMMITTEE

The reporting requirements of the main ethics committee responsible for the trial in each country should be established prior to the start of the study. These requirements will vary and therefore it should be detailed in the protocol/study specific SOP which SUSARs will need to be reported and where they should be sent e.g. the UK RECs evaluate UK SUSARs only.

1.10 REPORTING SUSARS TO THE COMPETENT AUTHORITIES

For trials taking place within the EU, the CI must ensure that **all** SUSARs are reported to the competent authority for each country in which the trial is taking place.

For trials where Imperial College AHSC is Sponsor, but where all sites are outside the EU, there is no requirement to report SUSARs to the MHRA. The reporting requirements of the authorities in the participating countries must be complied with.

1.11 ANNUAL SAFETY REPORTS/DEVELOPMENTAL SAFETY UPDATE REPORTS

An annual safety report should be submitted to the main REC and competent authority in each EU country that has a site participating in the trial (see section 3.5). This should include **all** SSARs and SUSARs occurring in **all** countries participating in the trial.

The requirements for countries outside the EU should be included in the protocol/study specific SOP. Annual reporting should take place as required.

1.12 TREND ANALYSES

The CI, in conjunction with the pharmaceutical company providing the IMP for the study, should conduct regular trend analyses and signal detection to determine the continued safety of the drug within the study. This is normally done post-marketing of the drug thus the company may request information to complete their dossier and submit their periodic safety update report (DSUR).

1.13 REFERENCES

Data Protection Act (2018)
Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use (cited 03 Dec 2023)

Detailed guidance on the European database of Suspected Unexpected Serious Adverse Reactions (Eudravigilance – Clinical Trial Module)
EudraVigilance Support Guide (cited on 03 Dec 2023)

The Medicines for Human Use (Clinical Trials) Regulations 2004 Part 5
(cited on 03 Dec 2023)

National Research Ethics Service guidance on safety reporting (cited on 02 June 2020)

MRC/DH joint project, Workstream 6: Pharmacovigilance (cited on 02 June 2020)

1.14 APPENDICES

The following Appendices list the following Templates associated to this SOP which can be found on the SOP, Associated Documents & Templates page.

Appendix 1: Sample SAE Form – RGIT_TEMP_003
Appendix 2: Flowchart for Reporting and Assessing Adverse Events in CTIMPs sponsored by Imperial College - RGIT_TEMP_004
Appendix 3: MHRA Addresses

Developmental Safety Update Reports should be provided to the MHRA using the MHRA Portal (cited on 14Dec2020)
The same guidance for submitting clinical trials applications via MHRA Portal applies, but please select regulatory activity G0042 - Development Safety Update Reports.

eSubmission Guidance**:** Guidance has been published on the structure and format of electronic submissions for both human & veterinary medicinal product submissions. (cited on 03 Dec 2023)

Guidance - Register to make submission to MHRA

Guidance on submitting clinical trial safety reports

Appendix 4 – CTIMPs Safety Report Form - RGIT_TEMP_006