Oxford University Hospitals NHS
NHS Trust

Safety Reporting in Clinical Research Policy
Final Version 4.0

Category:	Policy
Summary:	The Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments require that organisations which take on the role of Sponsor of Clinical Trials of Investigational Medicinal Products must have systems in place to record adverse events relating to those trials. The Department of Health Research Governance Framework for Health and Social Care 2005 requires that the safety of research participants should be given priority at all times. Regardless of the identity of the Sponsor, the host organisation retains a responsibility to ensure the safety of its patients.
Equality Impact Assessment undertaken:	21 November 2007
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Related Documents:	Trust Management Approval Policy Sponsorship of Clinical Research Policy Integrity in Research Policy Incident Reporting and Investigation Policy
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Contents

Introduction

1. The Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments require that organisations which take on the role of Sponsor of Clinical Trials of Investigational Medicinal Products must have systems in place to record adverse events relating to those trials.

2. The Department of Health Research Governance Framework for Health and Social Care 2005 requires that the safety of research participants should be given priority at all times.

3. Regardless of the identity of the Sponsor, the host organisation retains a responsibility to ensure the safety of its patients.

4. For studies that do not involve the trial of a medicinal product, any Serious Adverse Event (SAE) occurring in a participant that has possibly resulted from participation in the research and is deemed to be unexpected, must be reported to the main Research Ethics Committee (REC) within 15 days and copied to R&D.

Policy Statement

5. It is the policy of the Trust to:

   5.1 Protect the safety of all patients involved in clinical research.

   5.2 Ensure that arrangements for safety reporting in Clinical Trials of Investigational Medicinal Products (CTIMP), where the Trust has taken on the role of Sponsor, or Host Organisation, are compliant with the Regulations.

   5.3 Ensure that arrangements for safety reporting in other clinical research studies are compliant with the requirements of the National Research Ethics Service (NRES).

Scope

6. This policy applies to anyone conducting Clinical Trials of Investigational Medicinal Products (CTIMPs) within the Trust, regardless of whether they themselves are employed by the Trust.

Aim

7. The purpose of this policy is to describe the processes to be followed to ensure that the Trust fulfils its regulatory responsibilities for safety reporting both as Sponsor and host organisation

Definitions

The terms used in this document are defined as follows:

Reference Safety Information (RSI)

8. The information used for assessing whether an adverse reaction is expected. This is contained in either the Investigator's Brochure (IB) or in the Summary of Product Characteristics (SmPC).

Investigator's Brochure (IB)

9. A document containing a summary of the clinical and non-clinical data relating to an Investigational Medicinal Product (IMP) that is relevant to the study of the product in human subjects.

Summary of Product Characteristics (SmPC)

10. A document describing the properties and conditions for use of a particular licensed medical product, which is the basis of information for health professionals on how to use the medical product safely and effectively.

Adverse Event (AE)

11. Anything untoward medical occurrence in a participant to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product.

Adverse Reaction (AR)

12. Any untoward and unintended response in a participant to an Investigational Medicinal Product (IMP) which is related to any dose administrated to that participant.

Serious Adverse Event (SAE)

13. Any adverse event that:

- Results in death,
- Is life-threatening,

  NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

- Requires inpatient hospitalisation or prolongation of existing hospitalisation,
- Results in persistent or significant disability/incapacity, or
- Is a congenital anomaly/birth defect.
- Other important medical events.

NOTE: May be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the patient and may require medical or surgical intervention to prevent one of the outcomes listed above.

Pregnancy Safety Reporting

14. Any pregnancy that occurs during IMP administration, whilst not necessarily an adverse event, requires monitoring and follow-up to full pregnancy term. Each pregnancy will be followed up until outcome of the pregnancy is known.

Serious Adverse Reaction (SAR)

15. An adverse event (expected or unexpected) that is both serious and, in the opinion of the reporting investigator, believed with reasonable probability to be due to one of the study treatments, based on the information provided.

Suspected Unexpected Serious Adverse Reaction (SUSAR)

16. A serious adverse reaction, the nature and severity of which is not consistent with the Reference Safety Information

Incident

17. Any event or circumstance arising that could have or did lead to unintended or unexpected harm, loss or damage. Incidents may involve actual or potential injury, damage, loss, fire, theft, violence, abuse, accidents, ill health, infection, near misses and hazards.

Near Miss

18. Is an incident that did not lead to harm or cause harm, loss or damage but had potential to do so.

Development Safety Update Report (DSUR)

19. A legally required, annual safety report submitted to the Competent Authority, the Research Ethics Committee (REC), and other parties as applicable. The DSUR should take into account all new available safety information received during the reporting period for all trials with the same IMP and sponsored by the same organisation

Sponsor

20. The organisation taking responsibility for initiation, management and financing (or arranging the financing) of a clinical trial or research study.

Chief Investigator

21. The individual, as identified in the ethics application, who takes overall responsibility for the conduct of a clinical study.

Principal Investigator

22. The individual who takes on responsibility for conduct of the study at a particular site.

Responsibilities

Chief Investigator (CI) (OUH Sponsored)

23. Ensure that all SAEs, other than those specified in the protocol as not requiring immediate reporting, are promptly assessed in keeping with the requirement for expedited reporting to the regulatory authority and relevant ethics committee.

24. Ensure that SAEs, which require immediate reporting, are reviewed by an appropriate safety review committee for the monitoring of trial safety.

25. Ensure that all SUSARs are identified and reported in full to the regulatory authority and relevant ethics committee within the required timelines.

26. Promptly (within 3 calendar days) inform regulatory authorities, ethics committees and investigators of any urgent safety measures taken to protect participants in the study.

27. Ensure that DSURs and End of Study Reports are generated and submitted to the regulatory authority and relevant ethics committee within the required timeframes, and that copies are sent to the Trust R&D Department.

28. Ensure that all investigators are, at all times, in possession of the current RSI on the IMP (IB or SmPC).

Principal Investigator and delegated team (Hosted Trials)

29. Maintain detailed records of all AEs as specified in the protocol.

30. Ensure that all SAEs, which require immediate reporting, are reported to the Sponsor and the Trust R&D Department (where required to do so) within the timelines required in the protocol.

31. Provide prompt updates and further information as requested by R&D.

32. Ensure that any AE which qualifies as an incident or near miss is reported to Clinical Governance, within the specified timeframe (See Incident Reporting and Investigation Policy).

33. Ensure that departmental Safety Reporting SOPs outline the responsibilities for reporting SAEs to the Trust R&D Department.

Research and Development Staff

34. Maintain oversight and promote compliance with Regulatory requirements for safety reporting, on behalf of the Trust.

35. Facilitate communication with the Medical Monitor and Trials Safety Group, ensuring prompt review as appropriate.

36. Provide training to research teams as required.

    Highlight to research teams any SAEs which may constitute an adverse incident or near miss and which require reporting to Clinical Governance.

37. For **Trust Sponsored** trials, ensure that all DSURs are submitted to the MHRA and the REC within the required timeframe.

Medical Monitor

38. Conducts a medical review of SAEs reported on a weekly basis (+/- 3 days), following up SAEs to closure where required, requesting further information if appropriate

39. Review all identified fatal or life threatening SUSARs within three days, and all other SUSARs within seven days

40. Reviews safety reporting risk assessment form when requested by Head of Research Governance

Oxford University Hospitals NHS Trust / University of Oxford Trials Safety Group (TSG)

41. To pick up any trends, such as increases in unexpected events, and take appropriate action

42. To identify whether additional advice or information is required from investigators

43. To evaluate the risk of the trial continuing and take appropriate action where necessary e.g. recommend halting with the agreement of the OUH NHS Trust Medical Director

44. To act or advise, through the Chairman or other Consultant, on incidents occurring between meetings that require rapid assessment

45. To request provision of training to specific groups within the Trust or University, where necessary.

46. To request internal audits either in the Trust or University, where necessary

Content of the Policy

Risk assessment

47. Many clinical trials hosted by OUH Trust have the resources available to promote compliance with the safety reporting aspects of conducting a clinical trial. In order to focus attention on those trials that do not necessarily have the resources for intensive review of safety data, a risk assessment will be performed prior to the start of any trial hosted by the Trust.

48. Should there be any subsequent concerns about the trial; the risk assessment will be repeated.

49. The outcome of the risk assessment will determine the level of reporting to R&D that should be undertaken:

50. **Level 1**: All SAEs arising from the trial should be reported, as outlined in 34.

51. **Level 2**: Inform the R&D department promptly of any concerns regarding the safe conduct of the trial and/or any additional risks to the Trust.

52. The risk assessment will be undertaken as part of the governance review and will be clearly documented in the Trust Management Approval letter.

53. A risk based approach will also be used to select a representative selection of trials for audit or compliance checks to establish that safety reporting procedures are appropriately undertaken. Requests may also be made by the Trials Safety Group.

Reporting of SAE

54. The general Regulatory reporting process is presented in Appendix 1.

55. Trial specific reporting requirements will be outlined in the relevant trial protocol or sponsor provided guidance. In addition to the protocol, the requirements of the safety reporting level outlined in 26.4 and 26.5 must be followed.

56. The reporter must assess whether the event constitutes a near miss or an incident which requires reporting to Clinical Governance

Reporting of Level 1 SAE

57. All SAEs (other than those defined in the protocol as not requiring reporting) must be reported on the SAE Reporting Form to the Sponsor or delegate within 24 hours of Site Study Team becoming aware of the event being defined as serious. In addition, for Level 1 reporting, such SAEs must be reported to R&D.

58. Once the Investigator (or the delegated person) becomes aware of an SAE, an SAE Reporting Form should be completed.

59. The Investigator or (the delegated person) should then Email the report to the Sponsor, Trust R&D Department Email: ouhsae.reports@ouh.nhs.uk; and other relevant parties in accordance with the protocol.

60. The Trust R&D Department will assign an SAE number to each report and acknowledge receipt, which should be filed in the site file. Should any essential elements be missing in the initial SAE report, these will be requested from the Investigator. Further updates on the SAE should be forwarded promptly to the Trust R&D Department. All correspondence should be filed in the site file.

61. A medical monitor for the TSG will routinely review SAEs regularly (approximately weekly) to identify possible SUSARs (not categorised as such by the Investigator) and to check that there is sufficient information to make this decision.

62. All reported SAEs will be reviewed by the TSG on a quarterly basis.

63. For **Trust sponsored trials**, the SAE reporting form should be downloaded (with guidance notes) from the Trust R&D website, completed electronically (if possible), printed off and signed. This form may be used for other trials at the discretion of the sponsor.

Follow up of SAEs

64. The Medical Monitor will identify which SAE need to be followed up by R&D to resolution. Further and ongoing requests for information from the research team may be made.

Expedited Reporting of Suspected Unexpected Serious Adverse Reactions

65. If it is established by the Investigator that the event is a Suspected Unexpected Serious Adverse Reaction (SUSAR), the Investigator (or the delegated person) should inform the Trust R&D Department immediately. The SUSAR report will be forwarded immediately to a TSG medical monitor.

66. For **Trust Sponsored trials** the Chief Investigator (or the delegated person) will submit the report to the MHRA. The SUSAR report must reach the MHRA within 7 calendar days of the sponsor becoming aware for a fatal or life threatening event, with further information being provided within a further 8 calendar days. For all other SUSARs, these should be reported within 15 calendar days.

The Trust R&D Department will monitor the reporting timelines.

Development Safety Update Reports (DSUR)

67. For **Trust sponsored trials**, the CI, on behalf of the Trust shall submit once a year throughout the trial or on request, a safety report to the MHRA and the main REC, taking into account all new available safety information received during the reporting period. The report should be submitted within 60 days of the data lock point. The data lock point is defined as the cut-off date for data to be included in the DSUR.

68. If the trial is short term (i.e. less than 6 months), the DSUR is due within 90 days of the end of the trial, together with the notification of trial end.

69. The DSUR shall include all SAEs occurring in the period in trials in the UK or elsewhere and in trials with the same product in trials conducted outside the UK for which the Trust is the Sponsor.

Training

70. All staff involved in the conduct of clinical trials will undertake training in safety reporting prior to beginning their involvement in the trial.

71. Training required to fulfil this policy will be provided in accordance with the Trust's Training Needs Analysis. Management and monitoring of training will be in accordance with the Trust's *Learning and Development Policy*. This information can be accessed via the Learning and Development pages on the Trust intranet.

Monitoring Compliance

Aspect of compliance or effectiveness being monitored	Monitoring method	Responsibility for monitoring (job title)	Frequency of monitoring	Group or Committee that will review the findings and monitor completion of any resulting action plan
SAE Reporting	Review of reported SAEs	Quarterly	Head of Research Governance	Trials Safety Group
Identification of SAEs	GCP monitoring of Trust sponsored studies	Ongoing	Head of Research Governance	Trials Safety Group

Aspect of compliance or effectiveness being monitored	Monitoring method	Responsibility for monitoring (job title)	Frequency of monitoring	Group or Committee that will review the findings and monitor completion of any resulting action plan
Identification of SAEs	Audit of selected hosted studies	Ongoing	Head of Research Governance	Trials Safety Group

Review

72. This policy will be reviewed every 3 years, as set out in the Policy for the Development and Implementation of Procedural Documents.

73. Policies may need to be revised before this date, particularly if national guidance or local arrangements change, where implementation is unsuccessful or where audits necessitate a policy review.

References

74. The Medicines for Human Use (Clinical Trials) Regulations 2004 and amendments.

75. The Department of Health Research Governance Framework for Health and Social Care 2005

76. ICH Guideline for Clinical Safety Data Management: Definitions and Standard for Expedited Reporting

Equality Impact Assessment

77. In accordance with Equality & Diversity legislation, this Policy has had an Equality Impact Assessment undertaken. It has been determined that this Policy does not discriminate against any individual or group and a full copy of the assessment can be viewed on the Research and Development intranet page.

List of Appendices

78. The following appendices are attached to support this document:

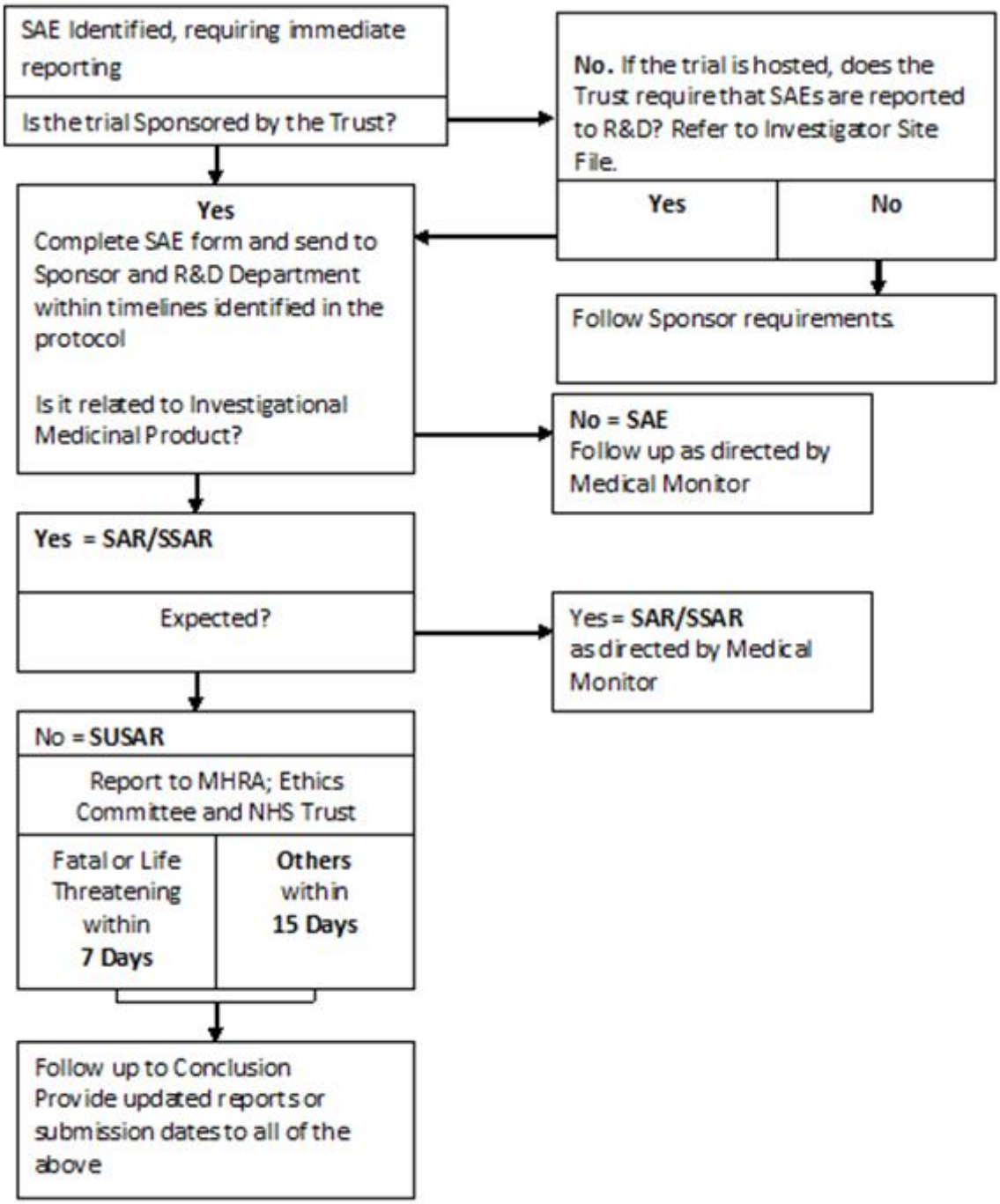
Appendix 1: Flowchart of the Reporting Process

Appendix 2: Equality Impact Assessment: Full Analysis

Document History

of revision	Version number	Reason for review or update
Mar 2005	1.5	Updated to incorporate change in policy
Nov 2007	2.0	General update
Jan 2014	3.0	General update

Appendix 1: Flowchart of the Reporting Process



PLEASE NOTE: For any type of report, if there are any safety concerns for patients or potential for adverse publicity, please contact the Trust R&D Department.

N.B. Where the SAE also constitutes an untoward incident, this must also be reported to Clinical Governance using the appropriate system.

Appendix 2: Equality Impact Assessment: Full Analysis

Equality Analysis
Policy / Plan / Proposal name: Safety Reporting in Clinical Research Policy
Date of Policy: July 2017
Date due for review: July 2020
Lead person for policy and equality analysis: Head of Research Governance
The only policies and proposals not relevant to equality considerations are those not involving people at all (for example equipment such as fridge temperature)
Identify the main aim and objectives and intended outcomes of the policy This policy sets out a consistent framework for the identification, evaluation and reporting of Serious Adverse Events (SAEs) occurring in clinical trials being conducted within the Trust.
Involvement of stakeholders Based on the previous version, update has drawn on feedback from researchers, regulators and OUH Trials Safety Group.
Evidence This policy applies to safety reports of events occurring in all trials conducted within the Trust, regardless of race, religion, disability, age, gender or sexuality
Disability This policy applies to safety reports of events occurring in all trials conducted within the Trust, regardless of race, religion, disability, sage or gender
Learning Disability This policy applies to safety reports of events occurring in all trials conducted within the Trust, regardless of race, religion, disability, age, gender or sexuality
Sex This policy applies to safety reports of events occurring in all trials conducted within the Trust, regardless of race, religion, disability, age, gender or sexuality
Age This policy applies to safety reports of events occurring in all trials conducted within the Trust, regardless of race, religion, disability, age, gender or sexuality
Race This policy applies to safety reports of events occurring in all trials conducted within the Trust, regardless of race, religion, disability, age, gender or sexuality
Sexual orientation This policy applies to safety reports of events occurring in all trials conducted within the Trust, regardless of race, religion, disability, age, gender or sexuality
Pregnancy and maternity This policy applies to safety reports of events occurring in all trials conducted within the Trust, regardless of race, religion, disability, age, gender or sexuality
Religion or belief. This policy applies to safety reports of events occurring in all trials conducted within the Trust, regardless of race, religion, disability, age, gender or sexuality
Gender re-assignment This policy applies to safety reports of events occurring in all trials conducted within the Trust, regardless of race, religion, disability, age, gender or sexuality
Marriage or civil partnerships This policy applies to safety reports of events occurring in all trials conducted within the Trust, regardless of race, religion, disability, age, gender or sexuality
Carers NA

Equality Analysis
Safeguarding people who are vulnerable This policy applies to safety reports of events occurring in all trials conducted within the Trust, regardless of race, religion, disability, age, gender or sexuality
Other potential impacts, for example culture, human rights, socio economic, for example homeless people **This policy applies to safety reports of events occurring in all trials conducted within the Trust, regardless of race, religion, disability, age, gender or sexuality**
Summary of Analysis
Does the evidence show any potential to discriminate? Safety reporting is governed by national Research Ethics Committees; Medicines and Healthcare products Regulatory Agency; and the Health Research Authority, which ensures all patients are adequately protected
How does the policy **advance equality of opportunity?** The policy applies to safety reporting of events, which are purely factual in nature.
How does the policy **promote good relations between groups** (promoting understanding)? All reports are assessed in a fair and open manner