Clinical Directorate Clinical Research Governance Team

Standard Operating Procedure

Sponsor Quality Assurance

SOP024

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Karen Jennings-Wilding	15th July 2024
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1. Introduction

Quality Assurance (QA) is the systematic and independent examination of study-related activities and documents performed to ensure that the data are generated, documented (recorded) and reported in compliance with Good Clinical Practice (GCP) and the applicable regulatory requirements. At the University of Liverpool (University) Quality Assurance of Sponsorship and Oversight refers to the University testing for itself the effectiveness of the Quality Systems that are in place in the Liverpool Clinical Trials Centre (LCTC), other Clinical Trial of Investigational Medicinal Product (CTIMP) activity that the University engages in, and for Non-CTIMP studies that the University sponsors through the timely execution of independent assessment.

Audit is the systematic and independent examination of study related activities and documents to determine whether they were conducted according to the protocol, local Standard Operating Procedures (SOPs), GCP and other applicable regulatory requirements. An audit of a study provides the University with an independent appraisal of the quality and completeness of the study and to assist in the identification of potential problem areas in order to implement solutions. It also provides a snapshot overview of study conduct.

In the University 'independence' is achieved through the appointment of members of staff with responsibility for QA, based in the Clinical Directorate, independent from the LCTC, external Clinical Trials Units (CTUs), individual studies or individual members of staff providing services on sponsored studies. This includes the roles of the Senior Clinical Research Governance Manager and Sponsorship Manager.,

The University has an established Quality System for Sponsorship and Oversight of University Sponsored studies, that works alongside the quality systems in place within the LCTC, co-sponsoring NHS trusts or elsewhere, to assure the quality of every aspect of a study whether Sponsored or otherwise involving the University. It will achieve adherence to the Protocol, the Medicines for Human Use (Clinical Trials) Regulations 2004 [as amended] (the Regulations) and the UK Policy Framework for Health and Social Care Research (UK Policy Framework) and other regulations and frameworks where applicable. Compliance with these standards provides public assurance that the rights, safety and well-being of study subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the study data are credible.

2. Scope of Procedure

The purpose of this SOP is to detail the systems in place within the University Clinical Research Governance Team to ensure appropriate levels of QA and oversight are used for University Sponsored studies. The Sponsorship of Clinical Research Quality Manual (QM001) provides detail of the Quality Management System used to ensure Sponsor oversight. The system contains policies, SOPs, work instructions, guidance documents and controlled documents such as templates and forms.

This SOP is intended as an overview of QA with more detailed guidance being provided in the specific SOPs referenced in section 9.

3. Who

This SOP is aimed at staff within the University Clinical Directorate who are involved in the QA and oversight processes for University Sponsored research.

This SOP is also applicable to Chief Investigators, students, trial coordinators and other members of University Staff involved in University Sponsored research.

4. When

This SOP should be referred to when completing any QA activity. Other University staff designated above should be aware of this SOP during the preparation of and throughout the conduct of a sponsored study to understand the QA expectations. This SOP should be read in conjunction with the Sponsorship of Clinical Research Quality Manual (QM001),

5. Quality Assurance

5.1 Regulations, frameworks and guidance

All research Sponsored by the University must adhere to applicable legislation. This includes, but is not limited to the UK Policy Framework for Health and Social Care Research, The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004 No. 1031) and subsequent amendments (the Regulations), The Medical Devices Regulations 2002, the Principles of Good Clinical Practice, the Data Protection Act 2018, UK General Data Protection Regulation (UK GDPR), the Mental Capacity Act 2005, the Human Tissue Act 2004 and Good Clinical Practice (GCP) guidelines.

5.2 Quality Manual

The Sponsorship of Clinical Research Quality Manual (QM001) must be adhered to for all research Sponsored by the University.

5.3 Policies and Standard Operating Procedures (SOPs)

Researchers and research related staff must adhere to all applicable University and Sponsor policies and SOPs during the conduct of the research study. Where research is being carried out on external premises (such as NHS Trusts) then relevant policies and SOPs must also be adhered to. Where policies or SOPs provide conflicting instructions, the Sponsor will define which policy or SOP must be followed.

For CTIMPs managed outside of a University CTU and for some other types of research it is required that a Quality Management System is established or evidenced to assure the Sponsor that there are appropriate procedures in place for the management of the trial. See SOP003 (Requirements for CTIMPs not being managed by a CTU) for further information.

5.4 Document Control

All SOPs (generic and study specific) and study related documentation should be document controlled to ensure that it is accountable, traceable and consistent and that all members of the study team are working to the most recent versions of each document.

The Senior Clinical Research Governance Manager is responsible for ensuring document control of all Clinical Research Governance SOPs. The LCTC Document Controller is responsible for controlling all LCTC generic SOPs and LCTC trial specific SOPs.

It is the responsibility of the CI or designated team member to ensure version control on all study related documents.

All documentation required to be submitted to the Research Ethics Committee (REC) or the MHRA must also be version controlled.

5.5 Staff Training

All staff members involved in CTIMPs must ensure that they have undergone Good Clinical Practice (GCP) training before the CTIMP opens to recruitment. The University recommends that this is undertaken as soon as possible to ensure the setup of the CTIMP is done appropriately.

GCP training must be updated on a three-yearly basis throughout the life of the CTIMP, or more regularly if there has been a change to regulations, or if it is requested by the Sponsor.

All staff working on Clinical research should ensure they are adequately trained and experienced to undertake their role. University members of staff are advised to access the courses provided by Epigeum before undertaking their research. It is noted here that training for a research related role does not have to be undertaken as a formal training course or specific research training but may be from non-research specific training courses, professional development courses, qualifications, competencies and experience, undertaking shadowing or mentorship, attending conferences, reading SOPs and participating in workshops.

Researchers should ensure they have training in the following areas;

- Informed consent
- Data protection and confidentiality
- Human Material

The Sponsor will expect to see copies of CVs and GCP certificates (where appropriate) for CI's to enable them to assess the level of training and experience held. Upon review the Sponsor may request that extra training is undertaken. CIs are required to ensure that members of their research team are appropriately trained to undertake their role. Researchers and their teams are also encouraged to maintain a training log (TEM003) and folder of certificates to produce at the time of audit or inspection.

All CIs must also ensure they have read and understood all applicable Sponsor policies and SOPs. This is demonstrated via the signature of the CI Declaration on each University Sponsorship Approval Letter.

5.6 LHP Joint Research Office (JRO) Sponsorship Committee and Non-Interventional Sponsorship Sub Committee (NISSC)

In all cases the decision on whether the University will Sponsor a piece of research is reserved to the Liverpool Health Partners (LHP) Joint Research Office (JRO) Sponsorship Committee or NISSC. All CTIMPs, Clinical Investigations of Medical Devices and research deemed to be higher risk will be reviewed by the JRO Sponsorship Committee, and lower risk studies will be assessed by NISSC. The Clinical Research Governance Team may use FORM004 JRO Sponsorship Algorithm in order to assist this decision-making process.

The Chairs of the JRO Sponsorship Committee and NISSC will also consider amendments made to Sponsored research of the University.

The JRO Sponsorship Committee and NISSC will receive various routine or non-routine reports on the conduct of research studies in order to maintain sponsor or organisational oversight, including but not limited to, annual progress reports, safety reports, monitoring compliance reports, summary audit reports, Trial Steering committee recommendations, notification of serious breaches of GCP or trial protocol etc. The procedure for how the JRO Sponsorship Committee provide oversight of University Sponsored CTIMPs activity is detailed in SOP029.

5.7 Audit of Quality

The Senior Clinical Research Governance Manager is responsible for ensuing an annual audit schedule is developed for auditing of sponsored studies and for oversight of the Clinical Trials Units. The CTUs may also undertake internal audit of managed studies. Where this audit may relate to Sponsorship it is expected that the Sponsor will receive a copy of the audit. Please also see SOP025.

5.8 Regulatory Inspection

In addition to monitoring and audit activity, CTIMPs may also be inspected by the MHRA. See also SOP002, Preparing and Hosting External Inspections.

6. Quality Control

Quality Control (QC) is an activity that involves the review of factors in a process as the process is occurring. The level and type of QC that is required is determined by the risk assessment in place for the trial. The following are examples of QC activities that may be carried out in the course of a trial, but it is noted here that the University, as Sponsor, delegates these activities to the CTU managing the trial.

6.1 Monitoring

Monitoring of quality is required for all CTIMPs. This may be done by a member of the study team employed to act as a study monitor or it may be done by a member of staff from the co-sponsoring Trust. The plan for how the study is to be monitored should be developed according to the risk management plan and signed off prior to approval of the sponsored study. See also SOP011. For higher risk Non-CTIMPs it may also be identified that monitoring should be undertaken, and discussions will be required with the study team at that time.

6.2 Independent Data and Safety Monitoring Committee

For University sponsored CTIMPs it is recommended that an Independent Data and Safety Monitoring Committee (IDSMC) is established to assess progress, safety and critical endpoints in an ongoing manner and provide the Sponsor with recommendations regarding trial modifications, continuation or termination of the trial. It is also recommended that the DMC is supplemented by a Trial Steering Committee (TSC) who provide overall, independent supervision of the trial to ensure conformity with required standards and the protocol. In some cases, it may also be required for a Non-CTIMP to convene a TSC or similar group to oversee the progress of the study. This will usually be recommended for complex studies that involve multiple organisations. The University will request that a Sponsor representative is a member of the committee.

6.3 Study Documentation

The CI and study team should draft all study related documentation including protocol, case-report forms (CRFs), patient information Sheets (PIS), study specific SOPs and ensure that documentation complies with all regulations and guidelines.

The CI should ensure that a Trial Master File (TMF) is set up for the study and ensure that the latest versions of all study specific documentation and essential documents are stored in the TMF.

7. Roles and Responsibilities

This procedure provides an overview of Quality Assurance activities within the University and therefore all University of Liverpool Clinical Research Governance Team staff, University Staff involved in working on CTIMPs and CIs should ensure that they are aware of this procedure.

8. Abbreviations

CI	Chief Investigator
CTIMP	Clinical Trial of Investigational Medicinal Product
CTU	Clinical Trials Unit
GCP	Good Clinical Practice
IDSMC	Independent Data and Safety Monitoring Committee

JRO	Joint Research Office
LHP	Liverpool Health Partners
LCTC	Liverpool Clinical Trials Centre
NISSC	Non-Interventional Sponsorship Sub Committee
QA	Quality Assurance
QC	Quality Control
SOP	Standard Operating Procedure
TSC	Trial Steering Committee
University	University of Liverpool

9. Associated Documents and References

QM001	Sponsorship of Clinical Research Quality Manual
SOP001	Production and Control of Standard Operating Procedures
SOP002	Preparing and Hosting External Inspections
SOP003	Requirements for CTIMPs not being managed by a CTU
SOP011	Monitoring of University Sponsored CTIMPs
SOP025	Internal Audit
SOP029	Organisational Oversight of CTIMPs
TEM003	Training log
FORM004	SPARK Sponsorship Algorithm

National Legislation and Guidance

UK Policy Framework for Health and Social Care Research

The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004 No. 1031)

The Medical Devices Regulations 2002

ICH E6 (R2) Principles of Good Clinical Practice

Data Protection Act 2018

UK General Data Protection Regulation (UK GDPR)

Mental Capacity Act 2005

Human Tissue Act 2004

10. Training and Resources

CIs, students, trial coordinators and other members of University Staff involved in University Sponsored research should be aware of and familiar with this SOP. Training can be provided by the Clinical Research Governance Team upon request.

11. Monitoring and Audit

An internal audit of Clinical Directorate SOPs will be conducted at a minimum of every two years.