QM-1 V7	
Title: Research & Development Quality Manual	
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GRAMPIAN CLINICAL RESEARCH OFFICE

NHS Grampian

1495 UNIVERSITY OF ABERDEEN

Research & Development Quality Manual

Document History

Version	Description of update	Date Effective
1	New document	29-05-15
2	Updated to reflect new SOP numbers in Q-Pulse	02-10-15
3	Reformatted and updated	01-04-17
4	Updated references to UK Policy Framework for Health & Social Care Research and GDPR. Reference to Genetically Modified Micro organisms	01-06-18
5	Updated accreditation and certification information at 5.4.3 Updated staffing at 6.1.2.4 6.12 updated regarding hosted trial monitoring	21-06-21
6	Updated regulatory references, reference to GRO and CIP throughout.	02-07-24
7	Updated reference to Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 throughout Reference to Document Controller at 3 Updated reference to GCP training requirement at 6.1.2 and 6.9 Updated ULT storage requirements at 6.16 Updated reference to Ideagen Quality Management System throughout	28-04-26

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1. Log of updates

Version	Date	Page(s) changed	Description of update
1	29-5-15	-	New document
2	2-10-15	Various	Updated to reflect new SOP numbers in Q-Pulse
3	1-1-17	All	Reformatted
		5-6	Inclusion of ADE, SADE, USADE and AMP at 4
		13 and 14	Inclusion of ADE, SADE and USADE
		6	Reference to Laboratory file
		9 and 16	Addition of customer feedback at 5.3.4 & 6.5.6
		9	Addition of Data Protection Act 1998 at 5.4.3
		10	Reference to QMS Matrix at 6.1.2
		12-13	Reference to environmental procedures at 6.1.4
		12 and 14	Reference to Study Specific SOPs
		16	Reference to corrections within CAPA at 6.5.3
		19	Reference to Biorepository and e-archiving 6.16
4	1-6-18	3, 9 and 12	Update reference to UK Policy Framework for Health & Social Care Research
		3 and 9	Update to include reference to GDPR and DPA (2018)
		19	Reference to Genetically Modified Micro organisms at 6.14
		19	Change of third party archive details at 6.16
5	1-6-21	9	Updated accreditation and certification information at 5.4.3
		11	Updated staffing at 6.1.2.4
		18	6.12 updated regarding hosted trial monitoring
6	2-7-24	3	Reference to GRO, ISO 14155:2020 and updated staff
		3.1 5.1 and 6.1.4	Reference to ISO 14155:2020/Medical Devices Regs 2002
		4	Removal of reference to EU directive
		5.1	Reference to GRO
		5.4.3 and 6.1.4	Updated references
		6.1.2.2	Reference to CIP
		6.1.2.3	Reference to Document Controller and NoSRES team
		6.4.1/6.4.3	Reference to SOP-QA-43
		6.5.2.3	Reference changed from CSOG to R&D Director
7	28-4-26	3,4,7,9,10,12, 17	Updated reference to Clinical Trials Regulations 2025
		3	Reference to Document Controller
		5	Reference to NIMP
		7, 14, 15, 16	Updated reference to Ideagen Quality Management
		10, 17	Updated GCP training requirements
		10	Reference to MHRA and R&D at 6.1.2.2
		16	Revised USM reporting requirements at 6.4.3
		12	Reference to Clinical Investigation Plan
		5, 10	Removal of reference to APR at 4 & 6.1.2.2
		17	Reference to risk adapted audit/monitoring at 6.12
		19	Reference to sample storage environment at 6.16

2. Index

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3. Outline of University of Aberdeen (UoA) and NHS Grampian (NHSG)

The University of Aberdeen was founded in 1495 and is Scotland's third oldest, and the UK's fifth oldest, university. In 1497 it was the first university in the English speaking world to create a chair of medicine.

The University of Aberdeen, which currently has 14,500 students, has invested heavily in medical research in Aberdeen. Located on the Foresterhill Health Campus are the Institute of Medical Science, The Health Sciences Building, Suttie Centre for Teaching and Learning in Healthcare, and The Rowett Institute of Nutrition and Health.

NHS Grampian came into being in 2004 after the dissolution of two NHS Trusts. It is overseen by an NHS Board responsible for improving the health of the Grampian population and for delivering the healthcare required. The Board oversees the implementation of Scotland's national health agenda, tailored to the needs of the Grampian population of approximately 500,000 spread over 3,000 square miles. From April 2016 NHS Grampian's fully integrated Health and Social Care Partnerships moved from shadow form to full operation across the three Local Authority areas of Aberdeen City, Aberdeenshire and Moray. The main NHS Grampian site is the Foresterhill Health Campus; which is shared with the University of Aberdeen. NHS Grampian works closely with the University of Aberdeen and Robert Gordon University in delivery of medical research and training.

This document sets out the Quality Management System for Clinical Trials of Investigational Medicinal Products (CTIMPs) and Medical Device Clinical Investigations (MDCIs) which are sponsored, or co-sponsored, by the University of Aberdeen and/or NHS Grampian. The sponsorship function of the University of Aberdeen and NHS Grampian is undertaken by the joint NHS Grampian and University of Aberdeen's Grampian Research Office (GRO), based at Foresterhill House Annexe, Aberdeen; under the direction of the Research & Development Director. The team consist of the Research and Development Director, Senior Research & Development Manager, Head of Commercial Research, Quality Assurance Manager, Research Governance Manager, Lead Research Nurse, Clinical Research Facilities Manager, Research Governance Officer, Assistant Research Governance Officer, Research Monitors, Quality Assurance Support Officer, Document Controller and various support and administrative roles. The team liaise with the Research Innovation & Enterprise team in the University of Aberdeen.

The remit of the Grampian Research Office (GRO) is to provide sponsorship, support and advice to researchers engaged in clinical research and to ensure the implementation and maintenance of quality assurance and research governance principles are applied to all projects, in accordance with the UK Policy Framework for Health & Social Care Research, The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 (SI 2025 No. 538), as amended, the Principles of Good Clinical Practice (GCP), ISO 14155:2020 – Clinical Investigation of medical devices for human subjects – Good clinical practice, the UK General Data Protection Regulation (UK GDPR), Data Protection Act (2018) and the Human Tissue (Scotland) Act 2006.

3.1 Research Governance and Quality Assurance Aims

- To facilitate high quality clinical research for Clinical Trials of Investigational Medicinal Products (CTIMPs) and Medical Device Clinical Investigations (MDCIs) within the University of Aberdeen and NHS Grampian.
- To ensure the scientific integrity of clinical research and clinical trials within the University of Aberdeen and NHS Grampian.
- To ensure the rights, safety and well-being of all participants in clinical research and clinical trials within the University of Aberdeen and NHS Grampian.
- To ensure compliance with the Principles of Good Clinical Practice (GCP).
- To ensure compliance with the requirements of The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 (SI 2025 No. 538) as amended.
- To ensure compliance with the requirements of The Medical Devices Regulations 2002 (SI 2002 No 618) as amended.
- To ensure compliance with the requirements of ISO 14155:2020 for MDCIs.
- To facilitate the readiness of University of Aberdeen and NHS Grampian for inspection by the Medicine and Healthcare products Regulatory Authority (MHRA).

4. Glossary of Terms

ADE	Adverse Device Effect
ADR	Adverse Drug Reaction
AE	Adverse Event
AMP	Auxiliary Medicinal Product
AR	Adverse Reaction
ARSAC	Administration of Radioactive Substances Advisory Committee
CAPA/CCAPA	Corrective Action and Preventive Action/Correction and CAPA
CAS	Central Allocations System
CC	Co-ordinating Centre
CI	Chief Investigator
CIP	Clinical Investigation Plan ('Protocol' for MDCIs)
CRF	Case Report Form **or** Clinical Research Facility
CRO	Contract Research Organisation
CROG	Clinical Research Operational Group
CSOG	Clinical Studies Oversight Group
CTFG	Clinical Trials Facilitation Group
CTA	Clinical Trial Application **or** Clinical Trial Authorisation
CTIMP	Clinical Trial of Investigational Medicinal Product
CTU	Clinical Trials Unit
DIBD	Development International Birth Date
DMC	Data Monitoring Committee
DSUR	Development Safety Update Report
EMA	European Medicines Agency
EudraCT	European Union drug regulating authorities Clinical Trials (EU Clinical Trials Database)
GCP	Good Clinical Practice (ICH GCP E6 (R3) – International Conference on Harmonisation)
GDPR	General Data Protection Regulation
GLP	Good Laboratory Practice
GMM	Genetically Modified Micro organisms
GMP	Good Manufacturing Practice
GRO	Grampian Research Office
GTAC	Gene Therapy Advisory Committee
HRA	Health Research Authority
HSE	Health and Safety Executive
IB	Investigator Brochure
ICF	Informed Consent Form
IRB	Institutional Review Board
ISO	International Organization for Standardization
IMP	Investigational Medicinal Product
IRAS	Integrated Research Application System
ISF/ITMF	Investigator Site File/Investigator Trial Master File*
MDCI	Medical Device Clinical Investigation
MHRA	Medicines and Healthcare products Regulatory Agency
NHSG	NHS Grampian
NIMP	Non Investigational Medicinal Product
NRES	National Research Ethics Service
NRS	NHS Research Scotland
NRS CMT	NHS Research Scotland Central Management Team
NRSPCC	NHS Research Permissions Coordinating Centre
PI	Principal Investigator
PIS	Patient Information Sheets
QA	Quality Assurance
QAM	Quality Assurance Manager

QC	Quality Control
QMS	Quality Management System
QP	Qualified Person
RAP	Risk Assessment Proforma
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
PMC	Project Management Committee
RI&E	Research Innovation & Enterprise
RGM	Research Governance Manager
RGT	Research Governance Team
RSI	Reference Safety Information
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SAP	Statistical Analysis Plan
SI	Statutory Instrument
SmPC/SPC	Summary of Product Characteristics
SOAR	Scottish On-line Appraisal Resource
SOP	Standard Operating Procedure
SSI	Site Specific Information
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial/Project Master File*
TSC	Trial/Project Steering Committee
USADE	Unexpected Serious Adverse Device Effect
UKCRC	United Kingdom Clinical Research Collaboration
UoA	University of Aberdeen

* TMF – Documentation from a CTIMP or MDCI **must** be filed in the TMF. This requirement is set down in UK legislation (2001/20/EC Article 15(5), SI 2025/538 [as amended] 31A).

The TMF forms the basis for an inspection to confirm compliance with regulatory requirements. The TMF is normally composed of a **Sponsor TMF**, held by the Sponsor organisation (or to whom this function is delegated), and an **Investigator TMF**, held by the investigator. These files together are regarded as comprising the entire TMF for the trial and should be established at the beginning of the trial.

In addition there may also be a **Pharmacy file** (held by the clinical trial pharmacy), **R&D file** (held by NHS R&D), **Laboratory file** held in the laboratory performing study analysis and **Site files** where there is more than one site.

5. Quality Management System

General

University of Aberdeen (UoA) and NHS Grampian (NHSG) have defined the quality framework for activities within UoA and NHSG. A Quality Manual (QM), Quality Statement and Standard Operating Procedures (SOPs) are in place; together these form the Quality Management System (QMS). This covers planning, operation and effective controls within research activities carried out in UoA and NHSG. Records shall be maintained by researchers to show evidence of compliance with the QMS and, where appropriate, the principles of GCP.

5.1 Quality Manual

This Quality Manual is the statement by UoA-NHSG of its documented Quality Management System which conforms with the principles of Good Clinical Practice (GCP), The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 Statutory Instrument No. 538 (SI 2025/538), as amended and ISO 14155:2020.

Conformance with the requirements stated in the Quality Manual and in the UoA-NHSG Standard Operating Procedures is required for all UoA-NHSG staff engaged in CTIMPs and MDCIs. Where improved methods or procedures are identified, the documentation so affected shall be officially and properly changed, when agreement has been reached between all Groups / Teams involved (see SOP-QA-1 - Management of SOPs).

This Quality Manual is a controlled document and is updated as required by the Quality Assurance Manager (QAM) and is reviewed at least every three years.

All staff shall be able to view the Quality Manual on the UoA-NHSG Grampian Research Office (GRO) website (www.adbd.ac.uk/grampian-research-office) and, where accessible, Ideagen Quality Management*. Only the current version shall be displayed. Printed copies shall be regarded as uncontrolled when printed and care should be taken to ensure that an out of date version is not being referred to.

*NHS Grampian Research and Development electronic Ideagen Quality Management system.

5.2 The Scope of the Quality Management System

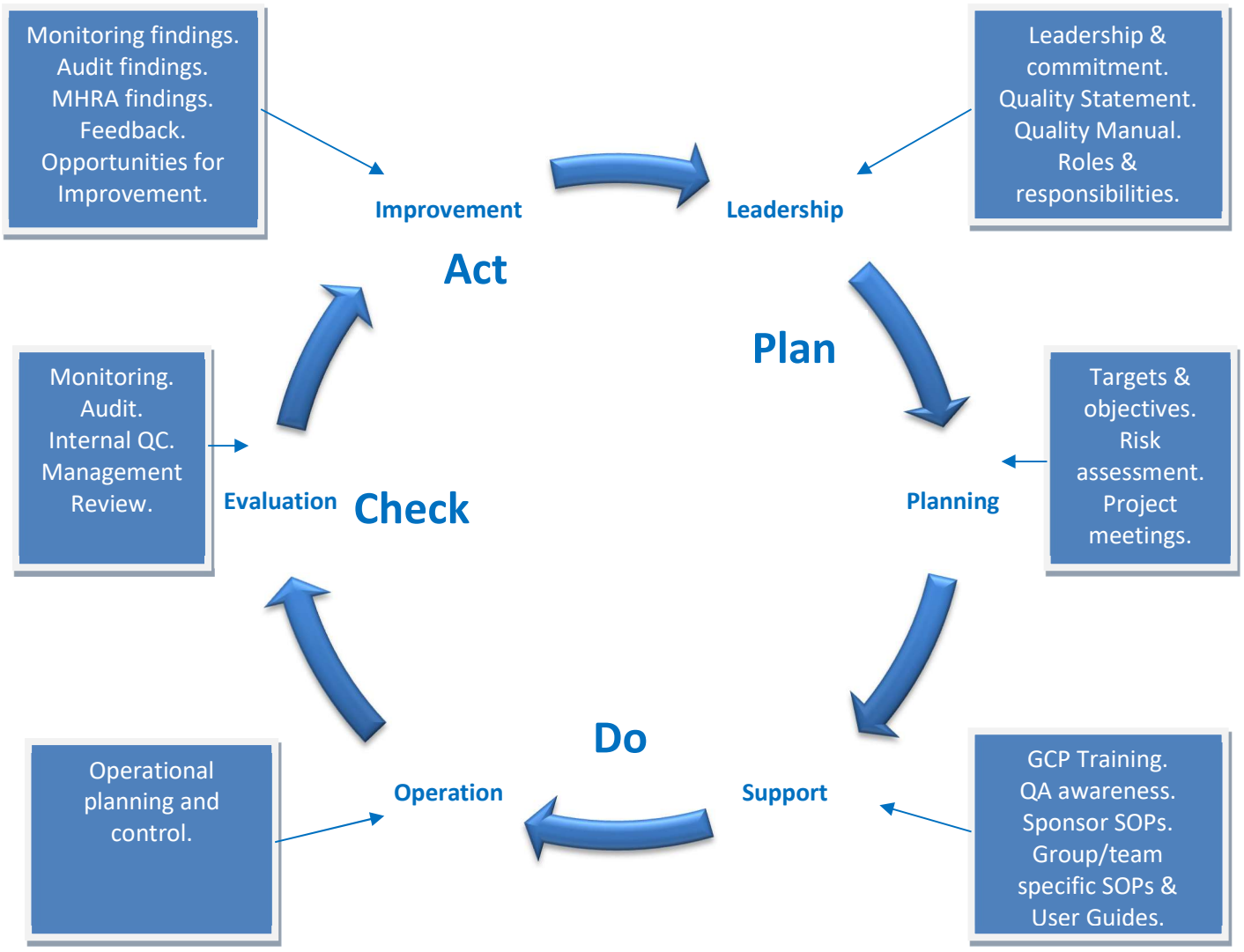
5.2.1 This Quality Manual applies to all researchers and Sponsor staff participating in CTIMPs and MDCIs which are sponsored, or co-sponsored, by University of Aberdeen (UoA) and/or NHS Grampian (NHSG).

5.2.2 For research projects which are sponsored externally to the UoA or NHSG, local researchers and support staff shall refer to the respective Sponsor's procedures and any timelines for handling Deviations, Breaches and Urgent Safety Measures (for UoA-NHSG procedure see SOP-QA-25 – Deviations and Breaches).

5.2.3 This Quality Manual demonstrates **'good practice'** in all clinical research conducted in UoA and NHSG. The principles contained within it may be applied to work not listed in 5.2.1 to demonstrate and encourage a quality culture which is compliant with various quality assurance standards and regulations.

5.2.4 This Quality Manual and UoA-NHSG SOPs may also be used by staff from other NHS areas, or organisations, with prior agreement.

5.3 The interaction within the research project governance processes of the Quality Management System.



5.3.1 Like all Quality Management Systems the one operated by UoA-NHSG uses the '**plan-do-check-act**' principle of continual improvement. There is demonstrable management commitment with a Quality Statement, the Quality Manual (this document) and documented roles and responsibilities for key staff.

5.3.2 Specific plans are formulated with targets, objectives and risk assessments performed. Plans, targets and objectives are realised through training and awareness sessions, QA support, Research Governance support and the preparation of group and team specific SOPs and User Guides. SOPs and User Guides are implemented and become operational.

5.3.3 The processes and activities are checked for effectiveness through a programme of risk adapted monitoring and audit to identify opportunities for improvement. Corrections, Corrective Action and Preventive Actions (CAPA) are identified and agreed, leading to continual improvement of the QMS.

5.3.4 The Quality Management System is regularly reviewed (Management Review) for effectiveness and any improvements opportunities are identified. Stakeholder feedback is also sought to identify any improvement opportunities and is reviewed by senior management during the Management Review. The cycle then starts again.

5.4 Quality Assurance

5.4.1 UoA-NHSG is dedicated to delivering research that consistently satisfies its stakeholders. As an organisation and as individuals, UoA-NHSG shall continuously strive to improve the quality of its activities.

5.4.2 UoA-NHSG is committed to providing the highest possible quality of research to its collaborators, funders and customers; who include the NHS, pharmaceutical companies, Government Departments, Charities, Local Authorities within the UK, and international bodies and organisations.

5.4.3 UoA and NHSG are diverse organisations and no single quality assurance scheme covers all of the activities of the organisations. As a result some of the different component sections within both UoA and NHSG have achieved and maintained accreditation and certification to a range of standards that meet the needs and activities of the various parts of the organisations.

The following list provides some details of the regulations and guidelines that UoA-NHSG currently comply with:

- UK Policy Framework for Health & Social Care Research.
- Principles of Good Clinical Practice (as outlined in Directive 2005/28/EC).
- UK Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 (SI 2025 No. 538) as amended.
- Medical Device Regulations 2002 (SI 2002 No. 618) as amended.
- Human Tissue (Scotland) Act 2006.
- UK General Data Protection Regulations (UK-GDPR).
- Data Protection Act (2018).
- ISO 14155:2020 Clinical investigation of medical devices for human subjects – Good Clinical Practice
- NHSG diagnostic laboratories are accredited by UKAS to ISO 15189:2022.
- NHSG Fertility Centre are accredited by UKAS to ISO 15189:2022.
- UoA Rowett Institute of Nutrition and Health hold certification to ISO 9001:2015.
- NHSG Biorepository holds accreditation from NRS CMT.
- The University of Aberdeen-NHSG Data Safe Haven (DaSH) hold certification to ISO 27001:2022.

5.4.4 The University of Aberdeen has developed a Handbook for Research Ethics and Governance which applies to all academic disciplines. It is managed centrally and is the central authority and reference point within the institution for matters relating to research governance which should be used and referred to accordingly by research staff and students.

5.4.5 Like all Higher Education Institutions (HEIs) in the UK, UoA maintains the academic standards of qualifications and the quality of the student learning experience through a quality system that complies with the Code of Practice for the Assurance of Academic Quality and Standards in Higher Education, published by the Quality Assurance Agency for Higher Education (QAA), an independent body established to provide public confidence in the quality and standards of higher education.

6 Quality Management System Requirements

6.1 Organisation

6.1.1 Management System

The UoA-NHSG Quality Management System covers clinical research work carried out in all parts of UoA and NHSG. Following the implementation of the Clinical Trials Directive 2001/20/EC, compliance with the principles of GCP became a legal requirement throughout the EU for persons involved in Clinical

Trials of Investigational Medicinal Products (CTIMP). Since 2026 n the UK these requirements are achieved through The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025, Statutory Instrument number 538 (SI 2025/538), as amended.

SI 2025/538 sets out the processes for regulatory and ethical review of all interventional trials in order for them to gain Clinical Trial Authorisation (CTA) from the MHRA (the competent authority in the UK) and favourable Research Ethics Committee (REC) opinion. SI 2025/538 provides the powers for inspection and enforcement by the MHRA.

6.1.2 Management – staff & specific duties

Records of qualifications, training and experience of all staff shall be maintained by each member of staff involved in clinical research activities. This shall include, as a minimum, an up to date CV, a job description, evidence of appropriate training (eg GCP, QA, trial specific training) and an organisational chart.

Before commencement of a clinical trial the Sponsor shall indicate which Sponsor SOPs should be read and understood by the CI (in addition to this Quality Manual) and recorded in their training file, or SOP sign-off sheet (TMP-QA-40). Similarly, in liaison with the Sponsor, the CI shall indicate which Sponsor SOPs and trial specific SOPs (if applicable) each member of the study team should read and understand, and record in their training file, or SOP sign-off sheet (TMP-QA-40). The Quality Management System Matrix (TMP-QA-44) indicates the component parts of the QMS which the various research roles should be familiar with and may be used in place of the SOP sign-off sheet.

Within UoA-NHSG appropriate GCP training shall be in place before a CTIMP or MDCI commences and shall be updated every three years.

For specific projects a training matrix may be required to detail specific training required to demonstrate competency before involvement in tasks (see SOP-QA-2 – Training record).

6.1.2.1 Specific responsibilities

6.1.2.2 Sponsor

The Sponsor is responsible for ensuring clinical trials comply with the legislation and principles of GCP. The Sponsor takes responsibility for the initiation, management, ensuring adequate finance is in place and having oversight of the TMF (including overseeing archiving after the conclusion of the trial). The Sponsor must perform a risk assessment of the proposed clinical trial at the protocol/Clinical Investigation Plan (CIP) development stage and, if a CTIMP, categorise the trial as risk type ‘A’, ‘B’ or ‘C’ (see below). The Sponsor must also oversee authorisation from the MHRA, R&D Permission and a favourable Research Ethics Committee (REC) opinion before the trial commences (although it is the CI who must apply to REC, MHRA and R&D using IRAS).

- Type A – no higher than the risk of standard medical care.
- Type B – somewhat higher than the risk of standard medical care.
- Type C – markedly higher than the risk of standard medical care.

The Sponsor must also ensure that the Investigator’s Brochure (IB) is produced and reviewed, at least annually, and that the MHRA are provided with an annual Development Safety Update Report (DSUR) for CTIMPs. The Sponsor shall also inform MHRA and REC of a temporary halt, early termination or the end of the trial. The UoA - NHSG Research Governance and Quality Assurance teams provide this function for all UoA-NHSG clinical research studies as either Sponsor or Co-sponsor. The Sponsor may delegate some of their functions but shall always remain responsible for them.

6.1.2.3 Quality Assurance Team

Consists of the Ethics & Quality Assurance Manager (QAM), Quality Assurance Support Officer, Research Monitors and Document Controller. The QA team ensure that effective quality management is in place for all clinical studies, manage the Quality Management System (QMS) and oversee all auditing and monitoring functions to demonstrate compliance.

The QA team is also responsible for any third party assessments which may be necessary, and archiving of trial documentation, in liaison with the Named Archivist.

All documentation which forms the QMS and all key trial documents must be controlled. The document control function is overseen by the QA Team (Document Controller).

The Ethics & Quality Assurance Manager also manages the North of Scotland Research Ethics Service (NoSRES). This consists of The Scientific Officer, Senior Ethics Co-ordinator/Deputy Regional Manager, two Assistant Ethics Co-ordinators, and two Ethics Committee Office Bearers.

6.1.2.4 Research Governance Team (RGT)

Consists of the Research Governance Manager (RGM) Research Governance Officer and Assistant Research Governance Officer. The Research Governance Team is responsible for setting standards to improve research quality and safeguard the public. It involves enhancing ethical and scientific quality, promoting good practice, reducing adverse incidents, ensuring lessons are learned and preventing poor performance and misconduct.

6.1.2.5 Research and Innovation Team (R&I)

The R&I team are responsible for preparing, reviewing and signing contracts for clinical research projects in liaison with the Quality Assurance team and Research Governance team. It manages the process for the submission of applications for funding to external bodies and the acceptance of such awards. The R&I team also deal with insurance or indemnity; to cover the liability of the Sponsor.

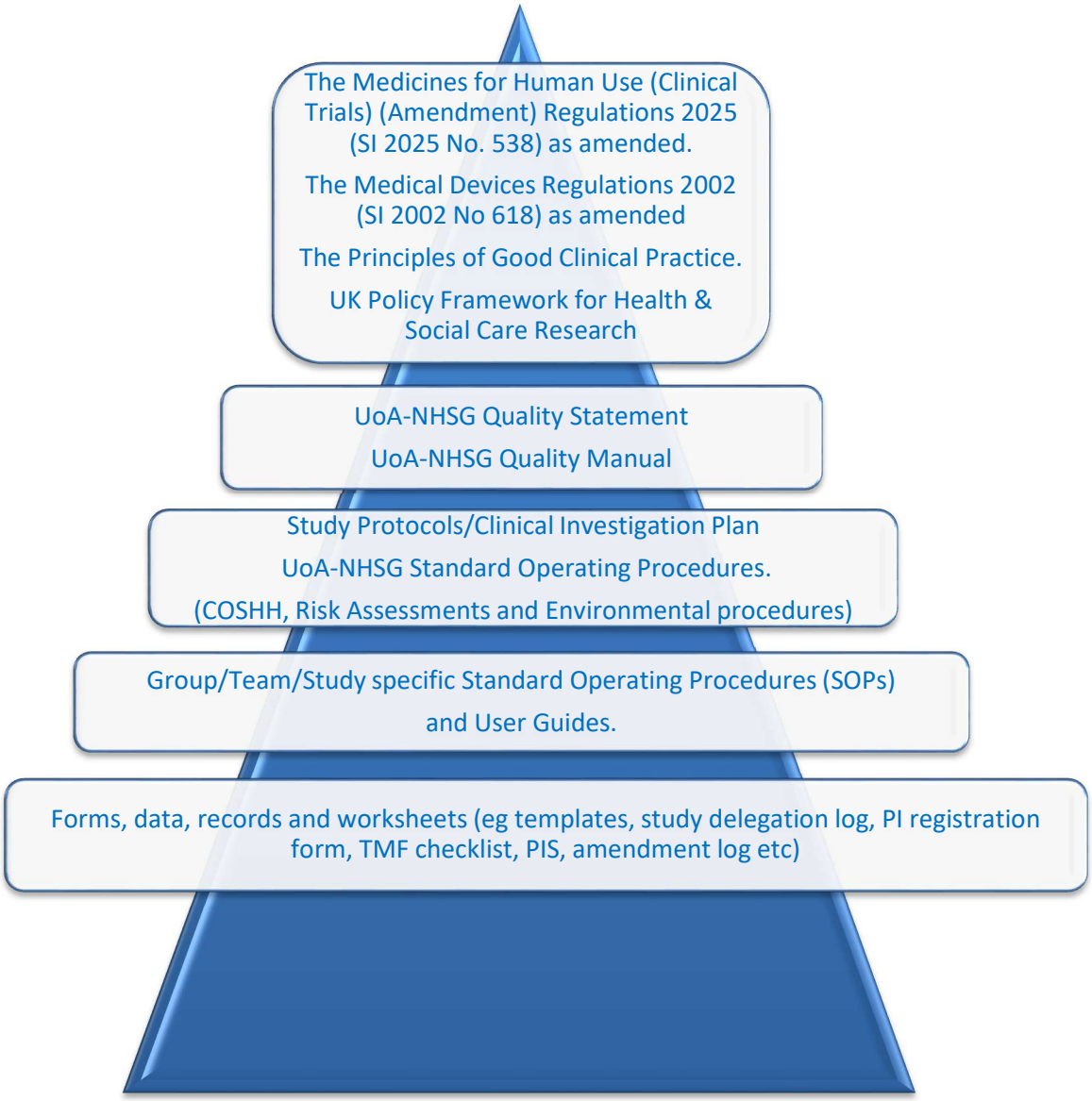
6.1.3 Authorised Deputies

In the absence of any of the above, any managerial and technical responsibilities shall be delegated to appropriate personnel. Such delegation shall be documented appropriately.

6.1.4 Management – General

Each person within UoA-NHSG is responsible for the quality of the work they do, and at all times are required to be familiar with the Quality Management System relevant to their role and activities. Each individual shall be responsible for ensuring they have a job description, which contains a brief summary of their key duties, and shall outline the extent and limitations of the job holder's responsibility.

The UoA-NHSG Quality Management System documentation is structured in five levels as follows:



Level 1 – Regulations and Guidelines

The regulations and guidelines for Research within UoA-NHSG are The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025 (SI 2025 No. 538), as amended, The Medical Devices Regulations 2002 (SI 2002 No 618), as amended, The Principles of Good Clinical Practice (as outlined in Directive 2005/28/EC) and the UK Policy Framework for Health & Social Care Research.

Other parts of UoA-NHSG may also be required to comply with ISO 9001:2015, ISO 15189:2022, ISO 27001:2022, ISO 14155:2020 or NRS CMT accreditation.

Level 2- Quality Statement and Quality Manual

The Quality Manual (this document) details the outline structure of the QMS and serves as a reference for its implementation and maintenance. It is a policy document, incorporating UoA-NHSG quality policies and

objectives, an outline structure of the organisation and the roles and responsibilities of key technical and management personnel.

The Quality Statement, signed by senior management, demonstrates the organisations' intent to comply with and maintain quality assurance procedures. It shall list brief objectives and be reviewed regularly.

Level 3 – Study Protocols/CIP and UoA-NHSG Standard Operating Procedures (also COSHH, Risk Assessments and any Environmental Management procedures).

The Study Protocol/CIP is a controlled document which details all aspects of the study and study arrangements. Full details of the requirements of a Study Protocol are detailed in SOP-QA-3 - Protocol guidance.

The trial protocol shall define the end of the trial and be signed by the CI. The protocol shall define the responsibilities concerning safety reporting. The standard Health Research Authority (HRA) template shall be used for all CTIMP protocols sponsored by UoA and/or NHSG, unless previously discussed and agreed with the Sponsor. The HRA protocol template is available on the HRA website. Protocol waivers occur when researchers prospectively agree and intentionally implement a deviation from protocol without prior approval of an amendment. **Protocol waivers are not permitted.** MDCIs shall use a Clinical Investigation Plan (CIP) in place of a protocol.

The UoA-NHSG Standard Operating Procedures (SOPs) define the purpose and scope of activities necessary to meet the requirements of regulations, guidelines and Sponsor. The procedures address the management requirements and technical requirements of the regulations and guidelines and outline how such activities are conducted, controlled and recorded. These SOPs shall be applicable to all UoA-NHSG sites engaged in clinical research and sponsored by University of Aberdeen and/or NHS Grampian.

SOPs shall be allocated a review date of three years, although they shall be reviewed when there is any reason to suspect they may no longer be valid (eg following an Adverse Event (AE), Serious Adverse Event (SAE), Adverse Device Effect (ADE), Serious Adverse Device Effect (SADE), Suspected Unexpected Serious Adverse Reaction (SUSAR), Unexpected Serious Adverse Device Effect (USADE) or a health and safety incident or near-miss), as significant new information becomes available, or when there have been significant changes to working procedures. Such reviews are unplanned reviews and are triggered by significant events or changes. Relevant new information may become available from various sources (eg new staff with different expertise and experience, new manufacturers and suppliers of raw materials and equipment, or as a result of technological or scientific developments).

If there is a change to an SOP during the active phase of a research project the original document **may** be used for the duration of the project in order to maintain continuity. Such a decision **must** be approved by Sponsor (including the Quality Assurance Manager) and documented in the Trial Master File (TMF).

COSHH (Control of Substances Hazardous to Health) and Risk Assessments shall be written and in place across UoA-NHSG, where appropriate. These are the responsibility of the respective Health and Safety teams in UoA and NHSG.

Environmental procedures may be in place to comply with environmental legislation, policies or Environmental Standard, such as ISO 14001:2015. This is the responsibility of the respective Environmental teams in UoA and NHSG.

Level 4 – Technical SOPs (or Group Specific SOPs/Study Specific SOPs) and User Guides.

This level of documentation outlines methods of implementation for specific activities associated with the individual groups and teams, and includes Technical SOP, Study Specific SOPs and User Guides.

Generally Technical SOPs, Group Specific SOPs and Study Specific SOPs shall only be applicable in the area pertaining to the work, although other groups or teams may use a document from another group or team if

it is appropriate. If minor changes are required to such a document (or location specific requirements) to make it applicable to another team or group, these can only be made with the prior approval of the document owner.

Technical SOPs, Group Specific SOPs or Study Specific SOPs shall be controlled and reviewed in the same way as the UoA-NHSG SOPs but shall be managed by local management rather than the Quality Assurance Manager or Document Controller.

User Guides are local controlled documents providing specific instructions, or further information, on a particular task (eg how to operate a specific autoclave or analyser, which samples to take for a specific trial, how to arrange archiving of documentation etc). User Guides may be displayed on a wall (eg adjacent to the particular autoclave or analyser, where samples will be taken etc) and may not need to be reviewed on a regular basis (eg valid for the lifetime of an item of equipment or until a local process changes).

Level 5 – Forms, data and records.

Documentation used for QA purposes in support of a project or clinical trial (eg templates, study delegation log, TMF checklist, PIS, amendment log etc). Laboratory workbooks and all documentation contained in the TMF are also included.

Forms, data and records shall be controlled in the same way as SOPs and User Guides.

Relevant email communications concerning a trial shall be printed out (singly and not as a conversation) and retained in the Investigator TMF, or Sponsor TMF, as appropriate.

6.1.5 Responsibility

The responsibility for the compilation, distribution, amendment and maintenance of the Quality Manual and Sponsor SOPs lies with the Quality Assurance Manager and Document Controller. The Master Copy of this Quality Manual and QMS SOPs, and all subsequent amendments, are held on file (Ideagen Quality Management) by the Document Controller.

Authors of Technical or Group Specific SOPs are responsible for their maintenance, although the QA Team may perform this task on their behalf (eg using Ideagen Quality Management).

6.2 Document Control

The Document Control procedure is included in SOP-QA-1 – Management of SOPs. All change requests and controlled changes shall be made using the approved Change Control procedure (eg Ideagen Quality Management), shall be managed by the Document Controller and may involve the Clinical Research Operational Group (CROG).

6.3 (Serious) Adverse Events, (Serious) Adverse Device Effects and SUSARs

AE/ADEs must be assessed against seriousness criteria and reported to the Sponsor if serious. If the investigator determined that the AE/ADE fulfils one of the seriousness criteria (as defined in the protocol) then the AE/ADE must be reported as a SAE/SADE within 24 hours. It will then be assessed to determine if it is reportable to the MHRA and REC. See SOP-QA-22 – Adverse Events in CTIMPs and SOP-QA-39 – Adverse Events in Medical Device Clinical Investigations.

6.4 Complaints and non-conformances (Deviations and Breaches)

6.4.1 Process

It is UoA-NHSG practice to ensure that all complaints and non-conformances identified within UoA or NHSG are investigated and resolved in a timely and effective manner, and that necessary Correction and Corrective Action and/or Preventive Action (CAPA) is identified to prevent recurrence. See SOP-QA-25 – Deviations and Breaches and SOP-QA-43 – Suspected Serious Breaches.

6.4.2 Non-conformances shall be recorded for a study and listed in the clinical study report or publication, if relevant. The Sponsor shall grade non-conformances as ‘serious’ or ‘non-serious’ and assess whether

non-conformances shall be reported to the MHRA as a serious breach of GCP or the protocol. Serious non-conformances identified through audit or monitoring shall be reported to the Clinical Studies Oversight Group (CSOG) and if necessary to the appropriate line management.

6.4.3 Urgent Safety Measures these are initiated in order to protect the subjects of a trial against any immediate hazard to their health or safety. Sponsor, MHRA and REC must be informed within seven days (although an initial telephone call is expected within 24 hours). See SOP-QA-25 – Deviations and Breaches and SOP-QA-43 – Suspected Serious Breaches.

6.5 Improvement

6.5.1 Practice

It is UoA-NHSG practice to ensure continual improvement of the effectiveness of the Quality Management System through the use of the quality framework, objectives, audit/monitoring results, analysis of data, Corrections and Corrective Actions and Preventive Actions (CAPA).

6.5.2 Audit and Monitoring

Studies, groups and facilities may be subject to audit and inspection by external parties, which may include regulatory authorities (eg MHRA). All UoA-NHSG staff are required to **fully co-operate** in such activities, under the direction of the Sponsor and QA Manager. Audit and inspection findings shall be dealt with by the appropriate staff and committees to provide a resolution within previously agreed timescales. It is the responsibility of researchers and team leaders to ensure Corrections and any Corrective Action and/or Preventive Actions (CAPA) are implemented; failure to do so shall be referred to senior management for appropriate action (see SOP-QA-28 – Monitoring, SOP-QA-29 – Audit and SOP-QA-30 - MHRA inspections).

6.5.2.1 Auditing – a QA activity, conducted independent of the trials team, examining trial related activities in accordance with the protocol, QMS, principles of GCP and regulatory requirements.

Audits shall only be conducted by competent and trained auditors. All audits shall be reported to CI or PI and Sponsor, and CAPA shall be progressed, using Ideagen Quality Management (see SOP-QA-29 - Audit).

6.5.2.2 Monitoring – overseeing the progress of a clinical trial and ensuring it is conducted, recorded and reported in accordance with the protocol, QMS, principles of GCP and regulatory requirements. Monitoring may be conducted by the trial team by someone trained in the trial, who can perform a QC check of the activities at the investigator site(s), or it may be performed by dedicated Trial Monitors. All monitoring shall be reported, and Corrections and any CAPA progressed, using Ideagen Quality Management (see SOP-QA-28 - Monitoring).

6.5.2.3 Audit/monitoring schedules shall be scheduled and prepared for each trial, ratified by R&D Director (for audit schedule), and be based on risk; with increased audit/monitoring activity for those projects judged by the QA team and/or Research Governance team to be at increased risk to the Sponsor. Additional audit or monitoring visits may also occur in response to Urgent Safety Measures or Breaches and may be unannounced. If required Ideagen Quality Management may be used to schedule study reports (reports to REC, DSUR reports etc) or maintenance/calibration checks on equipment.

6.5.3 Correction, Corrective Action and Preventive Action (CAPA or CCAPA)

Correction is any action to eliminate a non-conformance. Corrections shall also be implemented if deviations from the policies and procedures in the Quality Management System or technical operations are identified. Corrective Actions are steps which are taken to remove the causes of an existing non-conformance. All CAPA shall be processed using Ideagen Quality Management.

6.5.4 Corrective Action

Corrective action is any action which is taken to eliminate the cause of a non-conformance and therefore prevent a recurrence.

6.5.5 Preventive Action

Preventive actions is any action which is taken to eliminate the cause of a potential non-conformance, in order to prevent their occurrence. Preventive actions may be noted as 'Observations' or 'Opportunities for Improvement' during audit or monitoring.

6.5.6 Continuous Improvement

It is UoA-NHSG policy to ensure that opportunities for improvement and potential sources of non-conformances, either technical or concerning the Quality Management System, are identified where required. 'Stakeholder' feedback shall be regularly sought to identify any opportunities for improvement. Within UoA-NHSG this shall be managed by the Quality Assurance Manager and reviewed at Management Review Meetings (see 6.8).

6.6 Control of Records

Procedures for control of records is included in SOP-QA-1 – Management of SOPs. The Quality Assurance Manager has ultimate responsibility for all documents which form the Quality Management System.

Records held electronically shall be suitably controlled, secure and backed-up, with procedures appropriately documented. Software systems purchased 'off the shelf' may be considered suitably validated but any modified or bespoke software systems shall require validation before use. Any formulae or calculations used in data handling require regular checks to ensure they are still fit for purpose; such checks shall be recorded.

The Quality Manual, SOPs and User Guides shall be held, and controlled, using Ideagen Quality Management.

6.7 Contracts

Any contracts or Service Level Agreements (SLAs) prepared for CTIMPs or MDCIs shall refer to the Principles of GCP and SI 2025/538, as amended, if appropriate. Agreements with third party laboratories receiving samples for analysis from CTIMPs/MDCIs shall document all relevant facts concerning the procedure, including who receives results and data, to avoid accidental unblinding. Documentation detailing the same information for laboratories within the same institution (eg NHSG laboratories) may also be implemented where appropriate. The Sponsor shall maintain oversight and regular communication with third parties. The UoA R&I team assist the Sponsor in contractual matters.

Any potential third party laboratory service providers or IMP suppliers for a CTIMP or MDCI must be assessed by the Quality Assurance Manager for suitability prior to contracts being put in place. Only third parties which can demonstrate competence (eg certification or accreditation to a suitable quality standard) should be used. A list of pre-approved third parties is maintained in Ideagen Quality Management by QA as a 'preferred provider' list by the Sponsor.

A 'letter of intent' may take the place of a formal contract prior to a formal contract being agreed but the trial must not commence until the formal contract is in place.

6.8 Management Reviews

This is a periodic (at least annual) review of the Quality Management System by senior R&D Management, for its effectiveness, any opportunities for improvement and its fitness for purpose. It includes a review of findings since the last Management Review and identifies any concerns. See SOP-QA-37 – Management review.

6.8.1 Practice

It is UoA-NHSG policy to ensure the continuing suitability and effectiveness of the Quality Management System and research activities with regard to the Principles of GCP, The Medicines for Human Use (Clinical

Trials) (Amendment) Regulations 2025 (SI 2025 No. 538) as amended and Sponsor requirements, by performing a Management Review.

6.8.2 General

Management Reviews shall be held at least once per year. The objective of the review process is to continually develop and improve the performance of the Quality Management System and to identify and progress any relevant preventive action and opportunities for improvement.

The following agenda items may be discussed and reviewed:

- Feedback from researchers, CIs, PIs and any other stakeholders on the functioning of the QMS.
- Review of findings from any regulatory inspections.
- Review of non-conformances and observations raised during internal audits.
- Review of non-conformances and observations raised during monitoring.
- Systematic findings and trends noted in audit and monitoring.
- Effectiveness of CAPA.
- Possible areas of improvement and future development of the QMS.
- Review of Quality Manual for effectiveness.
- Review of Quality Statement for effectiveness.
- Staff training.
- Resource issues concerning the QMS.
- Review of feedback and satisfaction surveys.
- Planned assessment and regulatory inspections.

6.9 Human Resources

All staff involved in CTIMPs and MDCIs must be trained in GCP to comply with the requirements of SI 2025/538. It is recommended that all other researchers also attend GCP/GRP training. This training may be provided in-house (GRO Training Facilitators) or on-line, and must be updated as agreed locally. UoA-NHSG have agreed that GCP training for local researchers shall be **updated every three years**. All staff involved in a clinical trial must have documented training for equipment and procedures which form part of the trial (see SOP-QA-2 - Training record and SOP-QA-34 – Good Clinical Practice/Good Research Practice training).

6.10 Control of Customer Property

Customer property may be material or data supplied for analysis or intellectual property. UoA-NHSG shall ensure that any property supplied by the customer shall be stored and handled ethically in such a manner as to protect its integrity, security and confidentiality.

6.11 Process Control

UoA-NHSG shall ensure that all processes, which make up the service, are controlled by documented procedures. On-going personnel training shall be conducted and recorded to maintain and demonstrate the required standards.

6.12 Inspection and Testing

All CTIMPs and MDCIs in Grampian which are sponsored or co-sponsored by UoA and/or NHSG shall be subject to monitoring and audit. In addition, a percentage of hosted trials on the NHSG site shall also be monitored (see SOP-QA-28 – Monitoring and SOP-QA-29 - Audit). Sponsor may also request additional audit or monitoring of any study on a risk basis.

Study reports shall be reviewed on completion and before publication (see SOP-QA-31 - Research project closure and SOP-QA-33 - Research project publication and dissemination).

6.13 Equipment

All critical equipment must be functioning correctly, be fit for purpose and be capable of achieving the accuracy required. Only trained personnel shall use laboratory/medical equipment, and procedures must be in place to document the use, service and planned maintenance of all critical equipment. All critical equipment shall be maintained and serviced according to manufacturers' instructions. See SOP-QA-38 – Equipment and Facilities.

Each item of critical equipment shall be identified uniquely and intermediate checks shall be recorded appropriately to demonstrate confidence in the continued use of the equipment.

The frequency of intermediate checks must be justified based on national guidelines and/or regulations.

Any equipment that is used for a specific purpose/trial must be identified as such.

Any equipment that is out of use must be identified as such to preclude its use.

6.14 Facilities

All facilities must be fit for purpose with appropriate procedures in place to protect the integrity of samples, prevent cross-contamination between samples and prevent risk to staff or visitors. Procedures shall be in place to ensure security, safety, hygiene and biosecurity.

Appropriate measures shall be in place for Containment Level 2 and Containment Level 3 laboratories and facilities (there are currently no Containment Level 4 facilities in the UoA-NHSG site).

Any clinical research involving Genetically Modified Micro-organisms (GMM) shall only take place in premises for which the appropriate Health and Safety Executive (HSE) notification is in place. Involvement of the Biological Safety Officer of either UoA or NHSG and local approval from the Foresterhill Genetic Modification Safety Committee must also have been obtained. **Note**: different premises notifications exist with the HSE for University of Aberdeen and for NHS Grampian.

6.15 Health and Safety

Laboratories can be one of the most hazardous places in which to work and appropriate health and safety policies and procedures are available from the UoA Health and Safety team or NHSG Corporate Health and Safety department. Staff shall ensure appropriate risk assessments have been prepared and that COSHH data is available for any chemicals and reagents used.

6.16 Archiving

All data pertaining to CTIMPs and MDCIs shall be archived securely and confidentially for a period of **twenty-five years**, or for an alternate period providing this is documented and is consistent with both the terms of ethical approval and the funder's terms of award. This can be either on-site, in a suitable facility, or subcontracted to a suitable archiving contractor (see below):

Studies sponsored by University of Aberdeen shall be archived in the secure archive within the University of Aberdeen, Health Sciences Building, Foresterhill.

All studies sponsored by NHS Grampian shall be archived off-site by Oasis Information Secured.

Studies co-sponsored by University of Aberdeen and NHS Grampian shall be archived within the University of Aberdeen, Health Sciences Building, Foresterhill.

Unless specified by the Sponsor, commercial and hosted studies shall be archived off-site by Oasis Information Secured.

It is a legal requirement that a Sponsor appoints a Named Archivist who shall have oversight and control of all archiving functions (See SOP-QA-32 - Archiving).

Any samples to be archived for possible future use in research must have appropriate informed consent in place and shall be stored between - 80 C and -70C (±10 C), either in the approved NHSG Biorepository, under the management of the Biorepository Manager, or in an appropriately controlled ULT freeze or temperature/environment, agreed with Sponsor

Electronic data shall be locked and stored securely for twenty-five years in an approved location (e-archive) under the management of the appropriate IT department (see SOP-QA-20 – Data management for clinical trials). E-data shall not be stored on any intermediate storage medium unless agreed with Sponsor.