Research and Innovation Quality Manual

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Research and Innovation Quality Manual

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Introduction

NHS Greater Glasgow and Clyde is the largest health board and provider of healthcare in Scotland and one of the largest health care providers in the UK. Serving a population of 1.3 million (over 1/5 of the population of Scotland) with services provided by 43,500 staff. The geographical area covered includes: Glasgow City, West Dunbartonshire, Inverclyde, Renfrewshire, East Renfrewshire, East Dunbartonshire and North Glasgow (Stepps-Moodiesburn corridor).

The Research and Innovation Service in NHS Greater Glasgow and Clyde operates to support researchers in the NHS and academia, provides patients with access to novel care and has aims of improving healthcare. It has multiple roles including offering consultancy and advice, providing Management Approval and aiding in the achievement of a successful conclusion to research projects. Our goal is to release the potential to world class clinical studies across the region, and to play our part in enabling Scotland to grow as an internationally competitive location for medical research.

In 2021, Research and Innovation received in excess of **620** new research applications and have approximately **1000** studies ongoing at any one time.

1. Context of the Organisation

Research and Innovation comes under the Corporate Directorate of NHS Greater Glasgow and Clyde and is made up of a number of sub departments and teams which is represented in Figure 1 below.

This includes:

- Research Governance
  - Quality
  - Monitoring
  - Pharmacovigilance
- Pharmacy – Sponsor and site
- Systems – Sponsor, approvals and informatics
- Glasgow CRF
  - Clinical site teams
  - Education & Quality
  - Project Management Unit
- Research Imaging
- Innovation, (acting as Sponsor for Innovation trials)
- Bio-Repository
- Safe Haven

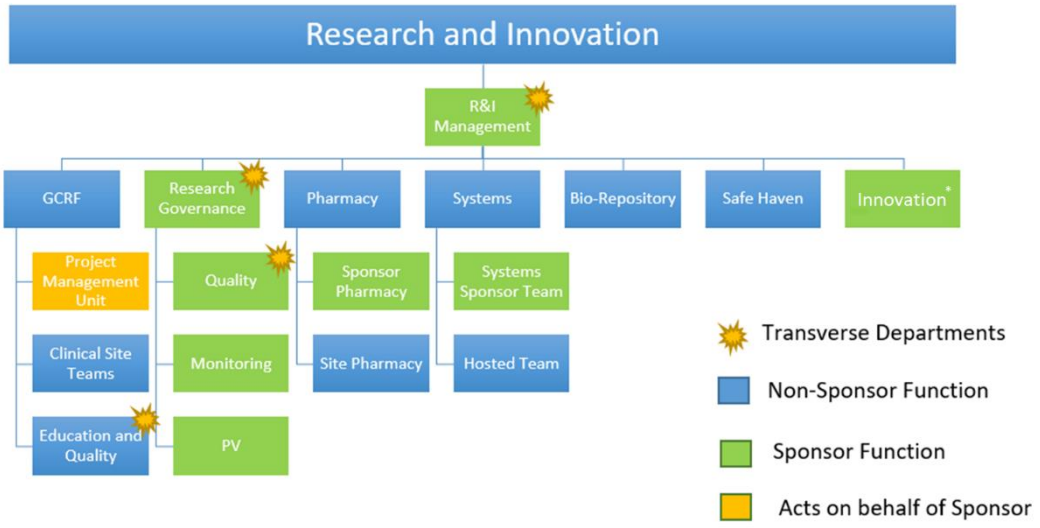

Figure 1 – Research and Innovation

As can be seen in Figure 1, Research and Innovation is made up of a number of discrete departments and several transverse departments which by their nature operate across the other functions.

R&I Management, Governance, Quality Assurance, Education and Training are all transverse departments as the nature of the activities they conduct are applicable and impact on all other departments. Research Governance and Quality Assurance have applicability and oversight across all functions, however some areas have delegated and assumed responsibilities to carry out these functions independently with clear reporting processes to ensure Research Governance and Quality Assurance maintain oversight. Details of these instances applicable to the relevant departments are:

- The Glasgow CRF and all teams and functions within come under the oversight of the GCRF QA Lead who has responsibility and oversight for Internal Audit, Management of SOPs and will maintain their own Quality Manual, QM-GCRF-1.
- Innovation will maintain their own Quality Manual, QM-IN-1.
- The Bio-Repository comes under the oversight of the Bio-Repository Manager and their own Governance Manager who will conduct their own Internal Audit schedule, manage SOPs and maintain their own Quality Manual, QM-BIO-1.
- The Safe Haven comes under the oversight of the Safe Haven Manager who will conduct their own Internal Audit schedule and maintain their own Quality Manual, QM-SH-1.

Although the above mentioned functions have responsibility to conduct the activities described, the accountability for these activities remain with Governance and Quality Assurance. To this end, oversight is maintained through the committees mentioned within section 5.1 to ensure audit schedules and activity are appropriate, SOPs are robust with sufficient coverage and that Quality Manuals are compliant with this Quality Manual and contain sufficient detail.

1.1. Mission

The mission for Research and Innovation is to fully embed a culture within NHSGGC to maximise the opportunities and support for researchers in order to increase the level of high quality, world leading clinical research and innovation for the health and economic benefits of our population. By playing a key role in delivering safe, effective and person-centred quality care within NHSGGC, nationally and globally.

Quality is a core service value in Healthcare provision for Participants in research

This will be achieved by:

- Put the needs and safety of participants at the forefront of all we do.
- Provide all the appropriate resources for staff to maximise what they can produce while nurturing a safe and healthy working environment.
- Providing a robust Quality Management System, covering all required processes, built around staff to produce high quality results which allow for activities be reconstructed and evidenced at a later date.
- Ensure staff have an appropriate level of training and experience to enable them to succeed and meet the needs of the organisation.
- Offer a high quality service to the investigators involved in research through the Organisation.

1.2. Applicable Regulations and standards

Across Research and Innovation there are a number of regulations and standards which apply and must be adhered to or in some cases aspired towards. The following list is not exhaustive but indicative of some of the major regulations and standards of impact within Research and Innovation.

- The Medicines for Human Use (Clinical Trials) Regulations 2004, as amended (MHU)
    - Directive 2001/20/EC as specified within MHU
    - Directive 2001/83/EC as specified within MHU
    - Commission Directive 2003/94/EC as specified within MHU
- UK policy framework for health and social care research 2017 as amended
- ISO 20387:2018 (General requirements for biobanking)
- Data Protection Act 2018
- Human Tissue Act 2004
- The Medical Devices Regulations 2002
- The Genetically Modified Organisms (Contained Use) Regulations 2014
- Genetically Modified Organisms (Deliberate Release) Regulations 2002

Other standards and examples of good practice are used to influence processes and practices within Research and Innovation but are not mandatory for compliance, some examples of these are:

- ISO 9001:2018
- ICH GCP Guideline (CPMP/ICH/135/95)

1.3. Sponsor

NHS Greater Glasgow and Clyde act as a Sponsor organisation where agreed for Glasgow-led clinical research. Certain Research and Innovation personnel represent NHS Greater Glasgow and Clyde as the Sponsor.

The staff groups which represent this function are:

- R&I Director
- R&I Senior Manager
- Innovation Manager
- R&I Systems & Operations Manager
    - Sponsor Research Co-Ordinator
- Research Governance Manager
    - Monitoring Team
    - Quality Team
    - PV Team
- Lead Clinical Trials Pharmacist
    - Sponsor Pharmacy Team
- Innovation Lead
    - Innovation Contract Manager

Each group that makes up the representation of Sponsor has set responsibilities of delegated actions, this level of information is contained within the relevant SOPs and must be complied with. There are some functions delegated to teams on behalf of the sponsor such as the PMU, the Biorepository where a central repository, Research Imaging where a central imaging lab.

1.4. Glasgow Clinical Trials Unit (GCTU)

Components of Research and Innovation together with the University of Glasgow, the Robertson Centre for Bio-Statistics and Population Health Research Facility form the Glasgow Clinical Trials Unit as detailed in SOP 01.001. Not all departments within Research and Innovation form part of the GCTU, instead representation includes Senior R&I Management, Research Governance, Sponsor Pharmacy, Systems and the Project Management Unit. The remit of the GCTU is to provide operational oversight and guidance for trials that are adopted by GCTU (SOP 01.002).

1.5. Cancer Research UK CTU (CRUK CTU)

Where CRUK CTU is responsible for oncology/haemato-oncology clinical trials, the Quality Management system of the CRUK CTU is followed by their staff for the activities delegated to them as denoted in the operational level agreements in place. Where these studies are sponsored/co-sponsored by NHSGGC relevant Sponsor SOPs apply and are cross referenced where appropriate, i.e. Risk Assessment, reporting Non-Compliances, Trial Master File structure, etc. The oversight of Governance within these trials remains the responsibility of Research Governance within Research and Innovation and this is achieved through a number of oversight groups as detailed in section 4.1.

1.5.1. Beatson CRF

The Beatson Clinical Research Facility (BCRF) hosts oncology and haemato-oncology trials. The BCRF Quality Management System sits outside the R&I QMS.

The BCRF maintains their own QMS which outlines the procedures they follow to manage trial activity.

1.6. Host sites

A large proportion of hosted activity will be supported by research teams in the Glasgow CRF or the BCRF, however, there are research teams outside these structures. All Research and Innovation in the Healthboard requires R&I management approval.

1.7. Chief Investigators

As the Chief Investigators lead on studies are provided with guidance on the relevant sections of the QMS. There are a number of SOPs that investigators must be aware and appropriately knowledgeable of as well as compliant to. These key SOPs have the Chief Investigators listed within their RACI matrix and they will be required to read and provide evidence they comprehend its contents. As such, investigators have the ability to feed into the development of SOPs by providing feedback to the relevant authors of the content.

2. Quality Management System

2.1. Scope

The Quality Management System for Research and Innovation is applicable to all those involved with trials and studies Sole or Co-Sponsored as well as Hosted by NHS Greater Glasgow and Clyde. As Research and Innovation form part of the GCTU, the Research and Innovation Quality Management System forms part of the overall QMS of the GCTU, together with the QMS of the University of Glasgow and the Robertson Centre for Bio-Statistics. Each area will manage their own QMS and work in compliance to its contents, there will be some areas of interaction between processes which is detailed within each of the relevant SOPs.

Glasgow CTU has a shared structure for its SOPs, Forms and Guidelines. They are divided in to different Chapters to cover specific content, each of which falls into the ownership of the individual QMS's as detailed in Figure 2.

RCB QMS	R&I QMS	PHRF QMS
Chapter 1		Chapter 90
Chapter 2	Chapter 17	Chapter 91
Chapter 3	Chapter 21	Chapter 92
Chapter 4	Chapter 22	
Chapter 5	Chapter 23	
Chapter 6	Chapter 50	
Chapter 7	Chapter 51	
Chapter 8	Chapter 52	
Chapter 9	Chapter 53	
Chapter 10	Chapter 54	
Chapter 11	Chapter 55	
Chapter 13	Chapter 56	
Chapter 14	Chapter 57	
Chapter 15	Chapter 58	
Chapter 18	Chapter 59	
Chapter 19	Chapter 60	
Chapter 24	Chapter 61	
Chapter 25		
Chapter 26		

Figure 2 – Chapters per QMS

2.2. Quality Manual

The Quality Manual for Research and Innovation describes the Quality Management System in use within Research and Innovation. It is used to provide an overview of the structure of the Quality Management System and its major components, how the system it is managed and developed, how it interacts in relation to other organisations and how the departments within Research and Innovation are organised.

The Research and Innovation Quality Manual acts as the overarching Quality Manual for the Research and Innovation QMS and interacts with the Quality Manuals for the departments within as detailed below in Figure 3. All other Quality Manuals are not standalone and must be considered alongside the R&I Quality Manual, QM-RI-1. In turn, the overarching R&I Quality Manual is informed by the contents of the sub Quality Manuals.

QM-RI-1		Research and Innovation Quality Manual
	QM-GCRF-1	Glasgow Clinical Research Facility Quality Manual
	QM-IN-1	Innovation Quality Manual
	QM-BIO-1	Bio-Repository Quality Manual
	QM-SH-1	Safe Haven Quality Manual

Figure 3 – Quality Manual Structure

The Quality Manuals for each department within will highlight and explain the specific requirements for the processes, procedures, standards and regulations of interest to their specific area of work. All of the processes detailed for each area will operate in compliance to any top level Research and Innovation process or procedure that may exist.

2.3. Policies and Procedures

2.3.1. Board Policy

Research and Innovation exists within the NHS Greater Glasgow and Clyde Health Board, as such there are a number of NHS Scotland and NHSGGC policies which are applicable to Research and Innovation and can be found with the links below:

NHS Scotland Policies

NHS Greater Glasgow and Clyde Policies

Where Research and Innovation author policies, they must be created and controlled through the board level process for the creation of policies. Research and Innovation specific policy documents created at the board level may be stored in Q-Pulse and identified as a policy document with the prefix of "POL-" followed by an identifier for their level of scope, i.e.

- POL-RI – Research and Innovation wide policy
    - POL-GCRF – Glasgow Clinical Research Facility Policy
    - POL-IN – Innovation Policy
    - POL-SH – Safe Haven Policy
    - POL-BIO – Bio-Repository Policy

This process may be utilised when it is a requirement to ensure staff are trained in the content of a policy.

2.3.2. Procedure

Procedures within Research and Innovation fall within the Chapters outlined in section 3.1, for each chapter the documents within will contain that chapter number within their ID and contain a prefix to donate the document type, i.e. SOP 50.xxx identifies the document as a Standard Operating Procedure within chapter 50. The 3 x's following this highlight a sequential number that is used to identify documents within this chapter, beginning at 001 and ending with 999. As well as the prefix of SOP, there are:

- FORM – Forms associated to an SOP, they will have the same number of the associated SOP and then an additional suffix of A, B, C, etc. For Example Form 50.011A would be associated to SOP 50.011.
- GUI – Guidelines associated to an SOP, as with Forms will have the same ID number as the SOP they are associated to and then a sequential letter suffix to separate.
- WI – Work instructions associated to an SOP, again will share the same ID number as the SOP they are associated to and a sequential letter suffix.

Research and Innovation Quality Manual

Each Chapter within the R&I QMS has its own intended content to help with the identification of the appropriate procedure, the titles of the chapters within the QMS are:

Chapter 17 - NHS GG&C Clinical Research Facility - Clinical

Chapter 21 - NHS GG&C Pharmacy - Sponsor IMP Management

Chapter 22 - NHS GG&C Pharmacy - Hosted CTIMP

Chapter 23 - NHS GG&C Pharmacy - Hosted Non-CTIMPs

Chapter 50 - NHS GG&C General

Chapter 51 - NHS GG&C Sponsor R&I

Chapter 52 - NHS GG&C Hosted R&I

Chapter 53 - NHS GG&C Sponsor Governance

Chapter 54 - NHS GG&C Hosted Governance

Chapter 55 - NHS GG&C Pharmacovigilance

Chapter 56 - NHS GG&C Sponsor Project Management Unit

Chapter 57 - NHS GG&C Clinical Research Facility - Administration

Chapter 58 - NHS GG&C Clinical Research Imaging Facility

Chapter 59 - West of Scotland Safe Haven

Chapter 61 - West of Scotland Innovation

The staff impacted by the content of each SOP is documented within a RACI matrix within the SOP and is distributed to the relevant staff for them to read and comprehend.

The process for the production, management and distribution of SOPs within Research and Innovation is detailed with SOP 50.023 and is applicable to all departments within R&I. If a department within Research and Innovation requires additional detail related to the production or management of SOPs the content must operate in addition to that outlined in SOP 50.023.

2.3.3. Interaction between Legislation, Standards, Policy and Procedures

There is a hierarchy and association built in to Legislation, Standards, Policy and Procedures, this is represented with Figure 4 below.

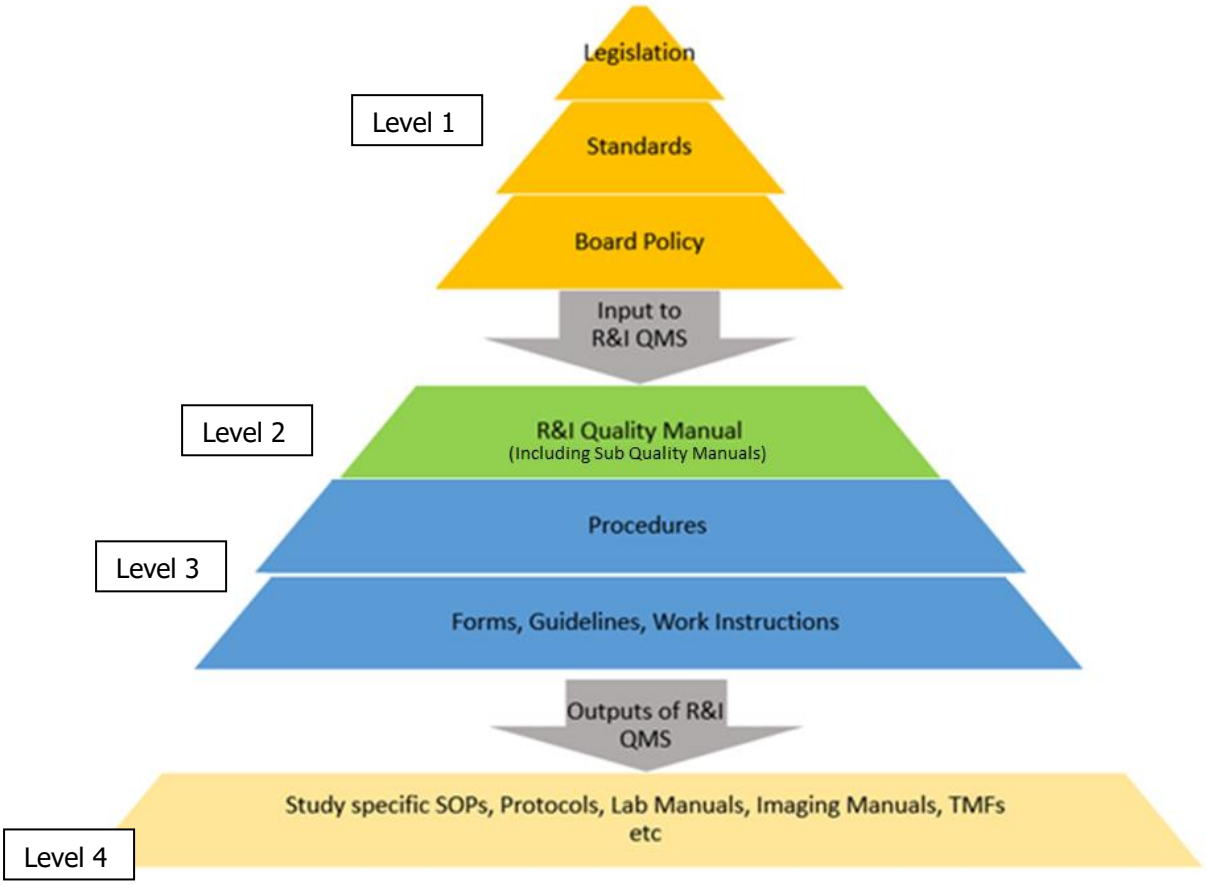

Figure 4 – Interaction and Hierachy

Level 1

- The requirements of Legislation and Regulations such as those detailed in Section 2.2 are a matter of law, they spell out what must be done or not done. It is essential and mandatory to comply with legislation.
- Standards are internationally agreed and recognised principles and practices of good conduct, they are an accepted benchmark of how best to operate and accrediation and compliance to these standards are a method of assurance to stakeholders of the robust nature of an organisations practices. Standards are not binding, it is not essential to comply with a standard unless it forms the basis of an agreement for an organisation to do business with R&I or to achieve and maintain accreditation to this standard.
- Board Policy documents are the statements of intent, they set the direction and end goals or achievements the organisation wishes to meet. They are informed by legislation and by applicable standards and are used to set direction.

Level 2

- The Research and Innovation Quality Manual, along with the Quality Manuals for any departments, are informed by all found in Level 1. The Quality Manual exists to set the scope and aims of the Quality Management System as detailed in section 3.2.

Level 3

- Procedures are the documented process by which policies are achieved, they contain the specific instructions and information which are required to complete the necessary activities. Good process should contain a sufficient level of information to explain all the necessary steps to complete an activity and demonstrate how legislation, standards and policies will be met.
- Forms, Guidelines and Work Instructions are the next step below procedures. They contain infromation relating to the end output of procedures or how to achieve the steps within a procedure. They are the documents that are used and referenced when the actual activity is taking place.

Level 4

- The output of the QMS takes the form of any controlled document that is produced as a result of following the procedures layed out within the Quality Management System. Examples of this output can be: Trial/Study Protocols, Risk Assessments, Lab Manuals, Imaging Manual, TMFs, study specific SOPs etc. The documents themselves do not form part of the QMS but are the result of following the contents of the QMS, as such they will fall under regular review to ensure compliance.

2.3.4. Change Requests

As the Quality Management System holds all of the relevant records for Procedures and Policies owned and developed by Research and Innovation, all members of staff within Research and Innovation have the ability to raise a Change Request against any document to provide user feedback to the relevant Author. This allows for all members of staff within Research and Innovation to feed into the Quality Management System and its contents.

3. Q-Pulse – Quality Management System Software

The Quality Management System within Research and Innovation is managed through the use of the application Q-Pulse.

Q-Pulse provides a database and user interface which allows for a number of aspects key to a successful Quality Management System. These features are divided into distinct modules with points of interaction across these modules. The functionality used within Q-Pulse for the relevant functions of the QMS are discussed within this Quality Manual as well as the relevant SOPs.

The modules available within Q-Pulse as used within Research and Innovation are:

3.1. Documents Module

The document module is central to the QMS and is the repository for all SOPs, Forms, Guidelines and Work Instructions. It also provides a controlled environment for the management of other controlled document types, such as Terms of References for committees, policy documents and agreements.

The functionality within Q-Pulse aids in the management of review, updates and dissemination of documents to the relevant staff groups. This allows for the complete history of a document to be retained and an audit trail of all relevant changes and updates to the controlled documents.

The interactions with this system for the control of the specific document types is detailed in the relevant SOPs, for example SOP 50.023 for the management and control of SOPs.

3.1.1. Electronic signature

Q-Pulse provides the functionality to enable electronic sign off of documents, this is conducted in a controlled manner which is linked to an individual account and restricts completion of the activities on this basis.

3.2. Audit and Monitoring Module

The Audit and Monitoring module within Q-Pulse is used to record all activity associated with individual audit and monitoring events. This provides an environment to record planned activity, identify scope areas to link record back to sites, trials, process areas and individuals involved. It also acts as a repository for relevant information and evidence of the activity. This activity can then be managed through the use of Q-Pulse and generated reports to update on activity and compare actual events against planned events to determine progress and compliance. The module has the capacity to create and attribute pre-defined checklists to an audit or monitoring visit to allow for specific questions and the responses to be captured.

This module interacts with the CAPA module to allow for findings to be raised and attributed to individual monitoring or audit events.

3.3. CAPA Module

The CAPA module allows for the creation of individual records of a variety of non-compliances ranging from monitoring and audit findings to Serious Breaches. The functionality within Q-Pulse allows for a bespoke workflow to be created to capture the appropriate stages in managing these non-compliances to satisfactory closure. The process for each is detailed within the relevant SOPs, i.e. SOP 51.008 for non-compliances, SOP 53.005 for Audit findings and SOP 53.004 for monitoring findings.

The individual CAPA records can be linked to relevant scope items such as trials, sites, process as well as associated to relevant owners of actions and monitoring or audit records. This allows for generation of reports and analysis of trends.

3.4. Sites

A record of all relevant trial sites is held within Q-Pulse which in turn links to associated activity such as monitoring visits and audits. The records will also have associated personnel for this site and allows for the generation of an overview of known activity for this site. This will also link to the CAPA module and provides oversight of known findings, non-compliances and serious breaches that may have been previously recorded for each site.

This module is also used to record details of vendors utilised within trials and their approval status as determined by the vendor assessment process, detail in section 7.6 and SOP 51.015.

3.5. People

All users within Q-Pulse have an individual record associated with their log in, this allows for traceability of actions they have performed and actions assigned to them for completion. This enables a record of SOPs that have been distributed to an individual user and evidence of when they have confirmed they have read and comprehended its contents.

In addition to this, it enables actions from audits, monitoring visits, non-compliances and a variety of other activities to be assigned to an individual and provide oversight of ongoing activity.

4. Quality Policy

In order to meet the needs of those involved in Research within Research and Innovation, the Organisation will:

- Implement and Maintain a Quality Management System which staff must adhere to.
- Ensure staff are familiar with the Quality Policy, Quality Manual and Quality Management system as relevant to their role.
- Establish a Quality Culture where all staff are empowered to take ownership of their role and responsibility for the Quality of their work.
- Ensure that all practices are conducted in line with those set out in the Quality Management System.
- Ensure that staff at all times act in compliance to all required legislation and standards.
- Ensure appropriate resources are in place to provide the services of the organisation.

5. Management Responsibility

In order to ensure the operation of the Quality Management System, a number of key management roles are in place with specific roles and responsibilities. These roles are identified within the Organogram below in Figure 5. It is the responsibility of Management within Research and Innovation to ensure the appropriateness of the areas relevant to their role within the Quality Management System within Research and Innovation. To this end, every SOP must be signed off by the appropriate Senior Manager for the process area and approved by the Director of R&I.

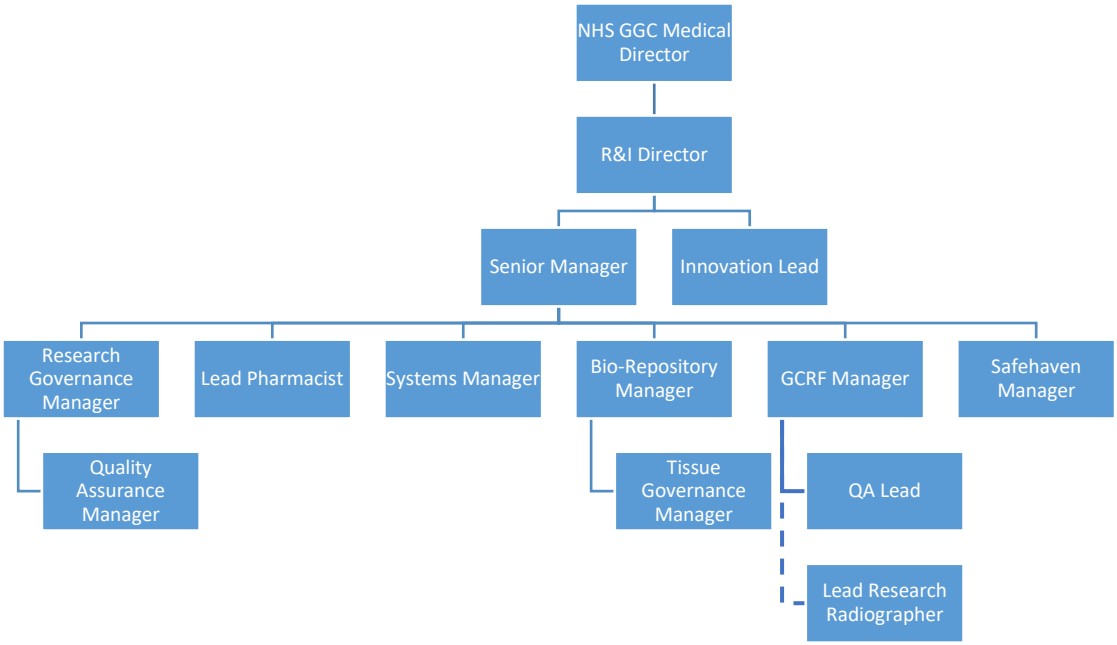

Figure 5 – Research and Innovation QMS Management

5.1. Management Review

A number of key groups are formed to provide oversight of the QMS with representation from the management team. At these committees and groups, key information relating to the outcome of audits, Non-Compliances, external inspections, management of SOPs and complaints are raised and discussed to determine the requirement for further action to be taken to make improvements to the Quality Management System. Each group will have its own terms of reference (SOP 50.022), minutes of meetings and a record of actions to be taken.

- Glasgow Health Science Partnership Regulatory Affairs Group (GHSP RAG)
- Glasgow Health Science Partnership Delivery Group (GHSP DG)
- Glasgow Clinical Trials Unit Management Committee
- R&I Senior Management Committee

A number of individual committees are formed to review and manage the content of activities and elements of the QMS, for each committee and appropriate level of management representation is present which in turn feeds into the above mentioned committees. Each committee will have a Terms of Reference which is stored in Q-Pulse and produced in compliance to SOP 50.022.

Examples include:

- Quality Oversight Committee
- R&I SOP Committee
- GCP Compliance (Hosted Activity)
- Sponsor Systems Meetings
- Sponsored CTIMP Oversight
- Sponsor Pharmacovigilance Group (with representation from CRUK)
- Joint Monitoring Group (with representation from CRUK)
- CRUK - Sponsored CTIMP Oversight

The output of all of this activity is compiled in an Annual report which is presented to the Board to report on activity.

As Research and Innovation sits within the Corporate Directorate of NHS Greater Glasgow and Clyde, Research & Innovation also report into Corporate Senior Management and the Board Clinical Governance Group.

Details of the Board and ongoing meetings can be found on the Greater Glasgow and Clyde website:

NHSGGC Board - NHSGGC

5.2. Resources

Management are responsible for the provision of adequate resources to achieve the aims of the organisation and requirements of the Quality Management System. The resources which must be provided and maintained by Senior Management fall under the following categories and are reviewed through the above mentioned committees:

5.2.1. Infrastructure and Environment

Research and Innovation provide facilities for the conduct of activities required by the QMS, this includes but is not limited to:

Buildings and the associated utilities (heat, light, electricity, internet access, etc.)

Equipment, i.e. hardware and software

Information and Communication Technology

All infrastructure will routinely be assessed and ensured to be adequate for the required purpose with the consideration of the appropriate human factors.

5.2.2. People

Research and Innovation employee a diverse range of staff in the appropriate numbers with the sufficient training and experience to implement the requirements of the Quality Management System.

6. Quality Assurance

Quality Assurance is the act of designing systems with the aim to assure the end result meets requirements, this differs from Quality Control in that it does not involve checking of the outcomes to ensure compliance. Quality Assurance and Quality Control are both essential elements of a robust Quality Management system, Quality Assurance is aimed at the preventative action before the work has even begun to ensure the QC checks find as few issues as possible.

These is achieved in a number of ways within the Research and Innovation Quality Management System.

6.1. Continuous Improvement

The Quality Management System within Research and Innovation operates under the principle of Continuous Improvement.

Continuous Improvement as the name implies, is an endless cycle of improving and adapting the Quality Management System to the changing environment. The Plan Do Check Act (PDCA) cycle is used within Research and Innovation and take input from factors such as the relevant legislation, findings from Audits and Monitoring Visits, user feedback and Non-Compliances to make plans and adapt the Quality Management System accordingly to produce an improved outcome.

As shown in Figure 6, at the heart of this is the Senior Management Team and Leadership within Research and Innovation to direct this cycle and feed in to the process to improve the Quality Management System.

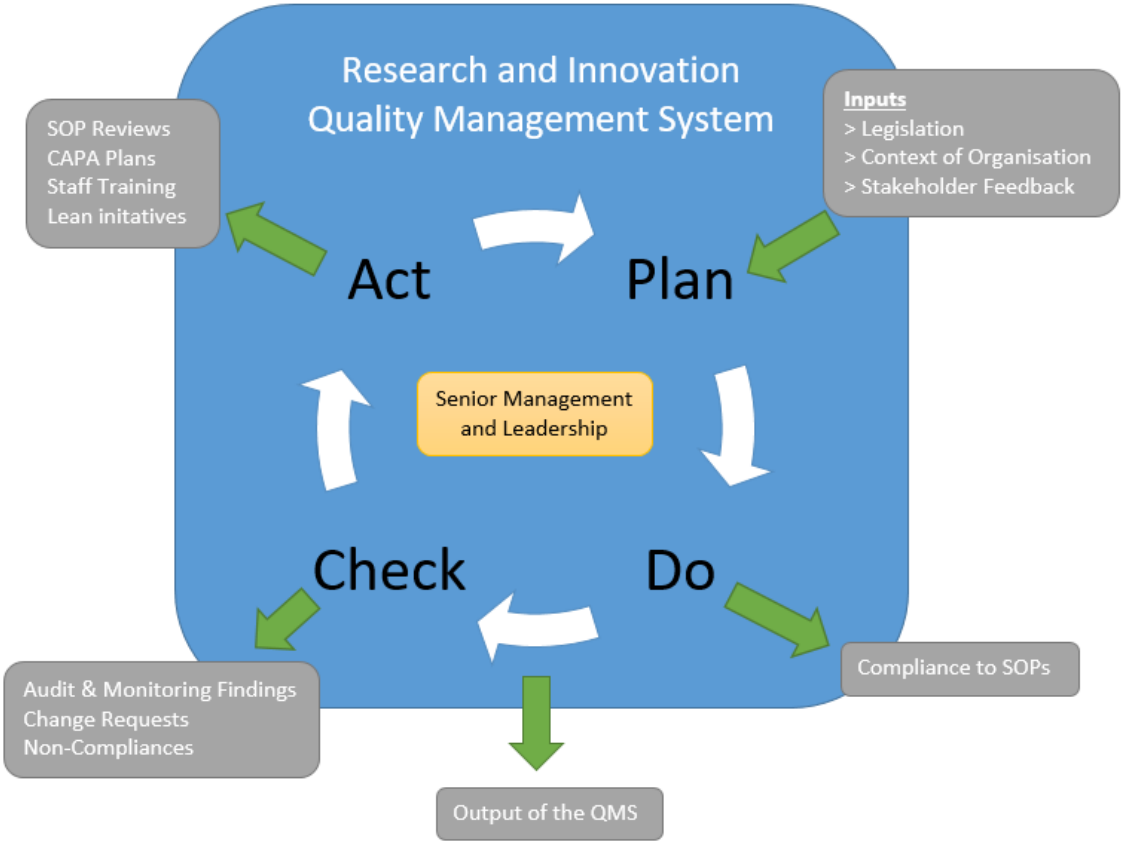

Figure 6 – Pland Do Check Act Cycle

6.2. Document Control

All documents within the Quality Management system must be produced and managed in accordance to SOP 50.023, this outlines the requirements for stakeholder engagement in the contents of the document and control of versions of the documents.

The requirements within this SOP are informed by the general SOP for Document Management within Research and Innovation, SOP 50.017. This outlines the principles of version control and document identification which must be applied to all controlled documents, including those used by trials and not contained within the Quality Management System.

A series of SOPs will exist throughout the departments of Research and Innovation which outline the particular requirements for the production and management of a variety of controlled documents, each of these SOPs exist to detail the particular requirements of the document in question but will remain in line with the requirements of SOP 50.017 and SOP 50.023 as applicable.

6.3. Audit

In line with good practices and the principles of Quality Assurance, Research and Innovation maintains an annual audit schedule of planned audit activity. This schedule is produced based on a review of the potential risks, previous audit reports, non-compliances and to ensure an adequate coverage of processes and trials. The process for preparation of this schedule, along with conducting and managing the outcomes of an audit are outlined in SOP 53.005 for Research and Innovation. Other departments within Research and Innovation may have SOPs that are used for the planning, conducting and managing their own audit activity which will be referenced in their respective Quality Manual, however the principles of these SOPs must act in line with SOP 53.005. If the relevant area does not have their own specific SOP they must follow SOP 53.005 directly.

The Research and Innovation audit schedule will take in all areas within the directorate and work alongside the audit schedules in place within the relevant departments, as shown in Figure 7. The combination of all of the audit schedules will form the complete picture of audit activity within Research and Innovation. While the specific audit schedules within each department will focus on their own area of activity, the main Research and Innovation Audit schedule will look across all areas and be conducted by the Quality Assurance Manager and the Quality Co-Ordinator.

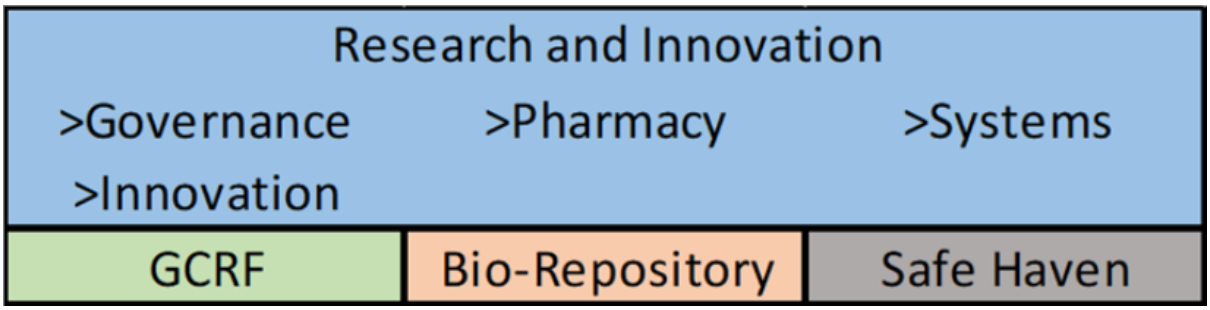

Figure 7 – Audit Schedules

The Research and Innovation audit schedule covers both compliance and system level audits, compliance audits are intended to ensure compliance to process and ensure correctness of outcome while the system level audits are intended to review the processes being followed to produce the outcome.

Audit activity within Research and Innovation is recorded and managed within the Q-Pulse application, this acts as the record of evidence of all of the activity associated with the audit including the scope of the audit, activity dates, names of auditors and auditees, records of any evidence and details of resultant findings. In turns, the resultant findings are also managed to completion within Q-Pulse to ensure a full trail of activity is available and that a set mythology for resolution is applied.

The audit schedule runs along the financial year and the output of this activity is reported to the Glasgow Health Science Partnership Regulatory Affairs Group (GHSP RAG) on an annual basis as well as any resulting outcomes from an individual audit on an ad-hoc basis should it be warranted, i.e. results in a category 3 or 4 non-compliance.

6.4. Risk Assessment and Management

SOPs within Research and Innovation are moving towards a risk weighted approach to the level of action required to be taken, key examples of this are SOP 53.010 (Preparation and Management of a Monitoring Plan), SOP 53.005 (Internal Audit) and SOP 51.008 (Handling Non-Compliance).

SOP 51.004 is in place to define a methodology for the assessment, documentation and recording of appropriate mitigation actions for risks associated to a trial with a bespoke approach depending on whether it is a Sponsored CTIMP, CIMD, Non-CTIMP, or a Hosted CTIMP.

6.4.1. Sponsored CTIMP or CIMD

The process involves engagement of all required stakeholders to assess the nature of the trial in line with set criteria as detailed within a controlled list (GUI 51.004A).

The risk assessment process requires a meeting with all of the relevant stakeholders to review the documented risks and agree the perceived level of risk based on impact and likelihood as well as the proposed mitigation actions and their ability to lower the risk profile associated with the trial.

The process of assessing the risk is continuous and begins at the earliest possible opportunity to review and gather the required information, the risk assessment for a trial can be revisited at any time during its lifecycle and updated to reflect new risks as they are identified. The process requires an assessment of risks to trials as a result of proposed amendments and documented where these risks are believed to be present.

CTIMP trials will have the risk assessment managed by the relevant Sponsor Co-Ordinator and for CIMDs run through Innovation this will be managed by the Innovation Contracts Manager.

6.4.2. Sponsored Non-CTIMP and Hosted CTIMPs

For both Sponsored Non-CTIMPs and hosted CTIMPs a process has been defined to categorise the risk level associated with the trial/study. In the event a high risk score (or medium with recurring high risk factors) is identified the Research Governance manager is to be informed to determine appropriate mitigation actions, this may include an enhanced monitoring plan, addition to the audit schedule or a variety of other approaches depending on the specifics of the trial.

6.4.3. Glasgow Clinical Research Facility Risk Assessment

For trials hosted by the Glasgow Clinical Research Facility, a specific SOP is in place for the purpose of assessing and putting in place mitigations for associated risks, this process is outlined within SOP 17.048.

6.4.4. Phase 1 and GMO Trials

In addition to the standard risk assessment process detailed above, Phase 1 and GMO trials have their own risk based approach in place which is designed to address the associated elevated risks of these trial types. To this end, specific SOPs are in place for each with the aim of a specialised committee being convened to review the specifics of the trial, identify risks and put mitigations in place. The relevant SOPs are:

- SOP 52.015 - Phase I First in Human Committee Review Process
- SOP 52.013 - Process for approving studies and trials involving a Genetically Modified Organism (GMO)

6.5. Archiving

It is a requirement of the Medicines for Human Use (Clinical Trials) Regulations to archive the Trial Master File for a defined minimum period of time, additional requirements and regulations are also in place to enhance the minimum archival period. The process and requirements of what is to be archived, for how long and by which method are outlined in the following SOPs for Research and Innovation:

- SOP 51.024 - Archiving Essential Documents from Clinical Research – Process for a Sponsored Clinical Trial of an Investigational Medicinal Product (CTIMP)
- SOP 51.025 - Archiving Essential Documents from Clinical Research – Process for a Sponsored Non CTIMP
- SOP 52.014 - Archiving Essential Documents from Clinical Research - Process for Hosted Research

The above SOPs outline the roles and responsibilities of the activities involved in archiving the Trial Master File as well as the process for the destruction of the documents at the end of the archival period.

For research hosted within the Glasgow Clinical Research Facility, the process for archiving essential documents is outlined within GUI 57.005B.

All documents that form the QMS are retained indefinitely within the Q-Pulse application, as detailed within SOP 50.023.

6.6. Vendor Assessment

In the conduct of a trial, a requirement may arise to make use of services that are not able to be provided internally. In these scenarios, an assessment is made of this potential vendor to determine if they are a suitable option to carry out the work required for the trial. A defined process is in place which is outlined in SOP 51.015.

This process requires engagement to be made with the potential vendor through a variety of means to assess their capability and their established QMS and practices. This engagement must take place before a contract is entered into with the vendor which is then dependent on a successful approval of this vendor for use. A list of approved vendors is maintained and reviewed on an ongoing basis.

6.7. Non-Compliance Management

In the natural course of operation, CAPAs to established updates to processes and protocols are likely to take place as a result of non-compliances. It is the ambition of the Quality Management System to reduce these occurrences as much as possible, to achieve this goal it is essential to identify and take appropriate actions to resolve non-compliances. Within Research and Innovation a process has been established and detailed with SOP 51.008 and within SOP 51.009 to specifically address serious breaches. Both processes are applicable across all of R&I, covering all areas highlighted in Figure 1 in Section 1.

Both of these processes are primarily aimed at the management of Category 3 and Category 4 non-compliances, however provision is made for the management of Category 1 and Category 2 Protocol deviations with SOP 51.008.

All Category 3 and Category 4 non-compliances are presented and reported to the Glasgow Health Science Partnership Regulatory Affairs Group (GHSP RAG).

Non-Compliances can also be identified and managed as a result of activities such as Monitoring and Audit, each of which have defined procedures for the management of these findings in their respective SOPs, SOP 53.004 and SOP 53.005.

6.8. Complaints

A defined policy and procedure is in place within Greater Glasgow and Clyde for reporting and managing Complaints from patients and for staff related matters, this can be located via the links in 3.3.1.

In the instance a complaint is raised it will be passed to the director and/or the Senior Manager for input and resolution.

Internal complaints that arise from investigators are directed to the Director and the Senior Manager in the first instance in order to investigate and determine the way forward.

6.9. Training

All staff must be appropriately trained to conduct the activities associated with their role, all roles will have a Job Description that outlines the requirements of training, education and experience the individual must possess prior to starting in the role.

All members of staff will be presented with the Research and Innovation Quality Manual as well as the Quality Manual for their area of work if applicable and evidence that they have read and understood its contents will be recorded. In addition to this, all SOPs relevant to the individual's role will be distributed to them and evidence they have read and understood its contents will be captured.

In the natural progression of an individual's role, their line manager will conduct a Personal Development Review using TURAS which includes a consideration of the individual's competencies against the Knowledge & Skills Framework (KSF). At this point, the requirement for any additional training may be identified.

Every individual within Research and Innovation must maintain a training file, as detailed in SOP 50.013. The contents of this training file demonstrate any training undertaken by the member of staff and can be used to demonstrate their skill set and competency, the contents of training files will be a routine subject of audit.

It is a policy requirement for all staff involved within Research to maintain an appropriate level of GCP certification.

6.10. GDPR

Among the applicable regulations which Research and Innovation must follow that are mentioned within section 2.2 is GDPR. As the work conducted by R&I involves the handling and management of data, the requirements of GDPR are built into all of the relevant processes within Research and Innovation.

An overarching Board Policy is in place to address the requirements of GDPR which is followed by Research and Innovation.

Confidentiality and Data Protection Policy

6.11. Incident Reporting (DATIX)

A board level process is in place for the reporting of Clinical and Non Clinical Incidents, DATIX. Incidents must be recorded through DATIX which is available to all staff through staffnet, the homepage of NHSGGC's intranet.

http://www.staffnet.ggc.scot.nhs.uk/

All incidents will then be reported to the appropriate manager in charge for further investigation and appropriate actions taken. This must take place alongside any processes undertaken to investigate issues within Research and Innovation.

6.12. Serious Adverse Events (SAEs) and Suspected Unexpected Serious Adverse Reaction (SUSARs)

SOPs 55.001, 55.004, and 55.007 detail the regulatory safety reporting requirements for CTIMPs, non CTIMPs, and clinical investigations of medical devices respectively. The SOPs document requirements for reporting and reviewing adverse events in line with the relevant regulatory framework, including expedited reporting of unexpected and related events to the national competent authority and research ethics committees were applicable. Annual reporting of serious adverse events to the national competent authority is documented within SOP 55.002. All pharmacovigilance and safety reporting activity is managed by the Pharmacovigilance Manager

6.13. Monitoring of Trials

Monitoring activity is carried out by the Clinical Trial Monitors within Research and Innovation for Sponsored CTIMPs, clinical investigations and selected high risk non-CTIMPs that are not managed by the CRUK CTU. For those trials managed by the CRUK CTU, they will provide their own monitoring resource.

The purpose of the monitoring activity is to assure compliance to the GCP, patient safety, data integrity and the output of the Quality Management System, as detailed in Level 4 in section 3.3.4 and the conduct of trials across sites.

A number of SOPs are in place to detail the monitoring processes and are contained in Chapter 53, the monitoring activity and subsequent findings from this activity are captured and managed in Q-Pulse.

Defintions

Acronym	Definition
BCRF	Beatson Clinical Research Facility
CAPA	Corrective and Preventative Action
CRF	Clinical Research Facility
CRUK	Cancer Research United Kingdom
CTIMP	Clinical Trial of an Investigational Medicinal Product
CTU	Clinical Trials Unit
GCP	Good Clinical Practice
GCRF	Glasgow Clinical Research Facility
GCTU	Glasgow Clinical Trials Unit
GDPR	General Data Protection Regulations
GHSP RAG	Glasgow Health Science Partnership Regulatory Affairs Group
ICH GCP	International Council for Harmonisation Good Clinical Practice
IMP	Investigational Medicinal Product
ISO	International Standards Organisation
KSF	Knowledge and Skills Framework
MHU	Medicines for Human Use
NHS	National Health Service
NHSGGC	National Health Service Greater Glasgow and Clyde
PDCA	Plan, Do, Check & Act
PHRF	Population Health Research Facility
PMU	Project Management Unit
PV	Pharmacovigilance
QA	Quality Assurance
QC	Quality Control
QMS	Quality Management System
R&I	Research and Innovation
RACI	Responsible, Accountable, Consulted & Informed
RCB	Robertson Centre for Bio-Statistics
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction
TMF	Trial Master File
UK	United Kingdom