Golden Jubilee Research Institute

Patients at the heart of progress

Research Quality Framework

11th September 2017

Version 1.1

Contents

Glossary....3
Background....4
Research Governance Policies and Procedures....5
Principle 1....5
Principle 2....5
Principle 3....6
Principle 4....6
Principle 5....6
Principle 6....6
Principle 7....7
Principle 8....7
Principle 9....7
Principle 10....8
Principle 11....8
Principle 12....9
Principle 13....9
Principle 14....10
Summary....10
Appendix 1: Policies and procedures relating to research at the Golden Jubilee National Hospital.....11

Glossary

CTIMP trial	Clinical Trial of an Investigational Medicinal Product – also known as a drug trial
MHRA	Medicines & Healthcare products Regulatory Agency is the competent authority for the regulation of drug (CTIMP) and device trials.
NHS Research Ethics Service	The UK Health Research Authority manages the UK Research Ethics Service. Further information can be found at: www.hra.nhs.uk. The application form can be found at: www.myresearchproject.org.
Research	For the purposes of research governance, 'research' means the attempt to derive generalisable new knowledge by addressing clearly defined questions with systematic and rigorous methods. Although some research projects include evaluation, where a project is considered to be solely audit or service/therapy evaluation, it will not be managed as research within the NHS or social care. Such projects do not require ethical review by a NHS or Social Care Research Ethics Committee or management permission through the NHS R&D office. See here for further information
Sponsor	The sponsor is the individual, company, institution or organisation, which takes on ultimate responsibility for the initiation, management (or arranging the initiation and management) of and/or financing (or arranging the financing) for that research. The sponsor takes primary responsibility for ensuring that the design of the study meets appropriate standards and that arrangements are in place to ensure appropriate conduct and reporting

Background

Research Governance concerns 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. A broad range of regulations, principles and standards of good practice exist to achieve, and continuously improve, research quality across all aspects of healthcare in the UK and worldwide. Research governance applies to everyone connected to healthcare research including Chief Investigators, Health Care Professionals, researchers, and support staff.

Note that both service evaluation and audit are terms that are generally used interchangeably with research. However, given that neither service evaluation – which examines an existing NHS service – nor audit – which compares existing NHS services to an established standard – carry any additional risk to patients, they are both out with the scope of this document.

The principles of Good Clinical Practice (GCP) in research underpin guidance relating to research governance and are outlined below.

The following principles are based on Articles 2 to 5 of the EU GCP Directive 2005/28/EC and include 2 new principles, no's 7 and 8, that are included in the Medicines for Human Use (Clinical Trials) Amendment Regulations 2006.

1. The rights, safety and well-being of the trial subjects shall prevail over the interests of science and society.
2. Each individual involved in conducting a trial shall be qualified by education, training and experience to perform his tasks.
3. Clinical trials shall be scientifically sound and guided by ethical principles in all their aspects.
4. The necessary procedures to secure that the quality of every aspect of the trial shall be complied with.
5. The available non-clinical and clinical information on an investigational medicinal product shall be adequate to support the proposed clinical trial
6. Clinical trials shall be conducted in accordance with the principles of the Declaration of Helsinki.
7. The protocol shall provide for the definition of inclusion and exclusion of subjects participating in a clinical trial.
8. The investigator and sponsor shall consider all relevant guidance with respect to commencing and conducting a clinical trial.
9. All clinical information shall be recorded, handled and stored in such a way that it can be accurately reported, interpreted and verified, while the confidentiality of records of the trial subjects remains protected.

Conditions based on Article 3 of the GCP Directive

10. Before the trial is initiated, foreseeable risks and inconveniences have been weighed against the anticipated benefit for the individual trial subject and other present and future patients. A trial should be initiated and continued only if the anticipated benefits justify the risks.
11. The medical care given to, and medical decisions made on behalf of, subjects shall always be the responsibility of an appropriately qualified doctor or, when appropriate, of a qualified dentist
12. A trial shall be initiated only if an ethics committee and the licensing authority comes to the conclusion that the anticipated therapeutic and public health benefits justify the risks and may be continued only if compliance with this requirement is permanently monitored.
13. The rights of each subject to physical and mental integrity, to privacy and to the protection of the data concerning him in accordance with the Data Protection Act 1998 are safeguarded.
14. Provision has been made for insurance or indemnity to cover the liability of the investigator and sponsor which may arise in relation to the clinical trial

The new ICH GCP E6 (R2) Addendum introduced 26 new items covering three main areas of clinical research: data management, and sponsor and investigator responsibilities (recent addition, November 2016).

15. The investigator should assure that there is a suitable monitoring plan in place to supervise the different individuals engaged in the study
16. The new duty of the principal investigator (PI) is to oversee the individual or party to whom the investigator delegates study tasks conducted at the trial site
17. The investigator must maintain records of the documents for critical processes and clear documented evidence of the PI's oversight and involvement in the trial.
18. Revision of the sponsor's responsibilities to include quality management, CRO, trial management, data handling, record keeping and noncompliance.
19. The sponsor should implement a system to manage quality throughout the design, conduct, recording, evaluation, reporting and archiving of clinical trials; the sponsor should focus on trial activities essential to ensuring human subject protection and the reliability of trial results

In practice, these responsibilities are distributed between the NHS Research Ethics Service, the study sponsor and each host NHS Organisation.

The Golden Jubilee is defined as the host origination for research projects that have been reviewed and approved by an NHS Research Ethics Committee **and** reviewed and approved by the Golden Jubilee Research & Development Department **and** where participants are recruited from the Golden Jubilee or where some element of research activity takes place in the Hospital or Research Institute. In addition, the hospital takes on the role of sponsor for about 10% of hosted projects and, for a subset of these studies, sponsor responsibilities include other NHS sites in Scotland, the devolved nations and occasionally, world-wide. Policies and procedures therefore have to be applicable to all of these scenarios.

Research Governance Policies and Procedures

The Golden Jubilee Research & Development Office has developed policies and procedures in line with the principles outlined above. The purpose of this document is to contextualise these policies and procedures and to note any gaps. Essentially, this document will provide assurance to patients, staff and the Golden Jubilee Board that any additional risks relating to research are managed effectively.

Note that principles 15-19 are relatively new additions. Sections 15, 16 and 17 relate to a clarification of the responsibilities of the Principle Investigator and are covered in GCP training which is required for each PI.

Principle 1

The rights, safety and well-being of the trial subjects shall prevail over the interests of science and society.

This the responsibility of the NHS Research Ethics Service however the Golden Jubilee provides supports in the following ways:

1. Where the Golden Jubilee is asked to sponsor a project, manage the Peer Review process (GJRI002: Research Project Protocol Peer Review – Guidance Document) which provides assurance that the protocol has scientific integrity.
2. Providing support to researchers in completion of the ethics application form.
3. Ensuring that a Research Ethics Committee approval letter is in place for each project.

The NHS Research Ethics Service is managed on a UK wide basis. Information on the service, including support for researchers, can be found at: http://www.hra.nhs.uk/. The application form and information about the application process can be found at: https://www.myresearchproject.org.uk/.

Principle 2

Each individual involved in conducting a trial shall be qualified by education, training and experience to perform his tasks.

This is the responsibility of the NHS site that recruits participants to research projects. Essentially, all researchers must have a Good Clinical Practice (GCP) in Research certificate. The GJ R&D Office ensures that there is a GCP certificate for each member of the research team at the point of study start up. The certificate is then renewed every 2 years – this is tracked by the R&D Office and reminders sent as appropriate. Points to note are as follows:

1. The GJ R&D Office provides licences for online GCP training free of charge to researchers. In addition, access to taught courses is available to researchers through the NHS GG&C Clinical Research Facility.
2. The GJ Lead Research Nurse has developed an induction package specifically for research support staff. The Senior Research Nurse in each topic area is responsible for coordinating the research specific induction process.
3. All GJ staff must maintain training relevant to their profession - this includes staff employed specifically to support research. This is monitored both by relevant professional bodies and through the established line management structure for research support staff.

4. For staff not substantively employed by the Golden Jubilee and who carry out research at this site, there is a process in place to ensure that individuals are adequately trained as described above (GJRI014, Honorary Research Contract / Letter of Access for research purposes – Guidance document).

Principle 3

Clinical trials shall be scientifically sound and guided by ethical principles in all their aspects.

This is the responsibility of the sponsor of each research project – the sponsor must provide an assurance in relation to this principle to the Research Ethics Committee. The Golden Jubilee fulfils this obligation in the following ways:

1. If the Jubilee is asked to take on sponsor responsibilities, the protocol is subject to peer review (GJRI002, Research Project Protocol Peer Review – Guidance Document). This process provides an assurance that, as far as is reasonably possible, the protocol is *scientifically sound and guided by ethical principles*. Once this process is completed, the Research Manager will sign the ethics application as the representative of the sponsor (the Golden Jubilee) in confirmation that the process has been followed.
2. If another organisation has signed the ethics application in the capacity of the project sponsor, in common with all NHS Organisations, the Jubilee takes this as confirmation that the organisation has followed a similar procedure and will not repeat the peer review process.

Principle 4

The necessary procedures to secure that the quality of every aspect of the trial shall be complied with.

This is the responsibility of the site that participants are recruited from. The Golden Jubilee fulfils this obligation in the followings ways:

1. Each project that is either actively recruiting or in the follow-up phase is monitored (GJRI005, Research Project Monitoring – Policy Document). As well as tracking recruitment, this process manages change including changes in the study team, changes in end dates etc. This is critical information which enables the Jubilee to closely performance manage research projects.
2. The Jubilee has an active research project audit system (GJRI006, Research Project Auditing – Policy Document). This allows for internal and external auditing of systems relating to research and of the research projects themselves. Reporting is through the Golden Jubilee Research & Development Steering Group.

Principle 5

The available non-clinical and clinical information on an investigational medicinal product shall be adequate to support the proposed clinical trial.

This principle relates to drug trials only (also known as Clinical Trials of Investigational Medicinal Products – CTIMP trials) and is the responsibility of the sponsor. In the UK *the available non-clinical and clinical information on an investigational medicinal product* must have been reviewed by the competent authority – the **Medicines & Healthcare products Regulatory Agency** (MHRA). At this point in time, the Jubilee does not sponsor drug trials and carries out this responsibility in the following way:

1. An MHRA 'no objection' letter must be on file for all research projects that are defined within the Research Ethics application as a drug trial.

Principle 6

Clinical trials shall be conducted in accordance with the principles of the Declaration of Helsinki.

The **Declaration of Helsinki** (**DoH**) is a set of ethical principles regarding human experimentation developed for the medical community by the World Medical Association (WMA). It is widely regarded as the cornerstone document on human research ethics and, in the UK, resulted in the development of what is now known as the NHS Research Ethics Service. The Jubilee provides assurance that all research conforms to **DoH** principles in the following way:

1. An NHS Research Ethics Committee 'no objection' letter must be on file for all projects that are categorised as research within an NHS environment. NHS Research Ethics Committees are overseen by the UK Health Research Authority (HRA) which provides advice on the categorisation of projects.

Principle 7

The protocol shall provide for the definition of inclusion and exclusion of subjects participating in a clinical trial.

Inclusion criteria are characteristics that the prospective trial participants must have if they are to be included in the study while exclusion criteria are those characteristics that disqualify prospective subjects from inclusion in the study. The purpose of inclusion and exclusion criteria is to ensure patients safety (by excluding patients who may be adversely affected), provide justification of participate appropriateness for the study, minimise withdrawal and ensure that primary end-points of study are reached. The Jubilee provides assurance in relation to this principle in the following way:

1. Following the peer review process (GJRI002, Research Project Protocol Peer Review – Guidance Document) which ensures that inclusion and exclusion criteria are included in the protocol and are appropriate to the aims of the research project
2. Ensuring that each research project has an associated NHS Research Ethics Committee 'no objection' letter – the REC will also review inclusion and exclusion criteria as part of their normal process

Principle 8

The investigator and sponsor shall consider all relevant guidance with respect to commencing and conducting a clinical trial.

Research within an NHS environment has common ground with areas where established guidance and legislation is in place. This includes, but is not limited to, the following:

1. Human Tissue (Scotland) Act 2006. This is relevant when tissue samples are taken for research purposes only (i.e. are not required for normal clinical care) **and** when samples taken for routine care are used for research purposes.
2. Data Protection Act 1988. This Act applies even if data is collected for research purposes only.
3. Ionising radiation – the use of ionising radiation in research must be formally documented in the research application form and is part of the review and approval process
4. Public Benefit and Privacy Panel (PBPP) review. This is applicable if patient data is (or may be) used and the patient has not explicitly consented to that use.
5. Adults with Incapacity (Scotland) Act 2000. This is relevant where patients do not have the capacity to consent to research. At the Golden Jubilee, this must be considered where there is the potential for participants to be admitted to the hospital in an emergency situation.

The Jubilee provides assurance in relation to this principle by reviewing each Research Ethics Application prior to accepting sponsor responsibility to ensure that consideration of guidance and legislation relevant to each protocol has been included in the application.

Principle 9

All clinical information shall be recorded, handled and stored in such a way that it can be accurately reported, interpreted and verified, while the confidentiality of records of the trial subjects remains protected.

The recording, handling and storage of data is carried out in line with processes that have been reviewed and approved by an NHS Research Ethics Committee. Data must be available for audit through the recruitment and follow-up processes and for a number of years thereafter – exact time is determined by the study sponsor. The Golden Jubilee is developing an archiving policy (GJRI010, Research Project Files – Archiving – Guidance Document) which will clarify roles and responsibilities in relation to the archiving and destruction of such data.

In line with the rest of the NHS, researchers must adhere to legislation and guidance in relation to the use of information gained for research purposes. The Data Protection Act 1988 applies and it is expected that the use of identifiable data will be explicitly consented to by each participant in the research project – NHS Research Ethics Committee's will review and approve the Informed Consent form for each project to ensure that the principles outline in the Act are followed. In general, it is expected that Informed Consent is taken and that data is anonomysed – usually link anonomysed – before it leave the NHS environment where it was taken.

Relevant points are as follows:

1. All Golden Jubilee staff must complete an online Information Governance course.
2. Procedures relating to the use of confidential information are reviewed and approved by an NHS Research Ethics Committee – a NHS REC approval letter must be on file prior to Golden Jubilee approval.
3. The use of each patient's data is explained to them as part of the Informed Consent process. The Golden Jubilee has a policy relating to this process (GJRI001, Informed Consent – Guidance Document) and encourages all researchers to attend a formal Informed Consent course which is available free of charge at the Glasgow Clinical Research Facility.
4. If Informed Consent is not considered necessary, or if it is not possible, then the proposed use must be reviewed and approved by the **Public Benefit and Privacy Panel for Health and Social Care (PBPP)**.

Principle 10

Before the trial is initiated, foreseeable risks and inconveniences have been weighed against the anticipated benefit for the individual trial subject and other present and future patients. A trial should be initiated and continued only if the anticipated benefits justify the risks.

Within the NHS, *research* is typically an activity that carries – or may carry – an additional risk to patients and therefore to the organisation. The principle role of the NHS Research Ethics Service is to review each application to ensure that anticipated benefit justifies any risk. In addition there are two levels of review prior to Golden Jubilee issuing an approval letter and the study beginning to recruit. The Golden Jubilee conforms to this principle in the following way:

1. The Golden Jubilee will not allow any research to commence unless an NHS REC letter of no objection is in place.
2. The high level 'Generic Review', resulting in a Governance Report must also be completed. For multisite studies, this is coordinated by the NHS Research Service Permission Coordination Centre (NRSPCC) and for single site projects, this is coordinated by the Golden Jubilee Research Manager.
3. A local review is also carried out to ensure that the project can be accommodated at the Golden Jubilee. This includes coordinating with services that will be involved – e.g. MRI, echo, labs – and confirming that funding agreed during the Generic Review is appropriate to the Golden Jubilee.

Principle 11

The medical care given to, and medical decisions made on behalf of, subjects shall always be the responsibility of an appropriately qualified doctor or, when appropriate, of a qualified dentist.

Each research project that has been reviewed and approved by an NHS Research Ethics Committee has an associate Site Specific Information (SSI) form. The Golden Jubilee Principle Investigator is identified in that form and is normally one of the medical staff responsible for the particular patient group that will be recruited to the

project. Note that other Health Care Professionals can be called upon to carry out their normal duties for patients that have been recruited to a research project - these individuals must be noted in the delegation log. In this way, an assurance is provided that *the medical care given to, and medical decisions made on behalf of, subjects shall always be the responsibility of an appropriately qualified doctor.*

The Jubilee provides assurance in relation to this principle in the following way:

1. Principle Investigators will either be substantively employed by the Golden Jubilee or will have applied for and obtained an appropriate document to allow them to carry out their responsibilities relating to the project. The process for obtaining the appropriate document is documented and is available (GJRI014 - Honorary Research Contract / Letter of Access for research purposes – Guidance document).
2. Each Principle Investigator will develop a delegation log (GJRI004 - Delegation Log - Guidance Document) which formally lists personnel that he/she has delegated a particular task to. The task must also be described and the both parties must sign the document.

Principle 12

A trial shall be initiated only if an ethics committee and the licensing authority comes to the conclusion that the anticipated therapeutic and public health benefits justify the risks and may be continued only if compliance with this requirement is permanently monitored.

1. NHS Research Ethics Committee approval is required for all research projects and a REC approval letter must be on file prior to Golden Jubilee approval.
2. Licensing authority – in the UK this is the **Medicines & Healthcare products Regulatory Agency** (MHRA). A 'no objection' letter must be in place when appropriate and in the following circumstance:
    a. All drug (CTIMP) trials. The only exceptions if a drug is used to cause a physiological effect (e.g. adenosine to change heart rate in some MRI tests) - this is generally not classed as a CTIMP trial. Given the 'grey area' nature of this circumstance, correspondence from the MHRA confirming that MHRA review and approval is not required must be lodged in the project file.
    b. Device trials – unless the device is being used with its established licence.
3. Continuous compliance with the principle is achieved using the processes outline in GJRI003, Review and Approval of Amendments – Guidance Document.

Principle 13

The rights of each subject to physical and mental integrity, to privacy and to the protection of the data concerning him in accordance with the Data Protection Act 1998 are safeguarded. ***Note that this is similar to Principle 9 where this text is taken from.***

In line with the rest of the NHS, researchers must adhere to legislation and guidance in relation to the use of information gained for research purposes. The Data Protection Act 1988 applies and it is expected that the use of identifiable data will be explicitly consented to by each participant in the research project – NHS Research Ethics Committee's will review and approve the Informed Consent document for each project to ensure that the principles outlined in the Act are followed. In general, it is expected that Informed Consent is taken and that data is anonomysed – usually link anonomysed – before it leave the NHS environment where it was taken.

Relevant points are as follows:

1. All Golden Jubilee staff must complete an online Information Governance course.
2. Procedures relating to the use of confidential information are reviewed and approved by an NHS Research Ethics Committee – an NHS REC approval letter must be on file prior to Golden Jubilee approval.
3. The use of each patient's data is explained to them as part of the Informed Consent process. The Golden Jubilee has a policy relating to this process (GJRI001, Informed Consent – Guidance Document) and encourages all researchers to attend a formal Informed Consent course which is available free of charge at the Glasgow Clinical Research Facility.

4. If Informed Consent is not considered necessary, or if it is not possible, then the proposed use must be reviewed and approved by the **Public Benefit and Privacy Panel for Health and Social Care (PBPP)**.

Principle 14

Provision has been made for insurance or indemnity to cover the liability of the investigator and sponsor which may arise in relation to the clinical trial.

All research studies conducted within the NHS must have appropriate indemnity in place. The sponsor must ensure adequate provision for indemnity or compensation in the event of injury or death attributed to a research study. Clarification of issues relating to indemnity is part of the Research Ethics Committee review and approval process and is detailed in the IRAS (Integrated Research Application System) form. The way in which the Golden Jubilee fulfils the obligation in respect of Principle 14 is described in the guidance document: GJRI015, Indemnity arrangements for research – guidance.

Summary

Research Governance in the NHS provides a system of documents and procedures that can be followed by parties involved in research to effectively manage that activity. Most documents relate to the principles of Good Clinical Practice (GCP) in research however, some are designed to provide support to certain aspects of research which are not explicitly mentioned in GCP. The full list of document can be found in Appendix 1 and where they are associated with a particular GCP principle, are mentioned with the explanatory text in the previous section for that principle.

All documents were evaluated by appropriate stakeholders prior to review and approval by the Golden Jubilee Research & Development Steering Group. Where the steering group recommended additional review – e.g. the Informed Consent guidance document by the Golden Jubilee Clinical Governance Group – the document review dates reflect the additional evaluation.

All documents are available to the wider Golden Jubilee staff community through Q-Pulse – Q-pulse references are listed in Appendix 1. In addition, the documents are available to research teams through the operational database CRF Manager.

Appendix 1: Policies and procedures relating to research at the Golden Jubilee National Hospital.

GJRI reference	*Q-Pulse Reference*	*Document name*	*Review date*
GJRI001	**GJRI001**	Informed Consent – Guidance Document	21st October 2018
GJRI002	**GJRI002**	Research Project Protocol Peer Review – Guidance Document	31st January 2019
GJRI003	**GJRI003**	Review and Approval of Amendments – Guidance Document	17th March 2019
GJRI004	**GJRI004**	Delegation Log - Guidance Document	15th March 2019
GJRI005	**GJRI005**	Research Project Monitoring – Policy Document	30th June 2019
GJRI006	**GJRI006**	Research Project Auditing – Policy Document	21st November 2019
GJRI008	**GJRI008**	Guidance for setting up and maintaining a Research Site File.	15th May 2020
GJRI009	**GJRI009**	Serious Adverse Event Reporting – Guidance Document	3rd August 2019
GJRI010	**TBC**	Research Project Files – Archiving – Guidance Document DRAFT	TBC
GJRI012	**TBC**	Management of Intellectual Property DRAFT	TBC
GJRI 013	**GJRI013**	Research Fraud and Misconduct – Policy Document	28th February 2020
GJRI014	**GJRI014**	Honorary Research Contract / Letter of Access for research purposes – Guidance document	4th August 2019
GJRI015	**GJRI015**	Indemnity arrangements for research - guidance	N/A

Note: At the time of approval by the appropriate Golden Jubilee Committee, documents are uploaded to Q-Pulse and to CRF Manager.