York Foundation Trust R&D Unit
Standard Operating Procedure
R&D/S64

Setting up Research Studies Involving Imaging (Including Studies using Ionising Radiation)

IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED

All staff should regularly check the R&D Unit's website and R&D Newsletter for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.

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This SOP will normally be reviewed every 2 years unless changes to the legislation require otherwise

Version History Log

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

Version	Date Implemented	Details of significant changes
1.0	15th November 2010	
2.0	30th April 2012	Change of SOP Controller. Removal of North and East Yorkshire R&D Alliance references

Contents

1 Introduction, Background and Purpose

ICH-GCP states that 'the investigator should have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely" (ICH GCP 4.2.3). A medical imaging service must therefore be 'adequate' for purpose and the responsibility to ensure that this is the case resides with the investigator.

The principles of GCP are also applicable to non-CTIMP research studies taking place in York Foundation Trust.

Research studies involving the use of ionising radiation are regulated by the Ionising Radiation (Medical Exposure) Regulations 2000 which, together with review by appropriate ethics committees, ensure that the exposures are justified and are authorised.

2 Who Should Use This SOP

This SOP is relevant to investigators setting up research studies sponsored or co-sponsored by York Foundation Trust.

3 When this SOP Should be Used

The procedure described in this SOP should be followed when setting up a research study involving imaging sponsored or co-sponsored by York Foundation Trust.

4 Procedure(s)

4.1 Research studies involving medical imaging

Imaging services involved in CTIMP work must meet essential requirements. Similar standards, whilst not essential, are desirable for non-CTIMP studies. It is the responsibility of the Chief Investigator (CI) or Principal Investigator (PI) to ensure that such requirements are met.

For York Foundation Trust CTIMPs the Sponsor will determine the scope and format of due diligence required. This is likely to include consideration of the following as a minimum: (i) staff and staff training, (ii) capacity of facility to deliver the required procedures, (iii) accreditation, (iv) quality assurance procedures (SOPs, quality control and audit), (v) inspection and maintenance of imagine equipment. The proposed imaging service should have such systems in place in order to demonstrate compliance with ICH GCP 2.13.

The CI/PI should undertake initial discussions with the proposed imaging department at an early stage of study development and is responsible for undertaking the required due diligence. The CI/PI must acquire the necessary documentation to demonstrate the competence of the designated imaging service to ensure that adequate GCP requirements are met.

Good Clinical Practice (GCP) is applicable throughout a research study and the general principles of GCP are applicable to imaging services.

Particularly relevant principles are: -

- *Each individual involved in conducting a trial should be qualified by education, training and experience to perform his or her respective task(s) (Section 2.8)*
- *All clinical trial information should be recorded, handled and stored in a way that allows its accurate reporting, interpretation and verification (Section 2.10)*
- *Systems with procedures that assure the quality of every aspect of the trial should be implemented (Section 2.13)*

N.B. Where research involves the administration of radioactive substances, an ARSAC certificate must be held at each research site where administrations take place. The certificate is site, procedure and holder specific. A "research ARSAC certificate" will be required if the research exposure is additional to those carried out by the certificate holder as part of normal clinical care.

Staff involved in undertaking imaging procedures as part of a clinical trial should receive GCP training commensurate with their roles and responsibilities. A record of training should be maintained for each individual involved in trial procedures and should be retained should a staff member leave employment.

It is the responsibility of the CI/PI to ensure the suitability and performance of the medical imaging service during the study. Periodic checks should be undertaken and documented to ensure that satisfactory arrangements remain in place for the duration of the study. If a Monitoring Plan has been devised for the study then this should include a visit to the imaging department where appropriate.

Any issues regarding suitability and performance of the service during the study should be raised with the Sponsor in a timely manner.

Formal agreements should be in place between the Sponsor and imaging department. These may be defined in the protocol, a study specific-SOP, or where imaging is to be undertaken by a separate organisation, in a contract.

4.2 Research studies using Ionising radiation

Procedures involving ionising radiation include:

- Diagnostic X-rays, CT scans or DXA scans
- Radiotherapy (including brachytherapy and therapy using unsealed sources)
- Radionuclide imaging

All studies involving ionising radiation must comply with the following:

- The Ionising Radiation (Medical Exposure) Regulations 2000 ("IRMER") as amended by the Ionising Radiation (Medical Exposure) (Amendment) Regulations 2006
- The Medicines (Administration of Radioactive Substances) Regulations 1978 ("MARS")
- The Ionising Radiation Regulations 1999

CTIMP studies involving ionising radiation must also additionally comply with The Medicines for Human Use (Clinical Trials) Regulations 2004[1] ("Clinical Trials Regulations").

The Ionising Radiation (Medical Exposure) Regulations 2000 (IRMER) govern the exposure to ionising radiation of patients or other persons voluntarily participating in medical or biomedical, diagnostic or therapeutic research programmes. The research provisions of IRMER apply to any *research exposure* involving ionising radiation, not only to exposures that are additional to routine care.

A "research exposure" is any exposure required by the research protocol following initial consent from the participant. It includes all exposures carried out on the participant as determined by the protocol, including those which would otherwise be part of routine clinical care for patients treated outside the research setting. Research exposures also include any exposure required by the *screening procedures* for the research. For example, where the protocol requires a diagnostic X-ray to confirm suitability for inclusion in the study, this would be a research exposure that must meet the requirements of IRMER relating to research exposures and for which a study participant must provide informed consent.

For example, in a comparative study of two radiotherapy schedules (conventional versus ultrafractionated), the control group might be receiving normal radiotherapy and additional diagnostic CT scans. However, all the exposures would be research exposures required by the protocol.

The following requirements apply to *all* research studies where patients recruited receive *any research exposures*:

- Dose constraints are established for biomedical and medical research programmes where no direct medical benefit for the individual is expected from the exposure.
- These dose constraints are adhered to.
- Individual target levels of doses are planned by the Practitioner for patients who voluntarily undergo an experimental diagnostic or therapeutic practice from which the patients are expected to receive a diagnostic or therapeutic benefit.
- The individuals concerned participate voluntarily in the research programme.
- The individuals concerned are informed in advance about the risks of the exposure.

All research involving ionising radiation should be reviewed by a Research Ethics Committee (REC), including ethical consideration of radiation exposures, and local employers' approval for these exposures under IRMER.

[1] The Medicines for Human Use (Clinical Trial) Regulations 2004 and the Medicines for Human Use (Clinical Trial) Amendment Regulations 2006 (SI 2006 No. 1928), the Medicines for Human Use (Clinical Trials) Amendment (No.2) Regulations 2006 (SI 2006 No. 2984), the Medicines for Human Use (Clinical Trials) and Blood Safety and Quality (Amendment) Regulations 2008 (SI 2008 No. 941), and the Medicines for Human Use (Miscellaneous Amendments) Regulations 2009 (SI 2009 No. 1164).

4.2.1 Responsibility of the CI/PI in preparing an application

It is the responsibility of the CI/PI to clearly summarise the radiation exposures (maximum number) of each type to which each volunteer could be subjected, and to present this information clearly to both the ethics committee and the local committee responsible for approval for these exposures under IRMER.

The research study must receive ethical approval and local Trust approval of IRMER compliance prior to commencement.

4.2.2 Ethics application

Input must be obtained from the following experts:

- A lead Medical Physics Expert (lead MPE), who performs a dose/risk assessment for all the radiation exposures proposed in the protocol.
- A lead Clinical Radiation Expert (lead CRE), who assesses whether the protocol could involve additional radiation exposure at any site in the study and advises the CI and the main REC on the suitability and ethical acceptability of additional exposures.

The dose and risk assessment should be accurately documented in the IRAS application. This should be prepared by a Medical Physics Expert (MPE) who is a registered health care professional and has expertise relevant to the planned exposures. MPEs are usually registered as clinical scientists by the Health Professions Council under the Health Professions Order 2001. Where the study involves different types of exposure (for example, both radioactive materials and other ionising radiation, or more than one imaging method), advice may need to be sought from other MPEs with relevant expertise. The lead MPE should produce a combined assessment for the ethics committee, giving the names of any other MPEs who have contributed to the assessment.

The Clinical Radiation Expert (CRE) should be a registered health professional with clinical expertise relevant to the planned exposures. Typically this might be a radiologist, a clinical oncologist (for radiotherapy) or a nuclear medicine specialist. Their assessment should cover potential exposure at all research sites, taking account of possible variation in normal clinical practice. Where the study involves different types of exposure (for example, both radiotherapy and other ionising radiation), advice may need to be sought from other CREs with relevant expertise. The lead CRE should produce a combined assessment for the ethics committee, giving the names of any other CREs who have contributed to the assessment.

During the development of the study protocol the Chief Investigator should seek advice from the lead experts at the earliest possible stage.

The ethical review will consider any research exposure that would be additional to exposure received by participants as part of normal clinical care if they opted not to participate in research. The main REC will consider whether the additional exposure is ethically acceptable, the risks and burdens involved in relation to the potential benefits, and the description of risk in the participant information sheet. Where there are differences between sites in radiation practice in clinical care, the main REC will need to consider whether this affects the ethical opinion.

4.2.3 Local Trust Approval

Arrangements for ensuring IRMER compliance at NHS Trusts will vary but usually this role is undertaken by a Medical Exposures Committee [MEC].

The Committee responsible for ensuring IRMER compliance has the responsibility of ensuring that an appropriate MPE has set appropriate dose constraints or targets for the exposure and that a CRE, acting as IRMER Practitioner for the project, has agreed that the exposures are justified and are authorised.

4.2.4 Sponsor Responsibilities

For studies involving research exposures under IRMER, the trial sponsor will require assurance that organisations hosting the study (whether NHS or non-NHS organisations) will comply with their IRMER responsibilities.

This should be addressed in the terms of the agreements between the sponsor and the host organisations. Sponsors should also ensure that local PIs are aware of the need to follow local IRMER procedures.

5 Related SOPs and Documents

International Conference on Harmonisation Guidance on Good Clinical Practice (Topic E6) (CPMP/ICH/135/95)

"Approval of research involving ionising radiation", available here: http://www.nres.npsa.nhs.uk/applicants/guidance/

http://www.arsac.org.uk/