Hull and East Yorkshire Hospitals NHS
NHS Trust

A Handbook for Researchers involved in Non-CTIMP studies

Version 1, 09.01.2015

Non-CTIMPS are studies which **do not** use Investigational Medicinal Products (IMPs) as defined by the Medicines and Healthcare products Regulatory Agency (MHRA)

Great Staff - Great Care - Great Future

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Research Governance: The Basics

Research Governance may loosely be defined as a range of regulations, principles and standards which exist to achieve and improve research quality across all aspects of health and social care.

Research Governance aims to:

- Safeguard research participants
- Protect researchers
- Enhance ethical and scientific quality
- Minimise risk
- Monitor performance
- Promote good practice

Of these aims, the touchstone of research governance is safeguarding the dignity, rights, safety and wellbeing of all research participants.

The Research Governance Framework (RGF) 1

The Research Governance Framework for Health and Social Care (RGF) is a Department of Health document which sets out the broad principles of good research governance. It ensures that health and social care research in England is conducted to the highest standards.

The RGF acts as a key text, underpinning the conduct of research in the NHS; it is implemented and enforced by the HEY Research & Development Department (R&D Department).

The aim of the RGF is not to provide a single document that addresses all legislation, standards and good practice guidelines – but to promote a quality research culture where excellence is promoted and where there is visible and strong research leadership and expert management.

The RGF applies to all research, both clinical and non-clinical, that is concerned with the protection and promotion of public health and which is to be undertaken in an organisation falling within the remit of the Secretary of State (NHS Trusts and Primary Care Trusts, for example). It also applies to research undertaken by industry (pharmaceutical companies), charities, research councils and universities that might have an impact on the quality of health and social care services.

When the HRA becomes a Non-Departmental Public Body (NDPB), from 01 January 2015, it will take responsibility from the Department of Health for issuing guidance for research in England, in place of the Research Governance Framework (RGF). The current version of the RGF will be withdrawn when the new framework is published. - See more at: http://www.hra.nhs.uk/about-the-hra/our-plans-and-projects/replacing-research-governance-framework/#sthash.hhD6A9Re.dpuf

1 Research Governance Framework for Health and Social Care: Second Edition, 2005. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4108962

Research Ethics Committee Approval

What is Research Ethics Committee (REC) Approval?

The Declaration of Helsinki (World Medical Association, as amended 2008), sets out the ethical principles for medical research involving human subjects – including research on identifiable human material and data. It is perhaps the most important document in the history of research ethics.

The role of Research Ethics Committees (RECs) is to safeguard the rights, safety, dignity and well-being of research participants by ensuring that research proposals have been designed and will be conducted in accordance with the Declaration of Helsinki. If they are satisfied that this is the case, they will offer a 'favourable opinion' for the research (often referred to as 'REC approval').

RECs are entirely independent of NHS Trusts and investigators.

When do I need it?

As a general rule of thumb, all research taking place within the NHS requires REC approval.

REC review is not normally required for research involving NHS or social care staff recruited as research participants by virtue of their professional role. However, NHS Research & Development (R&D) approval is still required.

How do I know if my project is 'research'?

Not all projects undertaken within the NHS are 'research.' The term 'research' has a specific meaning in the RGF and if a proposal does not fall within this definition it will not require review by a REC or approval by an NHS Research & Development (R&D) office.

Activities which do not fall within the definition of 'research' include:

- Audit
- Service Evaluation
- Patient & Staff Surveys
- Case Studies or Case Reports
- Consensus Methods

Applications for REC review may also be made on a voluntary basis for research tissue banks/bio banks and research databases.

The Health Research Authority (HRA) website has some useful guidance on categorising research proposals.

If having considered the guidance you are still unsure whether your project is classified as research, the Research & Development (R&D) office may be able to help. If the R&D office is uncertain, then a summary of the research can be sent to the chair of a REC for review.

How do I apply?

Applications for REC approval and for other approvals necessary for a project can be made online via the Integrated Research Application System (IRAS). This system streamlines the process for seeking relevant approvals by ensuring that, as far as possible, details only need to be entered once for a single project and much of the form then self populated.

Once you are ready to submit the forms in IRAS (i.e. the forms are signed by various parties and all supporting documentation outlined in the IRAS online checklist has been prepared and uploaded) follow instructions below.

- Refer to HRA website for information about RECs that could review your research and meeting dates
- When you telephone to book your application you will need to provide the IRAS Project ID and key information about your project.
- Phone the Central Booking Service (CBS) on 0161 625 7836.
- Confirmation of your REC booking will be provided via email

It is highly recommended that you arrange a time when you can attend, to answer any queries the REC may have.

When the booking process is completed, you will be given the name of the REC, a REC reference number and a submission date. The application should be submitted to the REC immediately after making the booking.

At the meeting of the REC, between 7 and 18 members will be present and will ask questions surrounding any ethical issues arising from your application. You should be prepared to clarify any ethical issues that may be raised.

How long does it take?

A REC is required to give an ethical opinion on an application within **60 calendar days** from receipt of a valid application. Where further information is required to give an opinion, the REC may make a request in writing for further information. The clock will be suspended pending receipt of this information.

A REC will typically issue an opinion within **10** working days after the meeting

NHS Research & Development (R&D) Approval

What is R&D Approval?

'R&D Approval' relates to the process of reviewing and checking applications for research to take place within an NHS organisation, prior to giving written permission. It is also frequently referred to as **NHS Permission or R&D Management Approval**. In most NHS organisations, an R&D office is responsible for carrying out these checks before permission is given by the R&D Manager or a delegated senior person.

When do I need it?

Approval will be required from the R&D departments for each NHS organisation involved in the research, if the research proposal is to involve any one or more of the following:

- Patients and service users of the NHS;
- Individuals identified as potential participants because they are relatives or carers of NHS patients and services users;
- Patient data, organs and other bodily materials of past or present NHS patients;
- Foetal material and IVF involving NHS patients;
- Use of or potential access to NHS premises or facilities; and/or
- NHS Staff (whether as participants or research personnel)

As a general rule, R&D approval will always be required if REC approval is required (see above). There may also be occasions where R&D approval is required when REC approval is not required (e.g. laboratory research on NHS premises).

How do I apply?

You can complete an application for R&D approval via the Integrated Research Application System (IRAS) which can be found at: http://www.myresearchproject.org.uk

This should be accompanied by a Site Specific Information (SSI) Form outlining the various activities to be carried out at HEY. Separate SSI forms can be generated for each organisation where the research will take place. The R&D form and SSI form generated within IRAS will then need to be submitted to the R&D office by email- research.development@hey.nhs.uk with a number of other documents, depending on the nature of the project. Checklists for these documents can be found in **Appendix A**.

What does the process involve?

The RGF requires NHS organisations to ensure that before any research involving human participants, their organs, tissue or data commences:

- there are adequate arrangements and resources (finance, staff and facilities capacity) to meet the standards set out in the RGF through to project completion;
- an identified sponsor has taken on responsibility for the project;
- the project has received ethical approval (where required);
- a 'Declaration of No Objection' has been received for a clinical investigation of a medical device;
- other regulatory approvals are in place depending on the nature of the research;
- honorary contract /letter of access if HEY is not your substantive employer
- the allocation of responsibilities is agreed and documented;
- appropriate contractual arrangements are in place; and
- Legislation relating to the research is followed within the organisation.

In order for the R&D office to confirm that adequate resources are in place, a member of the R&D team may need to arrange a short feasibility meeting with the Principal Investigator (or delegated member of the research team).

How long does it take?

The length of time taken to obtain R&D approval varies depending on each individual project, the other approvals necessary (see below), and the R&D offices at different NHS organisations.

We recommend that your application to the HEY R&D office is submitted at the same time as applying for REC approval (see above). If you provide us with all the documents required (see **Appendix A**) as early as possible, and are available to answer any further queries we may have, then this will help reduce the approval time.

The HEY R&D Office aims to complete initial feasibility within 30 days and issue NHS Permission within 15 days.

Research Involving NHS Staff

Do I need REC approval?

REC review is not normally required for research involving NHS or social care staff recruited as research participants by virtue of their professional role.

However, the Research Ethics Service may accept an application for review of research involving staff if the proposal raises material ethical issues. This can be requested by the sponsor, chief investigator or host organisation.

It is important to remember that ethics approval is required if the research involves any other activity that falls within the requirements for ethical review. Information regarding activity requiring ethical review is available on the **HRA Website**.

Do I need R&D Approval?

Yes. The Research Governance Framework for Health and Social Care still applies, and the research will continue to require R&D approval from each site involved.

The process for obtaining R&D approval for research involving NHS staff remains the same as for any other research project. Further information about the process for obtaining R&D approval is available in section 3, above.

Do I need to complete an R&D application form in IRAS?

As R&D approval is still required for research involving NHS staff, you still need to complete an application for R&D approval via the Integrated Research Application System (IRAS) which can be found at: **http://www.myresearchproject.org.uk**.

Within IRAS, it is possible to indicate in the Filter that a research project requires review by NHS R&D only. This will generate the necessary R&D application forms.

Sponsorship, Peer Review & Insurance

What is a sponsor?

A sponsor is an organisation (or group of organisations) that accepts responsibility for ensuring that there are proper arrangements to initiate, manage, monitor and finance a project. The RGF requires that all research taking place in an NHS or social care context must have a sponsor.

Evidence of sponsorship will be required by the R&D office before approval can be given.

Who may act as sponsor?

Any organisation that is a legal entity and which funds, initiates, hosts or employs staff involved in research may act as sponsor. While there is no official rule against individuals acting as sponsors, HEY will not indemnify research in these circumstances owing to the risks and legal liabilities involved.

The sponsor will usually be:

- The Chief Investigator's (CI) employing organisation;
- The University, for student research projects;
- The lead organisation providing health or social care to participants (e.g. NHS Trusts); or
- The primary funder (i.e. Commercial/Pharma Company).

Will HEY sponsor my research?

Hull and East Yorkshire Hospitals NHS Trust is registered with the Department of Health as willing and able to act as a sponsor under the RGF. This does not mean that HEY will accept sponsorship for all research requiring a sponsor.

HEY will consider accepting sponsorship where:

- The CI holds a substantive or honorary employment contract with the Trust;
- The research will only be carried out within the UK;
- The research does not pose significant legal, financial or reputational risks;
- The protocol is well-designed and is scientifically and statistically sound.

A request for HEY to act as sponsor can be made by emailing a copy of the research protocol and all other available information to research.development@hey.nhs.uk – including 'Sponsorship Request' in the subject line. This request should be made in conjunction with completing the REC application through IRAS.

What are the sponsor's responsibilities?

The sponsor's primary responsibility is to safeguard the rights, safety, dignity and well-being of research participants. This responsibility prevails over the interests of science.

In doing so, the sponsor will accept responsibility for securing the necessary arrangements to conduct the research and will ensure that all the necessary authorisations have been obtained before commencing.

Can the sponsor delegate its responsibilities?

No, but the sponsor can delegate any and all of their functions but cannot delegate responsibility, which always remains with them. The functions which have been delegated by the sponsor to the CI or Principal Investigator (PI) will usually be set out in an 'agreement. These responsibilities can further be delegated among members of the research team provided this is recorded in a 'delegation of duties log.'

Peer Review

Peer review is a system where a research proposal or protocol is scrutinised by independent experts to promote quality research and prevent poorly designed research from taking place. While the RGF places responsibility for assuring the quality of research through peer review to the funder, this will sometimes be undertaken by the sponsor (if they are not the same organisation). Depending on the type of research, this can also be carried out by the academic supervisor or within the research team.

The R&D office may require confirmation of peer review and in certain circumstances an independent peer review will be carried out.

Insurance & Indemnity

A key responsibility of the sponsor is to put in place arrangements for compensating participants if they suffer any harm as a result of their involvement in a project.

For research sponsored by HEY, the NHS Indemnity Scheme applies and provides unlimited cover for NHS staff, medical academic staff with honorary contracts and those conducting research for negligent harm. Non-negligent harm (i.e. harm that has been caused through no fault of those conducting research) is not covered by this scheme, however ex gratia payments may be considered by the Trust in limited circumstances.

For research sponsored by commercial companies and academic institutions the arrangements for indemnity are covered in the agreement that the R&D office negotiates with the company or institution.

Other Approvals

MHRA Declaration of No Objection

A Declaration of No Objection is required for clinical investigations (trials) of medical devices. This includes non-CE marked devices, CE-marked devices which have been modified or are being used outside their intended purpose(s), non-CE marked devices developed in-house or 'off-label' use.

Confidentiality Advisory Group (CAG)

NIGB approval is required for using patient information without consent. Approval will only be given where consent is impracticable and where pseudonymous or anonymous data will not suffice.

Administration of Radioactive Substances Advisory Committee (ARSAC) Certificate

An ARSAC certificate is required for any clinician (at each research site) who wishes to administer radioactive materials to human subjects, for example nuclear medicine scans (including PET scans) and nuclear medicine therapies. This does not apply to routine X-rays or CT scans.

Gene Therapy Advisory Committee (GTAC) Approval

GTAC has UK-wide responsibility for the ethical oversight of proposals to conduct clinical research involving gene or stem cell therapies.

Ionising Radiation (Medical Exposure) Regulations 2000 (IRMER) Approval

If the research involves (or might involve) ionising radiation (diagnostic X-rays, CT scans, DXA scans, radiotherapy, radionuclide imaging), the proposal will need to be reviewed by the HEY Medical Physics Expert who will sign-off on any use.

Human Tissue Authority (HTA) Licence

The storage of human tissue (or 'relevant material') for research purposes will require a licence from the HTA in certain circumstances. Samples may be held after the declaration of the end of the trial, for analysis or verification of research data for up to one year. After this period legal authority to hold any human tissue under the ethical approval will expire. To ensure that any continued storage is lawful, either the tissue must be held on premises with a storage licence from the Human Tissue Authority, or an application made for ethical approval of another project before the favourable ethical opinion of the existing project expires. Otherwise the tissue would need to be destroyed in accordance with the HTA Codes of Practice.

ICH GCP

What is ICH GCP?

Good Clinical Practice (GCP) is the ethical and practical standard to which all clinical research is conducted. The GCP guidelines were developed by the International Conference on Harmonisation (ICH). While these guidelines primarily relate to the conduct of clinical trials of Investigational Medicinal Products (CTIMPs), they are equally relevant and applicable to the conduct of <u>all</u> research.

"Good Clinical Practice is a set of internationally recognised ethical and scientific quality requirements which must be observed for designing, conducting, recording and reporting clinical trials that involve the participation of human subjects." (*Definition from EU Directive 2001/20/EC, article 1, clause 2)*

Compliance with this good practice provides assurance that the rights, safety and well-being of trial subjects are protected, and that the results of the clinical trials are credible and accurate.

The principles of good clinical practice are outlined in articles 2 to 5 in the EU Directive 2005/28/EC.

Do I need GCP training?
Everyone involved in the conduct of clinical research must have training to ensure they are best prepared to carry out their duties. This is laid down in the Research Governance Framework for Health and Social Care 2005, covering all research in the NHS in England, and in law for those people working on clinical trials.

The principles of GCP state that: Each individual involved in conducting a trial should be qualified by education, training and experience to perform his or her respective task(s). (*2.8, E6 Guideline for Good Clinical Practice*)

It is highly recommended by Hull and East Yorkshire Hospitals NHS Trust (HEYHT) that GCP training should be completed every 2 years and a copy of your certificate must be provided to the R&D office before NHS Permission will be given to your study.

How do I get GCP training?

NIHR CRN have developed GCP training courses which have a practical focus, with the key aim that participants know what to do to practise excellent GCP when they return to their workplace to ensure the rights, safety and well-being of patients and the quality of the research data. For those new to research there is an Introduction to GCP course which is an attended full day course and there is an online course for

Introduction to GCP. For those who have attended a GCP Introduction session there are GCP Refresher courses which are attended half day courses.

All the courses are appropriate for people conducting CTIMPs and non-CTIMPs research. Courses are available throughout the Yorkshire and Humber region. These courses are accessible to book on the NIHR Learning Management System (LMS) website - http://www.crn.nihr.ac.uk/learning-development/good-clinical-practice/ you will be required to register on the NIHR LMS website after which you will have access to all the training courses they provide.

What about medical devices?

A medical device is a product which is used for medical purposes in patients for diagnosis, therapy or surgery and can be anything from a plaster to a surgically implanted therapy.

There is at present no specific training for running medical device trials but the MHRA website gives clear information regarding clinical trials involving medical devices and they are happy to answer any questions that you may have about the UK regulatory process.

The link to the MHRA website is:
http://www.mhra.gov.uk/Howweregulate/Devices/Clinicaltrials/index.htm

Conducting your Research

To conduct your study you must:

- Identify a sponsor
- Have a favourable ethical opinion from a research ethics committee
- Have NHS Permission (R&D approval) to conduct the study
- Maintain a Trial Master File – *a List of Contents and documents are available on the R&D website,* http://www.hey.nhs.uk/rd
- Receive informed consent from the participant
- Collect accurate data. *A Data Collection Form template is available on the R&D website to adapt for your study*
- Create a clear audit trail
- Be aware of the safety reporting requirements
- Conduct the study to Good Clinical practice guidelines
- Be adequately funded

When can my Research begin?

Once all the necessary approvals required for any research have been received and NHS Permission has been granted, the research can proceed. Please note it is a condition of any Research Ethics favourable opinion that 'NHS Management Approval' is given for each NHS organisation participating in the research before commencing.

At study set up your study will have been risk-assessed by R&D and should it be considered a "high risk" study the R&D Clinical Trials Monitor will arrange a pre-study monitoring visit with you to ensure that everything is in place and appropriately set up before you begin your research. For all other studies an audit will be carried out by Hull and East Yorkshire Hospitals NHS Trust – Research and Development Department at specific time points during the life of your study.

When to contact the R&D office

It is important that you make contact with the R&D office in the following circumstances:

- Where approval is being sought for a substantial or non-substantial amendments
- Where there are concerns regarding research misconduct, a breach of GCP, or a breach of confidentiality or data protection laws
- If you are having difficulties with patient recruitment
- Submitting participant accruals information
- Providing annual progress or safety reports to REC
- When a project has closed to recruitment

Please also contact the R&D office if you have any queries or concerns or there is any information about your research that you think we would like to know. The R&D office is here to help and support you with the research you are undertaking.

Amendments

What are amendments?

Amendments are changes made to your study after a REC favourable opinion has been granted or, in the case of a non-CE marked medical device an MHRA letter of no objection, and REC favourable opinion has been granted. These amendments can be substantial or non-substantial.

For all studies, it is the responsibility of the Sponsor (HEYHT) to determine whether an amendment is substantial therefore, you must contact the R&D office to discuss any changes you wish to make. **R&D will then confirm whether the changes are a substantial or non-substantial amendment**

What are substantial amendments?

Substantial amendments are defined as amendments to the original REC application or to the protocol or any other supporting documentation that is likely to affect to a significant degree:

- The safety or physical or mental integrity of the subjects of the research;
- The scientific value of the research;
- The conduct or management of the research

Examples of substantial amendments:

- Changes to the design or methodology of the study, or to background information affecting its scientific value;
- Changes to the procedures undertaken by participants;
- Any change relating to the safety or physical or mental integrity of participants, or to the risk/benefit assessment for the study;
- Significant changes to study documentation such as participant information sheets, consent forms, questionnaires, letters of invitation, letters to GPs or other clinicians, information sheets for relatives or carers;
- A change of sponsor(s) or sponsor's legal representative;
- Appointment of a new Chief/Principal investigator;
- A change to the insurance or indemnity arrangements for the study;
- Temporary halt of a study to protect participants from harm, and the planned restart of a study following a temporary halt;
- A change to the definition of the end of the study;
- Any other significant change to the protocol or the terms of the REC application.

Examples of non-substantial amendments:

- Minor changes to the protocol or other study documentation, e.g. correcting typing errors, updating contact points, minor clarifications;
- Changes to the research team (other than appointment of key collaborators);
- Changes in funding arrangements;
- Changes in the documentation used by the research team for recording study data (Case Report Forms, Data Collection Forms);
- Changes in the logistical arrangements for storing or transporting samples;
- Extension of the study beyond the period specified in the application form.

Preparing amendments

Substantial Amendments

Notice of substantial amendment forms are created in IRAS; the system automatically generates the type of notice of substantial amendment form that is appropriate to the project category.

To generate the notice of substantial amendment form in IRAS open your study, highlight the REC application on the Navigate page and then select the Amendment tab and follow the instructions provided. Notice of Substantial Amendment forms and any accompanying documentation should be emailed to the REC

You should summarise the change(s) included in the amendment and briefly explain the reasons in each case on the notice of amendment.

You should submit the documents that have been modified, showing both the previous and new wording so that the changes can be readily identified, with the form.

The Notice of Substantial Amendment form generated in IRAS must be used. The form should be electronically authorised in IRAS by the sponsor and the Chief/Principal Investigator. Without any of the authorisations, the amendment will not be validated.

Please note: **You must not implement any amendment without notifying the R&D office, unless urgent safety measures have been taken. Urgent safety measures which would be equivalent to substantial amendments must be treated as such after the event.**

Non-substantial Amendments

If the R&D office is satisfied that an amendment is not substantial, there is no requirement to notify the REC at the time of the changes (although, you should inform REC of non-substantial changes when you next advise of a substantial amendment in order that they can maintain an up to date log of events).Although

non-substantial amendments may be notified for information only at R&D Manager's discretion. Sponsors may seek advice from the REC office directly on whether an amendment should be considered substantial or not.
How long does it take?

The REC coordinator will confirm receipt of a valid notification within 5 days. Amendments are normally reviewed by a REC sub-committee and an opinion issued within a maximum of 35 days from the date of receipt of a valid notice of amendment. If an unfavourable opinion is given, a modified amendment can be submitted and an opinion is usually issued within 14 days of receipt.

The R&D office will usually review amendments once they are received, but will not be able to provide 'ongoing' approval for the research until a favourable opinion has been received from REC. All amendments are processed by the R&D Administration Co-ordinator, email: research.development@hey.nhs.uk Tel: 01482 461883 (internal 761883).

MHRA (Medical Devices) review of amendments
The following guidance only applies to amendments to clinical investigations of medical devices subject to regulation by the Competent Authority (i.e. those that have received a Notice of No Objection from MHRA).

You must notify MHRA Devices of all proposed changes to the investigation (not only those classified as substantial amendments for the purposes of ethical review) and await a letter of no objection from MHRA Devices before you implement them. This includes changes made at the request of the REC.

For details of how to notify MHRA refer to the MHRA website. www.mhra.gov.uk

Annual Progress Reporting

What is Annual Progress Reporting?

Research Ethics Committees (RECs) are required to monitor research that has received a favourable opinion. Therefore, researchers must submit Annual Progress Reports in order to inform REC of the progress of the research.

The information required in an Annual Progress Report relates to research conduct, recruitment, amendments, and safety.

When are Annual Progress Reports required?

A Progress Report should be submitted to the REC which gave the favourable opinion (the 'main REC') 12 months after the date on which the favourable opinion was given. Annual Progress Reports should be submitted thereafter until the end of the study.

How do I submit an Annual Progress Report?

It is the responsibility of the Chief/Principal Investigator to complete and submit Annual Progress Reports.

Annual Progress Report Forms are available on the HRA website at: http://www.hra.nhs.uk/resources/during-and-after-your-study/nhs-rec-annual-progress-report-forms/

There are separate forms for submitting Annual Progress Reports, depending on the type of research:

- *Annual Progress Report Form for Clinical Trials of an Investigational Medicinal Product (CTIMP)*.
- *Annual Progress Report Form for All other research- this is what you will require*

A paper copy of the Annual Report Form should be sent to the main REC, and a copy sent to the R&D office. The REC office will acknowledge receipt of the Annual Progress Report, and it will be reviewed by REC. If necessary, the Chief Investigator may be invited to attend a meeting of the main REC or a sub-committee to discuss the progress of the research.

Can I continue with my research after submitting an Annual Progress Report?

The main REC does not need to re-confirm its favourable ethical opinion each time an Annual Progress Report is received. It is generally assumed that the opinion applies for the duration of the research, although the REC may review its opinion at any time.

Safety Reporting

To be compliant with Good Clinical Practice (GCP), Research Governance Framework (RGF), Medical Devices Regulations 2002, Chief/Principal Investigators of Non-CTIMP clinical studies have a responsibility to record and report SAEs.

In research a Serious Adverse Event (SAE) is defined as an untoward occurrence that:
(a) Results in death;
(b) Is life-threatening;
(c) Requires hospitalisation or prolongation of existing hospitalisation;
(d) Results in persistent or significant disability or incapacity;
(e) Consists of a congenital anomaly or birth defect; or
(f) Is otherwise considered medically significant by the investigator.

An SAE occurring to a research participant should be reported to the main REC (the REC that gave favourable opinion of the study) where in the opinion of the Chief/Principal Investigator the event was:

"**Related**" – that is, it resulted from administration of any of the research procedures, and "**unexpected**" – that is, the type of event is not listed in the protocol as an expected occurrence.

The Chief/Principal Investigator or Sponsor must submit reports of **related** and **unexpected** SAEs within 15 days of the Chief/Principal Investigator becoming aware of the event, using the SAE report form for non-CTIMPs available from:
Reports of SAEs in double-blind trials should be unblinded.
http://www.hra.nhs.uk/

The Coordinator of the main REC will acknowledge receipt of safety reports within 30 days.

Urgent Safety Measures

The Chief/Principal Investigator must notify the main REC immediately of any Urgent Safety Measures and in any event within three days. The R&D office must also be notified immediately or in any event within three days.

Audit

Audit is a systematic, independent and documented process for obtaining audit evidence and evaluating it objectively to determine the extent to which the audit criteria are fulfilled. However most importantly, the purpose of audit is to support and advise investigators with their studies and to promote good research within the Trust.

Audits of the Hull and East Yorkshire Hospitals NHS Trust Sponsored non-CTIMP study portfolio will consist of the following types of audit:

- Self-assessment audit
- Routine “face to face” audit
- Triggered “face to face” audit

The purpose of study audit is to verify that systems are in place to ensure:

- The rights and well-being of human subjects are protected
- To collect the study data as stated in the protocol
- The conduct of the study is in compliance with the approved study protocol/amendments, GCP and the Research Governance Framework and with the applicable regulatory requirements.

Risk Assessment

Low Risk Studies – IRAS Category 5

Any study where the following is selected on the IRAS Project Filter form should be deemed a “low risk” study.

- Basic science study involving procedures with human participants
- Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
- Study involving qualitative methods only
- Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)
- Study limited to working with data (specific project only)
- Research tissue bank
- Research database

“Low risk” studies will be audited by annual self-assessment forms unless it is deemed by the R&D facilitator to be of high enough risk to warrant more frequent self-assessment or “face to face” auditing to take place.

Moderate and High Risk Studies – IRAS Category 2 and 4

Any study where the following is selected on the IRAS Project Filter form should be treated as "moderate risk" or "high risk":

- Clinical investigation or other study of a medical device
- Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice

Moderate Risk Studies – IRAS Category 2 and 4

Trust sponsored non-CTIMP "moderate risk" studies will follow a further risk-based assessment during the sponsorship/governance process, and will be divided into either of the following 2 categories:

- Requires a one off "face to face" audit with corrective actions and escalation if necessary
  Or
- Requires self-assessment but more frequently than annual assessment (variable self-assessment), again with escalation to a "face to face" visit if necessary.

High Risk Studies – IRAS Category 2

Those studies assessed as "High risk" studies, for example non-CE marked medical device or major surgical intervention studies, will be reviewed by the R&D QA Manager and if deemed appropriate monitored by the R&D Clinical Trials Monitor, however these studies can be down-graded by the QA Manager and will then be considered as Category 2 moderate risk studies which require a one off "face to face" visit.

The Audit Process

Routine "face to face" audits

The auditor will contact the Chief/Principal Investigator to notify them of the audit visit, provide an agenda and arrange a mutually agreeable meeting time. The agenda will outline a list of the study documentation which should be available for the visit. This will include the documentation required in the Trial Master File (TMF). The following documents, but not limited to, will be checked:

- Regulatory approvals
- Agreements
- Delegation Log
- Recruitment log
- Consent Forms
- Honorary contracts and GCP Training

- Safety Reporting
- Study Data Capture

Reporting

After the visit, the auditor will prepare a report and where necessary an action plan. A copy of this report will be sent to the Chief/Principal Investigator within 5 days of the visit. This should be reviewed and agreed by the investigator.

The Chief/Principal Investigator will be given a minimum of 6 weeks to complete any actions. The auditor will follow-up with the Chief/Principal Investigator to ensure all actions have been completed/resolved. A confirmation that the actions have been completed/resolved will be issued and a copy of this should be filed in the relevant section of the Trial Master File.

Follow up/Escalation
Failure to complete the actions within the agreed timescales will be escalated to the R&D Manager for review and necessary action.

Triggered auditing Very occasionally where there are concerns in relation to the conduct of a study a triggered audit may be required as part of an investigation to better understand the root of the concerns. Findings from the audit may help to establish the extent and cause of the concerns which can hopefully be resolved.

Completion

When is a project complete?

The completion of a project should be defined in the protocol. In most cases, completion will be the date of the last patient's last visit (LPLV) or the completion of any patient follow-up and data collection.

What should I do when my project has completed?

1. **Communicate completion to relevant bodies and authorities**

   For all projects, a 'Declaration of End of Study' form must be completed and sent to the REC that granted a favourable ethical opinion for the project. This form can be found online: http://www.hra.nhs.uk/resources/during-and-after-your-study/end-of-study-notification-studies-other-than-clinical-trials-of-investigational-medicinal-products/

   The R&D office should be forwarded a copy of this notification

2. **Final analysis of data and locking of the project database (if applicable)**

3. **Complete all financial obligations**
   Any outstanding invoices payable or to be raised should be dealt with and arrangements in place for providing treatment to participants after completion (if agreed).

4. **Writing of final project reports, dissemination and publication of findings**

5. **Archiving of documentation- HEY R&D contract RESTORE Services for external archiving**

What should I do when my project has not completed on time?

Occasionally projects do not finish recruiting or following-up patients within the time specified in the REC-approved protocol. An extension to the study end date is normally considered by the HRA to be a non-substantial amendment. While formal approval is not needed from the REC, it is good practice to write to the REC for information purposes only. However, if the extensions are lengthy seek REC and R&D advice.

In all cases, you must information the R&D office of this change.

Research Governance Tips

- Inform us immediately if you have been contacted directly to undertake any research

- Use the Checklist found in Appendix A to ensure all the required documents are submitted to R&D via our generic email address- research.development@hey.nhs.uk to ensure your study is allocated with an R&D reference number

- Be sure to include your R&D reference number on all correspondence with the R&D office

- Feel free to phone the R&D office if you have not received an R&D number for your project or you want to check on the progress of your application

- Allow **5 working days** from submitting your application before following up on progress

- If you are asked for further information or documents, provide these as soon as possible

- For large projects, it is preferable to provide a single point of contact

- The R&D office operates a paperless system and all documents must be submitted electronically

- Submit your application for sponsorship in conjunction with completing your REC application.

- When emailing your R&D and SSI Forms in IRAS, do so in both PDF and XML formats – this will help us to process your application more efficiently

- Throughout the process and after approval, it is recommended that all versions of project documentation are saved, including tracked changes

- Always communicate to the R&D office anything that may be of interest (i.e. competitive recruitment of patients/participants)

Useful Links and Resources:

Integrated Research Application System (IRAS)
https://www.myresearchproject.org.uk/

Health Research Authority (HRA)
http://www.hra.nhs.uk/

HRA Decision Tool
http://www.hra-decisiontools.org.uk/research/

MHRA medical devices
http://www.mhra.gov.uk/Howweregulate/Devices/Clinicaltrials/index.htm

National Institute for Health Research (NIHR) Learning Management System (LMS)
http://www.crn.nihr.ac.uk/learning-development/good-clinical-practice/

Human Tissue Authority (HTA)
http://www.hta.gov.uk/

Data Protection
https://www.gov.uk/data-protection/the-data-protection-act

Research Governance Framework for Health and Social Care: Second Edition, 2005.
http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4108962

Confidentiality Advisory Group (CAG)
http://www.hra.nhs.uk/resources/confidentiality-advisory-group/

Gene Therapy Advisory Committee (GTAC)
http://www.hra.nhs.uk/resources/applying-to-recs/gene-therapy-advisory-committee-gtac/

Administration of Radioactive Substances Advisory Committee (ARSAC)
http://www.hra.nhs.uk/research-community/applying-for-approvals/administration-of-radioactive-substances-advisory-committee-arsac/

Help and Further Information

James Illingworth

R&D Manager

james.illingworth@hey.nhs.uk

01482 461 883

Susan Walker

R&D Accountant

susan.walker@hey.nhs.uk

01482 622 099

Jane Pacynko

QA and Training Manager

jane.pacynko@hey.nhs.uk

01482 461 908

Sarah Moffat

Clinical Trials Monitor

sarah.moffat@hey.nhs.uk

01482 461 887

Priyai Parkinson

R&D Facilitator

priyai.parkinson@hey.nhs.uk

01482 461 882

Mike Murrey

R&D Facilitator

mike.murrey@hey.nhs.uk

01482 461 881

Louise Hunn

R&D Facilitator

louise.hunn@hey.nhs.uk

01482 461 890

Carol Hirons

R&D Facilitator

carol.hirons@hey.nhs.uk

01482 461 884

Janice Brentano

R&D Administrator

janice.brentano@hey.nhs.uk

01482 461 883

Hayley Croft

R&D Finance Analyst

hayley.croft@hey.nhs.uk

01482 461 883

Useful contacts

Human Resources

Tracey Thomas

tracey.thomas@hey.nhs.uk

01482 605 209

NIHR Industry Manager

Hazel Brook

hazel.brook@nihr.ac.uk

01482 622 355

Stats Advice

Victoria Allgar

victoria.allgar@hyms.ac.uk

01904 321 384

Information Governance

Ann Johnson

information.governance@hey.nhs.uk

01482 477 845

Clinical Audit

Vicki Shaw

vicki.shaw@hey.nhs.uk

01482 608 779

HYMS

Liz Rowson

liz.rowson@hyms.ac.uk

University of Hull

Dr Andrew Taylor

A.F.Taylor@hull.ac.uk

01482 465 317

Radiology

Trevor Parker

trevor.parker@hey.nhs.uk

Medical Physics

Dr Craig Moore

craig.moore@hey.nhs.uk

Labs

Anne Anderson

anne.anderson@hey.nhs.uk

PALs

01482 623 065

pals@hey.nhs

HRA Central Booking Service

0161 625 7836

Appendix A – R&D Valid Submission Checklist

HEY Principal Investigator	
Full Study Title	
CSP Reference Number (if applicable)	

	Non - CTIMP	CTIMP	Enclosed (Yes/No/ NA)
Protocol			
R&D application form with HEY listed as a site			
REC Favourable Opinion			
Total number of participants expected to be recruited at HEY Trust - *mandatory*			
Estimated start date - month and year - *mandatory*			
Expected end of study – month and year - *mandatory*			
MHRA Approval			
Pharmacy Manual (if applicable)			
Investigator Brochure/ SmPC (as applicable)			
IMP Labels			
Participant Information Sheet – Informed Consent Form			
Confirmation email from Radiotherapy ***Only applicable for Oncology studies where radiotherapy is relevant, (not related to ionising radiation).***			

Please send above documents and the completed checklist to research.development@hey.nhs.uk

If documents are not available in the CSP documents repository we will ask for the study contact to request them from the sponsor. An R&D number will not be allocated until alldocuments required are received by R&D

Only applicable for Oncology studies where radiotherapy is relevant, (not related to ionising radiation). If you have any questions regarding submissions please do not hesitate to contact: Research & Development Department

Hull & East Yorkshire Hospitals NHS Trust, Office 13, 2nd Floor Daisy Building, Castle Hill Hospital, Castle Road, Cottingham, East Yorkshire, HU16 5JQ

Appendix B - Glossary

Commonly Used Research Abbreviations and Terms

ABPI	Association of the British Pharmaceutical Industry: A trade association for UK pharmaceutical companies
ADR	Adverse Drug Reaction (also known as AR)
AE	Adverse Event
Amendment	A written description of a change or formal clarification. Substantial amendments (See below under 'Substantial Amendment') to protocol, participant information/consent require REC, R&D, MHRA approval, Non-substantial amendments should be 'notified' to REC, R&D, MHRA
AMRC	Association of Medical Research Charities
AR	Adverse Reaction (also known as ADR)
ARSAC	Administration of Radioactive Substances Advisory Committee: Research studies wishing to administer radioactive medicinal products to human subjects need to obtain ARSAC approval before NHS R&D approval
ASR	Annual Safety Report: For studies involving the use of an Investigational Medicinal Product, this is the annual report which must be submitted to the MHRA detailing all SUSARs and SARs that have occurred in subjects on that study in the past year
ATMP	Advanced Therapy Medicinal Products
BP	Blood pressure
BRC	Biomedical Research Centre: larger centre covering a number of topics with facilities and research active clinicians/academics/research nurses to run clinical projects
BRU	Biomedical Research Unit: topic-focused centre which usually combines facilities and research active clinicians/academics/research nurses to run clinical projects, e.g. respiratory BRU
C/O	Complains of
CA	Competent Authority: organisation approving the testing of new drugs/devices or approving the marketing licences, in the UK this is the MHRA
CC	Coordinating Centre
CCRN	Comprehensive Clinical Research Network
CF	Consent Form (also ICF, Informed Consent Form)
CFR	Code of Federal Regulations (US)
CI (i)	Chief Investigator: The lead investigator with overall responsibility for the research. In a multi-site study, the CI has coordinating responsibility for research at all sites. The CI may also be the PI at the site in which they work. In the case of a single-site study, the CI and the PI will normally be the same person and are referred to as PI.
CI (ii)	Coordinating investigator
CLRN	Comprehensive Local Research Network: CLRNs are the primary vehicle for providing infrastructure to support study involvement at local NHS Trusts. There are 25 in England.
COREC	Central Office for Research Ethics Committees (replaced in 2007 by NRES)
CRA	Clinical Research Associate: usually a commercially employed person supporting the management of clinical studies, helps with obtaining R&D approval, site initiation, study monitoring and close out
CRF (i)	Case Report Forms: data collection tools provided by a sponsor on which the clinical data is recorded for each participant, such as weight, lab results, symptoms
CRF (ii)	Clinical Research Facility: hospital-like facility with consulting rooms, standard patient beds, ward medical equipment, research nurses supporting only research
CRN	Clinical Research Network
CRO	Clinical Research Organisation or Contract Research Organisation: A person or an organisation (commercial, academic or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions
CSAG	Clinical Studies Advisory Group
CSG	Clinical Studies Group
CSP	Coordinated System for gaining NHS Permissions: Standard process for adoption onto NIHR Portfolio of Studies in order to access NIHR CRN Support and funding; streamlines the process for gaining NHS permissions by collating the information for global and local approvals; researchers initiate this in IRAS by completing and submitting CSP Application Form
CTA (i)	Clinical Trials Administrator: person providing coordinating/secretarial support for running clinical studies
CTA (ii)	Clinical Trials Agreement: contract between the legal Sponsor and the hosting research sites
CTA (iii)	Clinical Trials Associate (similar to CRA): person involved in the management of a study from initiation, through conduct/monitoring to close-out
CTA (iv)	Clinical Trials Authorisation: The regulatory approval for a clinical trial of a medicinal product issued by the MHRA

CTAAC	Clinical Trials Advisory and Awards Committee
CTD	Clinical Trial Document
CTIMP	Clinical Trial of an Investigational Medicinal Product
CTU	Clinical Trials Unit: Design and manage CTIMPs, sometimes in specialist clinical areas, such as Cancer, or types of trial, such as RCTs
CV	Curriculum Vitae
D&V	Diarrhoea and Vomiting
DCF	Data Collection Form
DeNDRoN	Dementias and Neurodegenerative Diseases Research Network
DH	Department of Health (for England)
DIPEx	Database of Individual Patient Experience – the DIPEx website has a range of open source videos of real patient experiences www.healthtalkonline.org
DNA	Did not attend
DPA	Data Protection Act
DQ	Data query
DRN	Diabetes Research Network
DSMB	Data and Safety Monitoring Board: An independent committee composed of clinical research experts and community representatives that reviews data whilst a clinical trial is in progress to ensure that participants are not being exposed to undue risk
ECG	Electrocardiogram
ECMC	Experimental Cancer Medicine Centre
EM	Experimental Medicine
EMA	The European Medicines Agency: A body of the European Union which has responsibility for the protection and promotion of public health through the evaluation and supervision of medicines for human use
EU	European Union
EudraCT	European Clinical Trials Database: A database of all clinical trials in Europe, held since 1994 in accordance with EU directive 2001/20/EC
FAQ	Frequently Asked Questions
FDA	Food and Drug Administration: the Competent Authority in the United States, giving authorisation to conduct clinical trials and issuing marketing licences
GAfREC	Governance Arrangements for Research Ethics Committees
GCP	Good Clinical Practice: A specific internationally recognised version of this is ICH-GCP (see below)
GLP	Good Laboratory Practice: standard for laboratories involved in pre-clinical analyses (e.g. animal, in vitro); does not apply to Laboratories analysing samples from clinical trials involving humans
GMP	Good Manufacturing Practice: quality assurance standard for producing IMP, medicinal products
GTAC	Gene Therapy Advisory Committee: the ethics committee for clinical studies using genetically modified products; usually no REC approval required
HEI	Higher Education Institution
HEY	Hull and East Yorkshire Hospitals NHS Trust
HFEA	Human Fertilisation and Embryological Authority
HRC	Honorary Research Contract
HTA	Human Tissue Act or Human Tissue Authority
HTA	Health Technology Assessment – one of the NIHR research funding streams
IB	Investigator's
ICH-GCP	International Conference on Harmonisation (Europe, USA, and Japan): Defined standards for the terminology, design, conduct, monitoring, recording, analysis and reporting of a study. These standards give assurance that the reported results are accurate and credible and that the rights, integrity and confidentiality of all study participants have been protected throughout the study. Section E6 of ICH defines principles of Good Clinical Practice (referred to as ICH-GCP). Research teams on CTIMPs in the UK must follow GCP requirements as detailed in MfHU (CT) Statutory Instruments; all non-CTIMP studies conducted within the NHS adhere to GCP according to Research Governance Framework
IDMC	Independent Data Monitoring Committee
IMP	Investigational Medicinal Product: an unlicensed new drug, or an existing drug tested outside its licence, or existing drugs tested against each other for their efficacy/safety. The MHRA provide an algorithm to establish whether a study is a CTIMP: see Resource 2 or the MHRA website (provided on p67) http://www.mhra.gov.uk/home/groups/l-unit1/documents/websiteresources/con009394.pdf
IND	Investigational New Drug: sometimes used instead of IMP
Indemnity	Compensation for damage, loss or injury
Investigator	Researcher conducting the (clinical) study, those researchers leading the team are referred to as CI or PI

IRAS	Integrated Research Application System: A single, web-based system for completing applications for the permissions and approvals required for health and social care research in the UK. The various applications can be printed or submitted for this single system (includes REC, R&D, MHRA, GTAC, NIGB, ARSAC)
IRB	Independent Review Boards: US equivalent of authorised REC
IRMER	Ionising Radiation Medical Exposure Regulations: part of NHS R&D approval, usually done by the local hospital experts
ISF	Investigator Site File: A file designed for use in organising and collating all essential documentation required to conduct a study in accordance with the principles of GCP and the applicable regulatory requirements (e.g. REC approval letter/correspondence, MHRA approval, blank CRF, staff CVs, delegation of duties log etc.)
ISRCTN	International Standard Randomised Control Trial Number: A simple numeric system for the identification of randomised controlled clinical trials worldwide. Allows the identification of trials and provides a unique number that can be used to track all publications and reports resulting from each trial; can be obtained from www.isrctn.org or www.controlledtrials.com/mrct
LRN	Local Research Network
MCA	Mental Capacity Act
mCIA	model Clinical Investigation Agreement: for medical devices, covers the running of the study, not design of prototype or design of protocol; standard template for the UK (use is not obligatory)
MCRN	Medicines for Children Research Network
mCTA	model Clinical Trial Agreement: for IMP studies with commercial sponsor/CRO conducted; standard template for the UK (use is not obligatory)
MfHU (CT)	Medicines for Human Use (Clinical Trials) Regulations: SI 2004:1031 and subsequent amendments 2006:1928, 2006:2984 ,2008:941, 2009:1164 and 2010:1882 are the UK Statutory Instruments translating EU directives 2001/20/EC and 2005/28/EC into UK law, laying down the legal requirements for conducting CTIMPs in the UK
MHRA	Medicines and Healthcare products Regulatory Agency: The UK Competent Authority (CA) and licensing authority for medicines and medical devices. It replaced both the Medical Devices Agency (MDA) and the Medicines Control Agency (MCA) in April 2003
MHRN	Mental Health Research Network
mNCA	model Non-Commercial Agreement: for clinical research studies; standard template for the UK (use is not obligatory)
Monitor	The person designated by the sponsor to perform site visits and conduct the monitoring process; e.g. check whether there are any deviations from the protocol and that all source data was transferred into the Case Report Forms correctly
MRC	Medical Research Council
Multi Centre Study	A study conducted according to a single protocol but carried out at more than one site and by more than one investigator; one CI oversees several local PIs
NCRN	National Cancer Research Network
ND	Not done
NHS	National Health Service
NICE	National Institute for health and Clinical Excellence (decides which drugs are accepted into NHS treatment)
NIGB	National Information Governance Board for Health and Social Care Ethics and Confidentiality Committee
NIHR	National Institute for Health Research: established by Department of Health for England in 2006 to provide the framework through which DH will position, manage and maintain the research, research staff and infrastructure of the NHS in England as a virtual national research facility
NIHR CRN CC	National Institute for Health Research Clinical Research Network Coordinating Centre
NIHR IS	National Institute of Health Research Information Systems
NIMP (or non-IMP)	Non-Investigational Medicinal Product: product used alongside IMP but not directly under investigation in the research study, e.g. a challenge agent
NK	Not known
NOCRI	National Office for Clinical Research Infrastructure
Non-substantial amendments	Changes to the details of a study that have no significant implications for the subjects, the conduct, the management or the scientific value of the study (sometimes referred to as administrative amendments).
NRES	National Research Ethics Service: umbrella organisation responsible for all REC across the UK (replaced COREC in 2007)
OSCHR	The Office for Strategic Coordination of Health Research (UK wide)
PCF	Patient/Participant Consent Form
PCRN	Primary Care Research Network

PCT	Primary Care Trust
PI	Principal Investigator: The lead person at a single site designated as taking responsibility within the research team for the conduct of the study
PIAG	Patient Information Advisory Group (now NIGB)
PIC	Participant Identification Centre: NHS or other organisation which only identifies participants from a database etc., but recruitment/receiving consent and study conduct are managed elsewhere
PIS	Participant or Patient Information Sheet: An information leaflet given to those who have been invited to participate in a research study. The sheet is designed to provide the potential participant with sufficient information to allow that person to make an informed decision on whether or not they want to take part
PPI	Patient and Public Involvement
QA	Quality Assurance
QC	Quality Control
QLQ	Quality of Life Questionnaire
R&D	Research and Development: often name of Department within NHS hospitals giving permission to conduct projects on those facilities with patients/staff
RCT	Randomised Controlled Trial: A randomised controlled trial (RCT) is a clinical study in which two (or more) forms of care are compared; the participants are allocated to one of the forms of care in the study, in an unbiased way
RDS	Research Design Service: organisation with a number of experts who can help write the protocol/documents for NIHR grant applications
REC	Research Ethics Committee: authorised by NRES to review study documents for research taking place in the NHS, or social services. Some REC specialise in Clinical Trials, or topics such as research in children, MCA. See NRES website for more detail and other types of research http://www.nres.npsa.nhs.uk/ All Research in NHS/social services must have been reviewed by a UK REC
Research Passport	A system for HEI employed researchers/postgraduate students who need to undertake their research within NHS organisations, which provides evidence of the pre-engagement checks undertaken on that person in line with NHS Employment Check Standards (among them CRB and occupational health checks)
RfPB	Research for Patient Benefit: NIHR research funding stream
RGF	Research Governance Framework: DH guidance for the conduct of research within the NHS in England (use 2nd edition, 2005)
RM&G	Research Management and Governance
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SDV	Source Data Verification: checking the original data record, such as lab reports, patient medical notes against what was transferred onto the CRF/into a database
Serious-ADR	Adverse drug reaction which falls in to one of the serious criteria and therefore warrants expedited reporting (serious = resulting in hospitalisation, prolonged hospitalisation, death, life-threatening, congenital anomaly/birth defect or persistent or significant disability/incapacity)
SHA	Strategic Health Authority
SI (i)	Statutory Instruments: document which defines UK law in on a specific topic, e.g. how to manage a clinical trial
SI (ii)	Sub-Investigator (as in ICH-GCP, ICH does not use the term Co-investigator)
Site	The NHS organisation in which study activities and assessment are performed or the location(s) where trial-related activities are actually conducted. Each site/Trust needs to give R&D approval
SLA	Service Level Agreement
SMO	Site Management Organisation
SmPC	Summary of Product Characteristics: smaller version of Investigator Brochure with details on pharmacological effects, side effects, but issued for a product that already holds a marketing licence
SOP	Standard Operating Procedure: detailed written instructions designed to achieve uniformity of the performance of a specific function
SRN	Stroke Research Network
SSA	Site Specific Assessment: An assessment performed to establish the suitability of a Principal Investigator and a site for the conduct of research; SSA will be performed by the Participating CLRN for each research site (NHS organisation), using an SSI form available in IRAS
SSI	Site Specific Information: local detail to inform SSA including qualifications/expertise of the PI and wider research team, study procedures, departmental capacity to absorb project (includes Pharmacy, Pathology, Radiology) and departmental leads signatures; The SSI form is completed in IRAS

Substantial Amendment	A substantial amendment can be defined as an amendment to the protocol or any other study specific documentation, the terms of the REC application or the terms of the CTA application (as applicable) that is likely to affect to a significant degree the: □□The safety or physical or mental integrity of the subjects of the trial; □□The scientific value of the trial; □□The conduct or management of the trial; or □□The quality or safety of any investigational medicinal product used in the trial. Other changes to the particulars of a study that qualify as substantial amendments include: □□A change of sponsor(s) □□Appointment of a new Chief Investigator and □□Extension of the research beyond the planned closing date for recruitment A substantial amendment may not be made to a research study without the favourable opinion from the REC that gave a favourable opinion for the study (the main REC) and as applicable the MHRA. The only exceptions to this rule are: □□The Inclusion of a new research site or □□The Appointment of a new PI at an individual site Both of these qualify as substantial amendments but as they require further SSA and approval from the REC there is no requirement for notice of amendment to the REC. These changes do still however need to be notified to the MHRA (as applicable)
SUSAR	Suspected Unexpected Serious Adverse Reaction: A Serious Adverse Reaction (SAR) which is Unexpected (i.e. its nature and severity is not consistent with the known information about that product from the Investigator's Brochure or the SmPC) and suspected, as it is not possible to be certain of causal relationship with the IMP
TCRN	Topic specific Clinical Research Network: includes DRN, DeNDRoN, NCRN, MCRN, MHRN and SRN
TMF	Trial Master File (file with essential documents held by the Chief Investigator/Sponsor organisation)
UKCRC	United Kingdom Clinical Research Collaboration
WHO	World Health Organisation
WMA	World Medical Association
WT	Weight

This Glossary was taken from the NIHR Introduction to Good Clinical Practice (GCP) handbook and HEY R&D acknowledges that it was adapted with kind permission from The Southampton University Hospital Trust R&D Department and Basildon and Thurrock University Hospitals NHS Foundation Trust. *The NIHR are especially grateful for the contributions to this list from Dr Claudia Fellmer and the NIHR CRN GCP Facilitators.*