Hull University Teaching Hospitals NHS Trust

CP264 – Research And Development Operational Policy

Broad Recommendations / Summary

INTRODUCTION

This document is about both “research” - the attempt to derive generalizable new knowledge by addressing clearly defined questions with systematic and rigorous methods, and “development” - the implementation of research findings in local practice, particularly to establish their effectiveness.

The management, leadership and administration of all aspects of R&D fall within the responsibility of the R&D Office; which must ensure that all research is carried out in accordance with UK legislation, national and local policies, procedures and guidelines.

All research in the NHS must be conducted according to the standards of the UK policy framework for health and social care research, which sets out principles of good practice in the management and conduct of health and social care research that take account of legal requirements and other standards. These principles protect and promote the interests of patients, service users and the public in health and social care research, by describing ethical conduct and proportionate, assurance-based management of health and social care research, so as to support and facilitate high-quality research in the UK that has the confidence of patients, service users and the public.

CP264 –RESEARCH AND DEVELOPMENT OPERATIONAL POLICY

1. PURPOSE

This policy framework sets out principles and responsibilities at a high level that take account of relevant legislation in the UK. It will be supported by operational arrangements and guidance provided by the HRA and the Devolved Administrations, working in collaboration to ensure a consistent approach to co-ordinating and standardising regulatory practice. This will achieve compatibility across the UK for the management and conduct of health and social care research.

2. SCOPE

This Policy applies to all R&D being undertaken within Hull University Teaching Hospitals NHS Trust, research undertaken by HUTH staff and research requiring access to Trust premises or sites, service users, carers, clinical or Trust data, staff, human tissue or organs, however funded, and to all Trust staff and students.

Research governance is the responsibility of everyone and non-compliance with this policy and any research governance concerns should be reported to the R&D Office.

Any error, complaints, systems failures or other incidents, and learning points from such incidents will be addressed by members of the R&D Committee working closely with the researchers particularly the Chief/ Principal Investigator.

Research being undertaken for undergraduate or postgraduate qualifications also falls under the remit of this policy, though it will be the responsibility of the appropriate University to ensure sufficient scientific quality and Research Governance adherence is met.

For all the above classes of research, the following procedures should be followed.

3. POLICY STATEMENT

This policy sets out the procedures that should be followed when conducting any research and development (R&D) within Hull University Teaching Hospitals NHS Trust (the Trust). It refers to the legislation, policies, Standard Operating Procedures (SOPs) and guidelines that should be followed. The policy has been developed to ensure that all researchers, research teams and the Trust itself conform to the requirements of Research Governance, Research Ethics and regulatory and governance requirements, in particular:

- That HUTH upholds the principles of Research Governance and ensure that all researchers comply with the principals of Research and Clinical Governance, the Data Protection Act and the Trust Health & Safety Regulations.
- Ensure the design and conduct of studies is in accordance with robust scientific methods
- Adhere to agreed ethical standards of good clinical practice
- Comply with the requirements to the Department of Health and provide regular, accurate and comprehensive reports of all research activity as required, (i.e. PID Returns).
- Comply with the requirements of the UK Clinical Trial Regulations and all amendments therein,

This operational policy sets out the systems and processes which the R&D Department will adopt. This will ensure that:

- Management of research is carried out to high quality methodological, ethical and financial standards

- Support is provided for capacity building among HUTH staff (and those with honorary contracts accessing Trust facilities) to carry out research to the above standards
- Dissemination of new knowledge occurs to promote the implementation of research findings in practice

4. DEFINITIONS

See Appendix 1.

5. ROLES AND RESPONSIBILITIES

Chief Executive

The implementation of the UK Policy Framework for Health and Social Care Research and adherence to all relevant legislation, policies and guidelines is the responsibility of the Chief Executive.

Trust Board

The Trust Board are responsible for defining, agreeing and ratifying the proposed R&D strategy. In addition, the Trust Board has a specific responsibility in developing and maintaining the assurance framework which underpins the statement on internal control.

Chief Medical Officer

The Medical Director is the Executive Director with responsibility for developing and overseeing the organisation's framework for achieving the R&D strategy.

Director of Research and Development

The Director of Research and Development is responsible for facilitating, co-ordinating and monitoring key performance indicators in relation to the implementation of the R&D operational policy and strategy.

Clinical Quality Committee

The Clinical Quality Committee will review and approve the R&D operational policy, strategy and development plan for Research and Development which will be ratified by the Trust Board. The Research and Development Committee will serve as a sub-committee of the PQSE Committee and has specific responsibility for designated aspects of the Research and Development strategy and oversight of operational policy adherence.

The Clinical Quality Committee will review and prioritise the significant potential and actual risks to the Trust in relation to the implementation of the Research and Development operational policy and strategy.

Research and Development Committee

The Research and Development Committee are responsible for overseeing the implementation of the Research and Development operational policy and strategy and monitoring progress against annual objectives. The R&D Committee will receive updates against key performance indicators and the monitoring of departmental action plans against preparedness for external inspection. The committee are responsible for receiving research progress reports for all active research projects in the Trust and escalating any identified risks to the Clinical Quality Committee.

The Research and Development Office

The Research and Development Office are responsible for ensuring the Trust assessment of capability and capacity and application processes are adhered to and that no research takes place in the Trust without the relevant local and regulatory approvals. The R&D Office will be responsible for raising awareness of the systems and processes in relation to ensuring compliance with (but not exclusively) the UK Policy Framework for Health and Social Care

Research, HRA approvals, Good Clinical Practice and UK Regulations. The R&D Office will also be responsible for establishing and maintaining good relationships with key internal and external stakeholders including commercial companies.

HUTH Health Groups/Directorates
Business Units have a responsibility to ensure their developments are consistent with the Trust R&D Strategy and this Operational Policy. Heads of Service, Service Managers and General Managers are responsible for bringing to the attention of the Clinical Quality Committee the principal risks and control measures identified in relation to research activities.

Responsibilities as a Chief/Principal Investigator
The Principal Investigator is the person designated as taking overall responsibility within the team of researchers for the design, conduct and reporting of the study. They are accountable to their employing organisation, the host organisation/s (if different to the employing organisation) and the sponsor of the research for the conduct of the study.

Chief investigators must have suitable experience and expertise in the design and conduct of research.

Their responsibility is to ensure that:

- The dignity, rights, safety and well-being of participants are given priority at all times by the research team
- The research has received research ethics committee, Health Research Authority (HRA) approval, Medicines and Healthcare Products Regulatory Agency (MHRA) approval – where applicable and Trust managerial (local and R&D) confirmation of Capability and Capacity before commencing.
- Healthcare staff are suitably informed about the research their patients are taking part in.
- Each member of the research team is qualified by education, training and experience to discharge his/her role in the study.
- All research staff involved with the study are familiar with the protocol and have been trained in the study procedures (including informed consent procedure, AE reporting, breaking the study blind if applicable).
- The completion of the *study delegation and signature log* prior to the start of the study to confirm all the research staff involved with the study and their responsibilities. The signature and initials of staff ensure they can then be identified on forms, case notes etc.
- Students and new researchers must have adequate supervision, support and training including up to date GCP training.
- The protocol is written using the Guide to writing a Protocol for a Trust-sponsored CTIMP or HRA Template available from Trust R&D Officer or by visiting https://www.hey.nhs.uk/research/researchers/protocol-guides-for-hey-sponsored-ctimps-and-non-ctimps/ or https://www.hra.nhs.uk/planning-and-improving-research/research-planning/protocol/ to writing protocol
- The conduct of the trial is in compliance with the protocol approved by the HRA, MHRA, Ethics Committee (EC) and Trust R&D.
- There are no deviations from, or changes to, the protocol without agreement from the Trust R&D office and subsequent approvals from HRA,, MHRA, EC and Trust R&D
- The Trust R&D Office is notified promptly of any protocol violations and protocol deviations.
- Arrangements should be made for the appropriate archiving of data when the research has finished.
- Procedures are in place to ensure collection of high quality, accurate data and the integrity and confidentiality of data during processing and storage.

- Clear arrangements are in place for the management of financial and other resources provided for the study, including management of intellectual property arising from the work.
- Reports on the progress and outcomes of the work are produced on time and to an acceptable standard.
- The findings from the work are exposed to critical review through the accepted scientific and professional channels.
- Findings are disseminated promptly and fed back as appropriate to research participants.
- Any adverse events/adverse drug reactions or suspected misconduct are reported.
- All data and documentation associated with the study are available for audit at the request of the appropriate auditing authority.

Responsibilities as a Researcher Team Member
Researchers bear the day-to-day responsibility for the conduct of research. They are responsible for:

- Ensuring that the dignity, rights, safety and well-being of participants at all times
- ensuring that any research they undertake follows the agreed protocol
- ensuring that patients receive appropriate high quality care while involved in research
- protecting the integrity and confidentiality of clinical and other records and data generated by the research
- ensuring they are aware of their responsibilities under the Health and Safety Act both in respect of themselves and of other participants in research
- reporting any failures in any of the above, all adverse events and other potential harmful events or suspected research misconduct through the appropriate systems

Responsibilities as a HUTH Employee
Individual staff members have a personal duty to work within the provisions of this Trust-wide policy, and their associated procedures, protocols and guidelines.

Failure to observe and implement policy and their related procedures, protocols and guidelines is addressed through performance management mechanisms, training, or where appropriate, the Trust's Disciplinary Procedures.

All healthcare professionals, even if not involved in research, have a responsibility for the safety of their patients participating in research.

Before agreeing that patients be approached to take part in a study you should ensure that the research has been approved by the HRA and the appropriate research ethics committee and that Trust R&D confirmation of Capability and Capacity has been confirmed.
If you are unsure if the project has received appropriate Management, HRA or Ethical approval or Trust R&D confirmation of Capability and Capacity. You **must** contact the R&D Department **prior to** commencing any research activities.

Staff should report any concerns about the way informed consent is obtained or how the study is to be carried out to the R&D Department or Directorate Research Lead.

It should be noted that the responsibilities listed within this policy are not exhaustive and therefore additional responsibilities will be made clear in all research contracts and agreements, applicable legislation, nation and local policies and guidance.

6. CATEGORISING PROJECTS

It is a statutory requirement that all research involving NHS patients, staff or resources must be assessed by the HRA and research ethics committee. Furthermore, to comply with the Department of Health's UK Policy Framework for Health and Social Care Research, research activities must be formally approved by the HRA and Research Ethics Committee and confirmation of Capability and Capacity must also be confirmed by Trust R&D management prior to commencement; accountability for all research activity resides with the Chief Executive.

Seeking HRA and Ethics Committee approval and Trust R&D confirmation of Capability and Capacity can be a relatively time consuming process regardless of the nature of the research proposed. However, many other activities use similar methodologies to those in research but would not necessarily require assessment by a research ethics committee or formal approval within the UK Policy Framework for Health and Social Care Research; the boundaries between these different activities are not always clear. They include: clinical audit, local developments of existing research, introducing clinical innovations, service evaluations, patient or staff surveys and quality assurance programmes (list not exhaustive).

The increasing amount of evaluation, practice development, audit and research within the NHS has resulted in a number of grey areas where it is not easy to distinguish research from other forms of innovative work. Where a proposed project seems difficult to categorise, the aims of the project should be assessed. The project should be designed to match the purpose. The process for reviewing proposals in HUTH that do not clearly fall into a category is managed in collaboration with the Clinical Audit Department and considers what approval, authorisation or registration process is required for each category of project. . The HRA has introduced a decision tool to assist with the initial determination of your project – is it Research or is it Audit? http://www.hra-decisiontools.org.uk/research/

The following definitions of the above categories are used within this policy:

6.1 Research

"Research can be defined as the attempt to derive generalizable new knowledge by addressing clearly defined questions with systematic and rigorous methods."

UK Policy Framework for Health and Social Care Research for Health and Social Care, 11 Jan 2018 https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/
Research is likely to involve one or more of the following:

- Usually involves well-defined, often strict selection criteria for the sample selected
- Should be protocol-driven, although the design of qualitative research may require sufficient flexibility to respond to discoveries during the research process
- Quantitative research is designed so that it can be replicated. It may not be possible to replicate qualitative research, but it should be possible to form a judgement of the validity of the qualitative research process.
- In quantitative research, the sample size is usually defined by statistical methods. In qualitative research, statistical sample calculations and statistical sampling methods may not be applicable. There should however be a clear rationale for the sampling procedure used.
- Quantitative research usually involves statistical analysis to extrapolate from the sample to a wider population. This includes studies where only simple descriptive statistics such as percentages are appropriate.
- May test a new practice, therapy or drug
- May involve contact with participants

- May involve experiments on human subjects, whether patients, patients as volunteers or healthy volunteers
- May be invasive
- May involve collecting data from medical records
- May solely involve collecting data from medical records
- May involve examining tissue or body samples
- May involve extra disturbance or work beyond that required for normal clinical Management
- May use interviews or questionnaires
- Participants may be randomised
- Qualitative research uses a variety of methods, e.g. observation, interview, or other information, to describe, understand or interpret a situation or issue
- It is intended to publish and disseminate the results beyond the organisation, generally at conferences or in academic journals.
- The results may change practice if new interventions, tests, etc. are shown to be effective.

6.2 Clinical Audit

"Clinical audit is a quality improvement process that seeks to improve patient care and outcomes through systematic review of care against explicit criteria and the implementation of change. Aspects of the structure, processes, and outcomes of care are selected and systematically evaluated against explicit criteria. Where indicated, changes are implemented at an individual, team, or service level and further monitoring is used to confirm improvement in healthcare delivery."

Principles for Best Practice in Clinical Audit, National Institute for Clinical Excellence, 2002 -- https://www.nice.org.uk/guidance/published?type=cg

Clinical Audit is directly related to improving services against a standard that has already been set by examining:

- Whether or not what ought to be happening is happening
- Whether current practice meets required standards
- Whether current practice follows published guidelines
- Whether clinical practice is applying the knowledge that has been gained through research
- Whether current evidence is being applied in a given situation

Clinical Audit:

- May or may not involve patient contact but generally does not involve changes to normal clinical management
- Some audits can potentially require substantial patient/carer input and carry risks of distress and psychological harm
- Participants are never randomised to different treatments or services. Participants may receive different treatments or services but allocation of participants to different groups is through normal clinical decision-making processes
- Results are not transferable to other settings
- May use research methodologies e.g. interviews, random sampling, statistical analysis
- Standards of good practice are the basis of measurement not hypotheses and/or theoretical constructs
- Clinical audit outcome is improved quality of practice; Clinical research outcome is

mproved knowledge.

Surveys should be designed in such a manner as to cause minimal possible disruption to patients. Where substantial patient/carer input is necessary ethical approval may be appropriate. This may be from a clinical or university ethics committee. Issues such as confidentiality, validity, questionnaire design and whether participants might be distressed or harmed by their involvement should be reviewed by the NHS organisation but not necessarily by the R&D Department.

6.3 Student Research
Student projects should be assessed by the same criteria as above and managed appropriately. Further information on student research can be found on the HRA website https://www.hra.nhs.uk/planning-and-improving-research/research-planning/student-research/ or from the Trust R&D Office.

6.4 Clinical Investigation
Diagnostic tests may be the subject of a research study by a scientist within or outside the NHS. In situations where diagnosis of disease is difficult, NHS staff may request such a diagnostic test, in an attempt to obtain a diagnosis. Where the purpose of requesting the test is to obtain a diagnosis or to determine the appropriate care for a particular patient (or relatives, in the case of genetic disease), the request for the test should not be regarded as research. The person requesting the test does not need to be included in an ethics application and R&D approval from the NHS organisation of the person requesting the test is not required. Where the purpose for requesting the test is to help the scientist in developing a new diagnostic technique, and the aim is to develop the body of knowledge about the technique or the disease, the request for the test should be regarded as part of the research. For further discussion of this complex area see BMJ 2004; 329:624 http://bmj.bmjjournals.com/cgi/content/full/329/7466/624.

In international collaborations, other countries requirements for ethical approval for participating clinicians may be different.

6.5 Case Studies/ Case Reports
Case reports are usually anonymised and there are rarely ethical issues to be considered as long as consent is obtained, See Consent Policy CP. However, some journals may require confirmation that all appropriate regulatory approvals are in place prior to publication.

6.6 Data Management and Analysis
Data collected in the course of normal administrative functions of the NHS may be analysed to provide management information to monitor current provision or to plan future developments of the service. Routine data management and analysis is not research. Issues about data protection and confidential information should be handled through normal NHS processes in accordance with CP134 Confidentiality and Information Security Policy.

6.7 Consensus Methods
"The focus of consensus methods lays where unanimity of opinion does not exist owing to a lack of scientific evidence or where there is contradictory evidence on an issue. The methods attempt to assess the extent of agreement (consensus measurement) and to resolve disagreement (consensus development)."

J. Jones, D. Hunter; BMJ 1995; 311:376-380
http://bmj.bmjjournals.com/cgi/content/full/311/7001/376

Consensus techniques and consensus workshops are a communication process used to inform decision-making where evidence is lacking or contradictory. Consensus methods may

be used to agree guidelines, priorities, processes or policy. These include the Delphi method, the nominal group technique and consensus conferences. Consensus methods:

- May involve interviews and/or questionnaires
- Those involved are partners rather than participants and their names are usually included in any report or publication
- May be used to design a research project
- May be used to decide where research is required

Consensus methods would not normally require ethical approval. Consensus methods may also form part of a research project and, if so, should be managed as research.

6.8 Service Evaluation
"A set of procedures to judge a service's merit by providing a systematic assessment of its aims, objectives, activities, outputs, outcomes and costs"

Evaluation provides practical information to help decide whether a development or service should be continued or not. Evaluation also involves making judgements about the value of what is being evaluated.

Evaluation:
- May consist of or include audit, research or data management and analysis
- May provide cost and/or benefit information on a service
- Uses quantitative and qualitative data to explore activities and issues
- May identify strengths and weaknesses of services
- May include elements of research e.g. collecting additional data or changes to choices of treatment

If a large or complex evaluation study includes a research project (as defined above), the research should be managed within the UK Policy Framework for Health and Social Care Research. Where evaluation includes a clinical audit project (as defined above), the audit should be managed through the organisation's clinical audit management systems. In many cases, service evaluation will require collaboration between several departments within an organisation. Appropriate management of the evaluation should be agreed across the organisation, and the evaluation should not proceed without permission from a senior level in the organisation. Proper governance of research is essential to ensure that the public can have confidence in, and benefit from, quality research in health and social care. Research can involve an element of risk, both in terms of return on investment and sometimes for the safety and well-being of the research participants. Managing innovative work within the NHS requires an assessment of the risks involved and appropriate systems to manage these risks. In assessing the appropriate systems to manage projects which are difficult to categorise, a risk-based approach would include assessment of the risks to others of undertaking the work without appropriate rigour.

Service evaluation which is relevant only to the population or setting upon which it is based would generally be low risk. Evaluation concerned with producing internal recommendations for improvements that are not intended to be generalised beyond the setting in which the evaluation took place should therefore not be managed within the UK Policy Framework for Health and Social Care Research, and other appropriate systems should be used. These might include for example authorisation and oversight by a clinical effectiveness manager or a senior person in the department/ unit in which the evaluation is based.

If the results of the service evaluation are to be used to influence practices or processes outside the immediate setting and the work was not managed within the UK Policy

Framework for Health and Social Care Research, there would be a risk of the public being exposed to changes without a sound evidence base. Evaluation that will be generalised to other settings or populations should therefore be managed within the UK Policy Framework for Health and Social Care Research.

7. CENTRAL GUIDANCE AND LEGISLATION

All relevant guidance such as the Guidance on Good Practice and Clinical Trials in the NHS, the Medical Research Council guidance on the use of Personal Information in Medical Research, Data Protection Laws, Human Rights Act, NHS Guidelines on Research Governance etc. shall be adhered to when conducting R&D within HUTH:

7.1 UK Policy Framework for Health and Social Care Research (2017)

The Department of Health's UK Policy Framework for Health and Social Care Research for Health and Social Care sets legal requirements and recommended guidelines for hosting, conducting and managing research. It defines the roles and responsibilities of individuals and organisations and sets good practice standards. A full copy is available on: https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/

7.2 Mental Capacity Act (2005)

The Mental Capacity Act is designed to empower and protect vulnerable people who cannot make their own decisions. Research involving incapacitated or potentially incapacitated subjects must comply with the Act, which is available on: http://www.legislation.gov.uk/ukpga/2005/9/contents

7.3 Data Protection Act (1998)

This Act was introduced to protect individual's rights regarding the access and use of their personal information. The Act is designed to ensure that the inappropriate use of data does not lead to any unnecessary harm or distress in individuals. The act stipulates that any data must be fairly and lawfully processed for limited purposes, and should be adequate, relevant, not excessive, accurate and up to date. Any data should not be kept any longer than necessary, must be stored in a secure environment and processed in accordance with the individual's rights. Further information on the Act can be found on: http://www.legislation.gov.uk/ukpga/1998/29/contents

7.4 Medicines for Human Use (Clinical Trials) Regulations (2004) and Amendment Regulations (2006)

These Regulations apply to studies that investigate the efficacy and safety of a medicinal product. Before starting a clinical trial involving medicines, regulatory approval in the form of a Clinical Trial Authorisation (CTA) must be received from the Medicines and Healthcare products Regulatory Agency (MHRA). An algorithm to help people identify whether their research falls under the EU Clinical Trials Directive is available on: http://www.legislation.gov.uk/uksi/2004/1031/contents/made

7.5 Human Tissue Act

The Human Tissue Act 2004 covers England, Wales and Northern Ireland. It established the HTA to regulate activities concerning the removal, storage, use and disposal of human tissue. Consent is the fundamental principle of the legislation and underpins the lawful removal, storage and use of body parts, organs and tissue. Different consent requirements apply when dealing with tissue from the deceased and the living. For further information please go to: - https://www.hta.gov.uk/policies/human-tissue-act-2004

For further information regarding undertaking a clinical trial please contact the Trust R&D Office details of which can be found at: https://www.hey.nhs.uk/research/contact-research/

The above represents the core legislation requirements for most research applications. It should be noted that this list is not exhaustive. Researchers are asked to visit the Health Research Authority (HRA) website at www.hra.nhs.uk or contact the R&D Office for advice on any other specific research legislation, policies and guidance.

8. GENERAL INFORMATION

8.1 General Management

All research activity within the Trust, regardless of funding source, must be approved by the HRA and Ethics Committee and furthermore Trust R&D Capability and Capacity to undertake the research must also be confirmed prior to commencement. Failure to comply will mean that researchers will not be covered by the Trust's indemnity policy for this element of their work.

No research should commence at Hull University Teaching Hospitals NHS Trust without HRA and Ethics Committee approval as well as Trust R&D confirmation of Capability and Capacity.

The R&D Manager will act on behalf of the Trust in the Capability and Capacity process (delegated to a Research Development Unit "RDU" lead). Clinical Trials Agreements and Indemnity Agreements for commercially funded trials to be executed by the Director of R&D or Chief Medical Officer.

All applications for research activity taking place at HUTH must follow the Health Research Authority (HRA) approval process and include Trust R&D confirmation of Capability and Capacity. For further information on the process and the documentation required for approval, please visit www.hra.nhs.uk or contact the local Trust R&D office.

8.2 HUTH Trust R&D - Confirmation of Capability and Capacity

All research, including commercial studies, research conducted in collaboration with other organisations, single site research and student research requires Trust R&D confirmation of Capability and Capacity in addition to HRA and Research Ethics Committee (REC) approval before it can start.

Research that is of insufficient quality to be meaningful is a waste of resources and unethical. HRA and Research Ethics Committee approvals are required to ensure that the proposed research is:

- Ethically sound
- Scientifically robust
- Able to demonstrate financial probity
- Compliant with the UK Policy Framework for Health and Social Care Research
- Will not adversely affect service delivery, registered with the Trust and therefore, monitored and relevant to the Trust's R&D strategy.

All research projects to be submitted for HRA and ethical review must use the online Integrated Research Application System, (IRAS) available from: https://www.myresearchproject.org.uk/

8.3 HUTH R&D - Confirmation of Capability and Capacity Review Process

Following receipt of all regulatory approvals, R&D offices must confirm the Trust's Capability and Capacity to adopt the research project before it can commence. Information required by the Trust includes (list not exhaustive):

- Evidence that the appropriate clinical lead(s) or service manager(s) have agreed to support the study, and if applicable a CI/PI has been appointed
- A copy of the completed HRA and Ethics application form and any supporting documents have been provided
- For studies involving IMPs, a copy of the notice of acceptance from the MHRA
- Evidence of peer review
- Clinical Trial Agreement/SLA with third party
- Finance Authorisation

8.4 Research Ethics Service (RES)

The Research Ethics Service (RES) is a core function of the HRA and is committed to enabling and supporting ethical research in the NHS. It protects the rights, safety, dignity and wellbeing of research participants. They have a duty to provide an efficient and robust ethics review service that maximises UK competitiveness for health research and maximises the return from investment in the UK, whilst protecting participants and researchers. - See more at: https://www.hra.nhs.uk/about-us/news-updates/update-research-ethics-service-res-standard-operating-procedures-sops/

The Research Ethics Service (RES) includes reviews of research involving:

- Patients and users of the NHS. This includes all potential research participants recruited by virtue of the patient or user's past or present treatment by, or use of, the NHS. It includes NHS patients treated under contracts with private sector institutions.
- Individuals identified as potential research participants because of their status as relatives of carers of patients and users of the NHS, as defined above
- Access to data, organs or other bodily material of past or present NHS patients
- Fetal material and IVF involving NHS patients
- The recently dead in NHS premises
- The use of, or potential access to, NHS premises or facilities
- NHS staff – recruited as research participants by virtue of their "professional role"

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All relevant legislation and guidance such as the UK Medicines for Human Use (clinical trials) regulations, Good Clinical Practice in Clinical Trials, the Medical Research Council guidance on the use of Personal Information in Medical Research, Data Protection Laws, Human Rights Act, The Mental Health Act, Mental Capacity Act, and NHS Guidelines on Research Governance shall be adhered to when conducting R&D within the Trust. Further information on research submissions can be found at: www.hra.nhs.uk

Researchers are obliged to justify those instances where REC approval is not required. Failure to comply will result in suspension of insurance and indemnity and therefore of the study.

In order to reduce delays, HRA and Ethical approval should be sought in parallel on the same IRAS application form. Where the Trust and research applicant are in doubt, or disagree, over the categorisation of the project, The HRA decision tool will be used to make a determination.

For further information on projects that do not require approval by an NHS Research Ethics Committee see the information available at www.hra.nhs.uk or contact the Trust R&D office. The HRA decision tool can be used as a guide.

8.5 Research Protocol

Research which is poorly designed is regarded as being unethical, and is also not the best use of staff/clients' time. Therefore, researchers should get advice on methodology at an

early stage (and before submission of the IRAS application). Information can be obtained directly from the Health Research Authority (HRA) website at www.hra.nhs.uk or from the Trust R&D Office or the local Regional NIHR R&D Study Support Unit.

Researchers should undertake a literature review in the area of research being proposed, to ensure that the work does not unnecessarily duplicate existing work. Similarly, researchers should explore the NIHR UK Clinical Trials Gateway and appropriate Clinical Trial registers (such as the Medical Research Council and National Clinical Trials Database).Wherever possible, service users and/or carers should be involved in the research throughout the project, including the design, data collection and analysis stages of the research.

Research protocols for potential Trust sponsored research should be submitted to the Trust R&D Office as part of the IRAS submission process for review and approval of scientific methodology and relevance to the Trust, according to the agreed process, prior to commencing the project. The Trust will assess the proposed research and make a decision on whether the research can proceed, where appropriate making recommendations on research methodology and design.

For Trust-sponsored CTIMPs, all protocols must follow the template available at: NIHR GCP Resources:https://www.nihr.ac.uk/our-faculty/clinical-research-staff/learning-and-development/national-directory/good-clinical-practice/gcp-resources/gcp.htm or upon request from the Trust R&D office. It is a condition that this template be used for all HUTH-sponsored CTIMPs and should be accompanied by a Trust R&D sponsorship request form, available from the Trust R&D office. Or from our website at: - https://www.hey.nhs.uk/research/researchers/protocol-guides-for-hey-sponsored-ctimps-and-non-ctimps/

For externally funded R&D (both non-commercially and commercially funded) and research which has an external Sponsor, this review will not be an additional hurdle to projects which have already been subject to independent review (by recognised ‘partner organisations’ of the NHS). It will not unnecessarily duplicate any scientific review undertaken by other outside funding agencies during the process of consideration of the grant being awarded. However, approval must still be obtained.

Further information and guidance on the Trust’s peer review is available from the HUTH R&D Office or online at www.hra.nhs.uk

8.6 Sponsorship

Under UK Policy Framework for Health and Social Care Research, all research in the NHS needs to have a formally agreed research governance Sponsor. If this responsibility is to be met by the Trust then this needs to be agreed with the R&D Office prior to submission of the IRAS application.

In the case of multi-centre studies, where this Trust is not the sponsor, the Lead Centre (sponsor) will add our Trust details to the IRAS application, (which is submitted electronically to the Health Research Authority {HRA}) who will, in turn, invite us to participate in the research. The Trust R&D office will then undertake a “Capability and Capacity” review with the research team concerned. This review will consider available capacity within the Trust, trial complexity, duration and any anticipated risks. Following the review, a decision will be made and the HRA will be notified through the completion and return of their standard confirmation documentation.

The responsibilities of non-commercial clinical trial external sponsors will be made explicit by the implementation of a study agreement.

In the case of research carried out by students, and supervised via the university sector, HUTH will be deemed as sponsor & host of the study. The academic supervisor will be expected to assure the R&D Manager (or nominated deputy) of the relevance, scientific merit, and value for money of the study through the normal submission process.

The Trust should endeavour to provide independent scientific review of Trust sponsored projects submitted for approval. Project reviewers have been identified from inside the Trust; however, it may be necessary to occasionally seek external advice. Submissions therefore should include the nomination of a clinical expert to review the project for its relevance, scientific merit and value for money. This nominated reviewer must be unconnected to the applicants and should be a recognised expert within the relevant field. Further information on the peer review process and associated documentation can be obtained from the HRA website at www.hra.nhs.uk or from the Trust R&D office.

8.7 Application for Sponsorship of a CTIMP at HUTH
Sponsorship of CTIMPs represents a significant risk and responsibility for HUTH and therefore requires appropriate planning at the earliest opportunity. The protocol and all documentation and procedures associated with it must be developed in detail; monitoring must be arranged and the monitor involved in the trial initiation process; all investigators must be trained; there must be sufficient financial and human resources available for safe and effective conduct of the trial. Investigator teams will need to work with the R&D Office and all relevant Support Services on all these matters in conjunction with the Trust SOPs, available at https://www.hey.nhs.uk/research/researchers/gcp-sops-for-hey-sponsored-ctimps/

8.8 Research involving medicinal products (CTIMPs)
Research involving pharmaceutical products, clinical trials or other studies primarily examining efficacy, effectiveness or adverse events of medicinal products for human use need to have the appropriate clinical trial approval from the Medicines and Healthcare Regulatory Authority (MHRA).

An algorithm has been developed by the MHRA to help researchers find out whether a project comes within the Medicines for Human Use (Clinical Trials) Regulations 2004: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/317952/Algothrim.pdf

Written confirmation of the requirement to submit an application for Clinical Trial Authorisation to the MHRA must be obtained in all cases of doubt by submitting the protocol to the MHRA Clinical Trial Helpline: clintrialhelpline@mhra..gov.uk The Trust will not rely on the MHRA algorithm alone and in all cases where doubt remains, written confirmation from the MHRA will be sought.

8.9 Research involving medical devices
Research involving a medical device that does not have a CE mark or is CE marked but being used outside its intended purpose, your study is likely to require approval from the Medicines and Healthcare products regulatory Agency (MHRA) as well as approval from the HRA and Research Ethics Committee. MHRA approval for a device study is referred to as a 'notice of no objection'.

- An application must be made to the MHRA as part of the IRAS application process. A study cannot proceed if the MHRA raises any grounds for objection. Further details can be found at:- https://www.gov.uk/government/collections/regulatory-guidance-for-medical-devices

8.10 Commercial / Industrial Research

All commercially sponsored research carried out at HUTH must have a fully executed contract otherwise known as a Clinical Trial Agreement (CTA) before the study starts. All parties must sign a written agreement that defines the scope of work and formalises the understanding between the parties. This agreement must define the scope of work, establish acceptable payment arrangements, and address important issues such as the right to publish research results, protection of confidential information, and indemnification of third parties and/or case injury.

The Department of Health and the Association of the British Pharmaceutical Industry have agreed a model CTA as a standard contractual framework for commercial trials involving NHS patients. The model agreement should be used in all commercially sponsored studies that are conducted within the Trust.

All commercial research will be contracted by the organisation employing the Chief Investigator. Trust employed staff will be governed by these contracts. All commercial and non-commercial contracts for research projects should be sent for review and approval by the R&D Office RDU Lead and for subsequent Trust authorisation by the Trust's Director of R&D or authorised signatory.

All commercially-sponsored research or research involving collaboration with commercial companies should adhere to the Trust Business Integrity Policy:
http://intranet/policies/policies/11.pdf

8.11 Contractual Agreements

The Trust's R&D and Finance Departments must be notified of all financial and research agreements with outside agencies (including commercial companies) prior to signing. Where appropriate the Trust will seek legal advice on the appropriateness of the agreement. Only the Trust's Director of R&D or Chief Medical Officer (or other delegated authority) should sign all such agreements on behalf of the Trust.

The following is required by the Trust for all research related contracts and agreements:

- Written arrangements to be made with research sponsors and funders prior to commencement of each study.
- All research projects to be appropriately costed and managed.
- A mechanism to be in place to ensure financial probity.
- Intellectual Property Rights to be identified.
- Agreements to be in place for ownership, exploitation and income from Intellectual Property.

Review and negotiation of agreements, including the templates accepted for use in the Trust are detailed in the 'Contracts and Agreements Working Instructions'. Nationally approved model agreements are to be used unmodified where possible and appropriate.

The Chief or Principal Investigators should be aware of their personal obligations, and those of the research team, with regard to all research contracts signed by the Trust on their behalf.

The key responsibilities of all collaborators to be clearly defined within a Memorandum of Understanding or a Clinical Trials Agreement (CTA) (dependent on the financial and sponsorship arrangements of the study) and approved by the Director of R&D, Chief Medical Officer or nominated deputy prior to commencement of the project.

The Chief or Principal Investigator is responsible for informing the R&D Manager of any changes to these arrangements, which might be made during the life of the research study. No changes can be made without the approval of the Trust R&D Office.

Vendor Selection, Assessment and Contracting
Some or the research activity sponsored by HUTH may require the use of external vendors to support its management and delivery. External vendors include Clinical Trial Units, external laboratories, consultancy staff, randomisation services, IMP procurement and management.

A vendor is a person, organisation or agency external to HUTH that provides functions, services or products related to the conduct of research sponsored by HUTH. It does not include research collaborators or other research sites.

The requirement for the use of external vendors must be identified during the development of the study protocol or grant application submission as part of the sponsor risk assessment following the CI completing the sponsorship request form. The CI must ensure appropriate procurement processes are followed when selecting an external vendor and must liaise with the R&D Office to ensure appropriate assessment and contract negotiations can take place. The sponsor is ultimately responsible for all activities outsourced to an external vendor. Where specialist services are being contracted, the CI and sponsor will liaise with the relevant expertise and support services (i.e. HUTH Clinical Trials Pharmacy Team).

A risk based approach to the selection of vendors should be adopted. The CI and R&D Office will need to look at the risks associated with the tasks to be delegated as well as previous experiences and intelligence on the vendor (i.e. has the CI or Trust used the vendor in other work). Vendor assessment methods include:

- Pre-qualification assessment questionnaires
- Assessment of CVs and previous experience
- Obtaining suitable references
- Referring to prior knowledge from use in other trials
- Assessing quality systems/written procedures/SOPs
- Conducting audits

The decisions made to select must be documented and held in the TMF. Maintaining oversight of the vendor should be done via regular contact (i.e. emails, teleconferences, site visits, audits, review of agreed deadlines and contractual milestones) and must be proportionate to the activity undertaken as well as the initial and ongoing risk assessment made by the sponsor. Oversight correspondence must be documented and held in the TMF.

A clear ‘two-way’ communication and update process should be established so that any changes originating from both parties regarding the delivery, management or oversight can be risk assessed and formally agreed. An escalation process must be in place to ensure any identified non-compliance or performance issues can be assessed and dealt with.

It is acknowledged that some trial set-up activities may be undertaken prior to formal execution of a contract so as not to delay study progress against milestones. In this instance, a ‘letter of intent’ outlining the specific set-up activities, standards to adhere to and timelines must be put in place. To be clear, study start-up does not include shipment of IMP, trial specific screening or dosing.

Non Commercial Studies

For non-commercial studies, you should prepare the HRA the **Statement(s) of Activities and Schedule(s) of Events** documents for each type of research site in your study. Please ensure that you refer to the guidance provided when completing these documents.

For commercial studies, you should prepare the draft template agreement you propose to use with sites, the costing template and a template delegation log. For studies which are part of the NIHR CRN Portfolio you should ask the lead CRN to validate the costing template at least one week before application for HRA Approval.

For both commercial contract and non-commercial studies applying for the **NIHR CRN Portfolio**, you should **request inclusion on the NIHR CRN Portfolio** prior to your application to HRA Approval. As part of HRA Approval, we will share information about your application with the CRN to allow them to make a decision on NIHR CRN Portfolio eligibility.

8.12 Finance
When submitting projects to the Trust for approval, full details about project funding are required by the R&D Department.

For any study involving resources of other departments, costings must be declared and agreed by the appropriate departmental head in conjunction with the R&D Medical Education Accountant.

The NHS R&D application form should be completed when a researcher is completing the IRAS form. This form outlines any cost implications (clinical and non-clinical) attributed to the research project. For hosted studies, the schedule of events should be completed.

Before an application is made for any research grants, from whatever source, researchers should obtain financial advice via the R&D Office and the Finance Department in conjunction with the finance department of any external employing organisation of the grant applicant.

In the case of multi-centre studies led by another site, agreement to take part should not be given until a financial appraisal has been carried out. This will be facilitated as part of the Trust confirmation of capability and capacity process.

Where applicable, identified financial problems will be investigated in accordance with the procedure as laid down in the Trust's Fraud and Corruption Policy:
https://pattie.interactgo.com/Interact/Pages/Content/Document.aspx?id=3503&SearchId=

8.13 Fees for Commercial Research
As a minimum, the full costs of commercially funded research should be recovered. As per the correct Trust income distribution policy.

The Trust requires a payment of £1,500 for the processing of commercially Sponsored research to be invoiced on issuing Trust approval. For NIHR industry adopted studies that utilise the costing and DoH model agreements will be charged a fee as designated by the costing template (usually around £1000). NIHR costing template is available from: www.ukcrn.org.uk/index/industry/costing`. Researchers are advised to use this template as a guide for all research when identifying appropriate study costs.

Companies that deviate from the ABPI approved model clinical trial agreements may also be asked to pay legal costs for study review when required.

8.14 Treatment costs and Service Support costs for externally funded non-commercial R&D.
In all cases where there are associated treatment costs, excess treatment costs and/or service support costs, the Trust should be notified with the appropriate information about the proposed R&D as early as possible, in line with the requirement in the Department of Health's 'Non-Commercial External Funded R&D in the NHS: Guidance for Researchers'. Contact the R&D Office for further information or to discuss any queries.

In the case of the costs being associated with external R&D grant proposals originating from Trust staff, notification to the Trust should be prior to submission of the grant to the external non-commercial funder.

In the case of the costs being associated with external R&D grant proposals being led from other bodies such as a University or other Trust, notification must be prior to formal agreement to participate/collaborate with the research.

Excess Treatment Costs
Excess Treatment Costs (ETCs) borne by host sites are seen in particular as a significant risk. Whilst ETCs are the biggest single issue, there are other costs to Trusts in supporting research that can make Trusts cautious in undertaking new research.

8.15 Indemnity
The Clinical Trials EU Directive 2001/20 makes it a legal requirement that provision has been made for insurance or indemnity to cover the liability of the investigator and sponsor before a clinical trial using medicinal products may be undertaken.

- The UK Policy Framework for Health and Social Care Research requires that financial arrangements are in place to compensate anyone harmed as a result of negligent or non-negligent harm.

- The NHS cannot purchase advance insurance to cover indemnity because it is backed by the resources of the Treasury.

8.16 Negligent harm
Indemnity arrangements within public bodies, especially the NHS, can address only negligent harm. This is the legal liability that arises from the NHS Trust's duty of care towards patients.

Negligent harm is where an NHS patient is harmed in the course of research and an individual or group of individuals can be demonstrated to have caused that harm because of their negligence through, for example, not following an agreed procedure according to set policy or protocol. In such cases, the Trust is liable or vicariously liable and would be responsible for dealing with claims arising against the Trust for the harm caused.

The Trust participates in the Clinical Negligence Scheme for Trusts (CNST), run by the NHS Litigation Authority, which pools the risk of clinical negligence claims.
www.nhsla.com/Claims/Pages/Clinical.aspx

The Trust will only extend NHS indemnity cover (for negligent harm) to its employees, both substantive and honorary, conducting research projects that have been approved by the R&D Department. The Trust cannot accept liability for any activity that has not been properly registered and the Trust Has formal confirmation of capability and capacity.

8.17 Non-negligent harm
Non-negligent harm arises where an individual has been harmed in the course of research, through no fault of an individual or institution involved in the research and even though all the correct policies and procedures have been followed.

It is the role of ethics committees to decide whether or not a study can go ahead without a scheme of compensation for harm caused where there is no negligence.

NHS indemnity arrangements do not extend to non-negligent harm and NHS bodies cannot purchase commercial insurance for this purpose. NHS bodies cannot give advance undertaking to pay compensation when there is no negligence attributable to their vicarious liability.

The agreements between research partners clarifying who holds the respective responsibilities for the research, as well as the patient information leaflets, should specify clearly whether there are arrangements in place for non-negligent harm or if there are no arrangements in place for non-negligent harm.

If the principal investigator is employed by the University of Hull, the University has the responsibility for providing financial cover for damages or compensation arising from non-negligent harm (where applicable).

Hull University Teaching Hospitals NHS Trust has indemnity to cover claims arising from negligent harm, but not non-negligent harm.

In most circumstances, formal Trust confirmation of capability and capacity will secure indemnity for negligent harm via the CNST scheme.

If the research proposal involves a novel treatment, intervention or clinical procedure, and/or new equipment, device or drug, then appropriate procedures for patient indemnity must be arranged. If a commercial company is supplying a drug or clinical device then the Standard Association of British Pharmaceutical Industry indemnity of the Model NHS: ABPI Clinical Trial Agreement must be obtained (contact the R&D Office for advice).

When commercial research involving a medicinal product is undertaken, a contract of indemnity usually based on Association of British Pharmaceutical Industry (ABPI) guidelines is required. Model Clinical trial Agreement templates are available from the DoH at: http://www.ukcrc.org/regulation-governance/model-agreements/

Arrangements for compensation under such a scheme should be detailed in the patient information and consent form. For non-commercial research, the NHS has no special compensation arrangements for non-negligent harm; indemnity may be available from the academic partner. The participant information sheet and consent form must make clear whether compensation for non-negligent harm is available. For further information contact the R&D Office for advice or check the Health Research Authority and www.hra.nhs.uk

8.18 Intellectual Property Rights (IPR)
IPR is any data, information, equipment, research tool (such as questionnaires or assessments), product, or research result which as well as being of value to the evidence base, is also potentially commercially exploitable.

The Trust-agreed policy on Intellectual Property Rights shall be observed (contact the R&D Office for further information: http://intranet/policies/policies/257.pdf).

Researchers must inform the R&D Department if they consider the output from research has potential for the generation of intellectual property.

The Trust will collaborate with the NHS Intellectual Property Hub (Medipex Ltd) and advise researchers as appropriate. The R&D Office will advise researchers if there is a potential for exploitation of Intellectual Property.

Intellectual Property Rights, their ownership and management are to be appropriately included in research contracts or terms of grant awards.

Agreements with sponsors and funders must be made prior to the start of the study. This includes clearly identified ownership of data and the right to publish findings.

Advances in health and social care may need to be developed commercially in order for them to be made widely available and successful commercial development depends on protection of any intellectual property rights (IPR). Potential IPR issues must be discussed with the R&D Office.

8.19 Data Protection and Information Security
The Trust is committed to ensuring the confidentiality and security of all information it processes.

Information held in a wide variety of media is essential to the running of the Trust's business.

In order to ensure the confidence of patients and other data subjects in those who use information about them, and for the use of information to adhere to the law, it is essential that confidentiality is respected. This is not simply a matter of restricting access to information to those who have authority to use it, but also involves establishing this authority.

With some exceptions, authority to use information must rely on the consent of information subjects, based on their knowledge of the potential recipients of information about them, and understanding of the uses to which information may be put.

Information Security provisions will be assessed as part of the approval process submitted to the HRA http://www.hra.nhs.uk

All researchers submitting projects to the Trust for approval through the Integrated Research Application System "IRAS" will be e asked to give information about the collection and storage of data and its archiving when the research is completed. Within the "IRAS" application, researchers will be asked to declare that they will comply with the Data Protection Act (1998) and sign the application as a condition of approval. . Any issues identified from the capability and capacity review will be escalated to the R&D Manager in the first instance. Issues that remain unresolved will be escalated to the Information Governance Manager and Trust Caldicott Guardian.

The following policies should be read in conjunction with this policy with regards to Information Governance:

- Confidentiality and Information Security Policy (and incorporated procedures): http://intranet/policies/policies/134.pdf
- Information Governance Policy: http://intranet/policies/policies/292.pdf
- Information Technology Procurement Policy: http://intranet/policies/policies/44.pdf
- Health Records Management Policy: http://intranet/policies/policies/281.pdf
- Freedom of Information Policy: http://intranet/policies/policies/239.pdf

Section 251 of the NHS Act 2006 was introduced to allow organisations to obtain patient identifiable information, for medical purposes, in circumstances where it was impracticable to obtain informed consent from the patients concerned.

Scrutiny of the use of these arrangements by the Confidentiality Advisory Group (CAG): https://www.hra.nhs.uk/approvals-amendments/what-approvals-do-i-need/confidentiality-advisory-group/ formerly the Patient Information Advisory Group (PIAG), as well as wider consultation and Parliamentary approval for controversial activities, were built into the legislation to prevent the use of these powers for trivial or inappropriate purposes.

The Patient Information Advisory Group was established to provide advice on issues of national significance involving the use of patient information and to oversee arrangements created under Section 60 of the Health and Social Care Act 2001.

Applications for research that involves the use of patient identifiable information, for medical purposes, in circumstances where it was impracticable to obtain informed consent from the patients should be made via the IRAS system: https://www.myresearchproject.org.uk/ Guidance on the process is available on the IRAS website and the following link: https://www.myresearchproject.org.uk/help/hlpsubmissions.aspx

8.20 Human Tissue Authority (HTA)
All research activity undertaken by HUTH must adhere to the Human Tissue Act 2004 as applicable. The HTA regulates the removal, storage, use and disposal of human bodies, organs and tissue from the living and the deceased.

All applicable codes of practices relating to the removal, storage, use and disposal of human tissue and organs must be adhered to in conducting research at HUTH. For further guidance please contact the R&D Office and the following links: https://www.hta.gov.uk/ ; https://www.hta.gov.uk/hta-codes-practice-and-standards-0

8.21 The Ionising Radiation (Medical Exposure) Regulations 2000 and Ionising Radiation (Medical Exposure) (Amendment) Regulations 2006 (IRMER)

All research activity undertaken by HUTH must adhere to the Ionising Radiation (Medical Exposure) Regulations as applicable. All research applications will be subject to review against these regulations in conjunction with the Trust Radiology and Medical Physics Department.

For further guidance please contact the R&D Office and the following links:
http://www.opsi.gov.uk/si/si2000/20001059.htm
https://www.gov.uk/government/organisations/administration-of-radioactive-substances-advisory-committee

8.22 Informed Consent
Except in instances approved by the REC, all research requires the process of obtaining informed consent to be adhered to.

ICH GCP 1.28 states that informed consent is *'A process by which a study subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form.'*

The HUTH Informed Consent SOP describes the procedure for obtaining written informed consent from a patient or healthy volunteer participating in a clinical trial/study. The SOP is applicable to all research staff involved with clinical trials sponsored by Hull University Teaching Hospitals NHS Trust (HUTH) and also for non-HUTH sponsored trials that do not have their own procedures for consent. https://www.hey.nhs.uk/wp/wp-content/uploads/2016/03/SOP06.pdf

Patient information should be provided to potential study subjects in both an oral and written form.

The HRA website has useful information on the requirements for patient information sheets and gives guidance on the design and layout of patient information sheets and consent form. . http://www.hra.nhs.uk/

For all research, the lead researcher of the project team involved in recruiting participants will sign an undertaking to follow study protocols and to always advise patients that even if they give initial consent to take part in the study they can withdraw at any time.

8.23 Pharmacovigilance: clinical trials

Researchers must understand the types of untoward occurrences that may occur and how they are managed and communicated.

The requirements for safety reporting can be found in Part 5 (Pharmacovigilance Regulations 32, 33, 34 and 35) of the Medicines for Human Use (Clinical Trials) Regulations 2004: SI 2004/1031. These regulations specify the reporting requirements for research related adverse events. Compliance with these requirements ensures that the safety of trial subjects is protected. It is a legal requirement for trials involving IMPs to comply with the safety reporting procedures within the UK Clinical Trial Regulations. The requirements for investigators at HUTH have been transcribed into investigator and sponsor responsibilities within the 'Safety reporting in HEY-sponsored CTIMPs SOP'. https://www.hey.nhs.uk/wp/wp-content/uploads/2016/03/SOP07.pdf

Pharmacovigilance definitions:

- **AE - Adverse event:** any untoward medical occurrence in a clinical trial subject administered a medicinal product which may or may not be caused by or related to that product.

- **Adverse reaction or adverse drug reaction (ADR):** any untoward and unintended response in a subject to an investigational medicinal product which is related to any dose administered to that subject.

- **Unexpected adverse reaction:** an adverse reaction the nature and severity of which is not consistent with the information about the medicinal product in question set out:

  (a) in the case of a product with a marketing authorisation, in the summary of product characteristics for that product using MHRA approved R51
  (b) in the case of any other investigational medicinal product, in the investigator's brochure relating to the trial in question.

- **SAE - Serious adverse event or serious adverse reaction:** any adverse event, adverse reaction or unexpected adverse reaction, respectively, 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.

Important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the patient or may require intervention to prevent one of the other outcomes listed in the definition above should also be considered serious.

- SSAR - Suspected serious adverse reaction **is any serious adverse reaction that is suspected (possibly or probably) to be related to the investigational medicinal product.**

- SUSAR – Suspected unexpected serious adverse reaction **is an SSAR which is unexpected, meaning that its nature and severity are not consistent with the information about the medicinal product in question set out:**

  (a) in the case of a product with a marketing authorisation, in the summary of product characteristics, (SPC) for that product using the approved R51 via MHRA.

  (b) in the case of any other investigational medicinal product, in the investigator's brochure relating to the trial in question.

An SAE becomes a SUSAR if the event is suspected (possibly or probably) to be related to the IMP and unexpected i.e. not previously documented in any of the product information (SPC, investigator brochure, patient information leaflet) or protocol.

8.24 Research Incidents: Datix reporting
The safety of research participants and research staff must be given priority at all times and Health & Safety regulations strictly observed. Staff working on research projects should report incidents in line with the procedure outlined in the Trust's 'Incident Reporting Policy' (CP379).

All incidents and near misses, involving staff, patients and others are reported by completing an incident report via the electronic incident reporting system (DATIX) which is available on the front page of the Trust Intranet site (Pattie).

An incident is an event or omission, or series of events or omissions that have occurred and have caused, or may have caused, harm, loss or damage. An incident may involve patients, staff, or members of the public, Trust property, quality of services or affect the reputation of the organisation.

To assist staff in determining what research related incidents need to be reported onto the Trust incident reporting system, the following guidance (table below) should be used.

Please contact the R&D Office for any further advice. However, if in doubt, and you feel you have witnessed an event which has harmed or caused distress to patients, staff, or any other visitor to the Trust or has the potential to harm or cause distress to patients, staff, or visitors, report it as an incident.

Research Incident Type	Definition	Datix (Yes or No)
Serious Breaches	MHRA Serious Breach Guidance	Yes (Sponsor reporting instructions to be followed in addition).
Adverse Events (AEs)	**Non-serious AEs**	No (should be reported as per the sponsors instructions, the protocol and SOPs).
Serious Adverse Events (SAEs)	See section 8.23	No - when SAE definitely not classified as related by PI and Sponsor. (Should be reported as per the sponsors instructions, protocol and SOPs).
Adverse Reactions (ARs)	**Non-serious ARs related to study intervention and expected** (i.e. listed in protocol or MHRA approved SmPC).	No (should be reported as per the sponsors instructions, protocol and SOPs).
Unexpected Adverse Reactions (UARs)	See section 8.23	Yes (all UARs) (Sponsor and protocol reporting instructions to be followed in addition).
Serious Adverse Reactions (SARs)	See section 8.23	Yes (Sponsor and protocol reporting instructions to be followed in addition).
Suspected Unexpected Serious Adverse Reactions (SUSARs)	See section 8.23	Yes (Sponsor and protocol reporting instructions to be followed in addition).
Drug administration or prescribing error	**All incidents involving Clinical Trials Pharmacy**	Yes (Sponsor to be notified in addition).
Participant eligibility error	Participant found to be ineligible **after randomisation and receipt of treatment or intervention**.	Yes (Sponsor to be notified in addition).
Participant eligibility error	Participant found to be ineligible **after randomisation but before receipt of treatment or intervention**.	Yes (near miss) (Sponsor to be notified in addition).
Participant eligibility (screen failure)	Participant consents and undergoes screening procedures but found to be ineligible.. Participant is a **screen failure and does not receive any study interventions.**	No (should be reported as per the sponsors instructions and SOPs).
Protocol Deviations	**If deviations occurred through no fault of the**	No (should be reported as per the sponsors

	sponsor, host site or research staff and resulted in no harm to the participant.	instructions and SOPs).
Protocol Deviations	**If deviations occurred as a direct result of the Trust or sponsors inability to fulfil the study protocol** (i.e. issues with resources, facilities, equipment, staffing and any other issue outside of the control of the study participant.	Yes (Sponsor to be notified in addition).
Sponsor monitoring visit reports	Sponsors may put in place central or on-site monitoring visits that may highlight **areas of GCP non-compliance.** Sponsors will provide the research study team with a report of any findings and actions required.	Monitoring actions to be reviewed by the site study team and assessed against the definitions listed in this section.
Information Governance breaches and potential issues	See CP292 Information Governance Policy.	Yes (Sponsor to be notified in addition).
Other operational issues related to research delivery and oversight affecting staff and patients	For example, laboratory freezers fail and go out of allowed temperature range potentially rendering research samples unusable.	Yes (Sponsor to be notified in addition).

For advice on how to complete the form please contact your Line or Service Manager or Datix team.

Clinical Governance mechanisms for Risk Management are to be utilised in the process for dealing with adverse events resulting from a research study. All researchers will follow the Trust's Risk Management Policy CP363: https://pattie.info/Interact/Pages/Content/Document.aspx?id=3500&SearchId=409517 and Policy on Reporting Incidents CP379: https://pattie.info/Interact/Pages/Content/Document.aspx?id=5523&SearchId=409527

The Sponsor Oversight Committee will be informed of all Trust-sponsored research related incidents reported via Datix and the R&D Committee will be informed of all research related incidents reported via Datix.

8.25 Support Services Facilitation

All research activity within the Trust must be undertaken in conjunction with all relevant support services (Pharmacy, Radiology, IT, Medical Records, Medical Physics, Pathology) – list not exhaustive. In doing so, investigators shall adhere to all support services operating procedures, policies and guidelines.

Authorisation for the research activity to take place within HUTH will be sought as part of the Trust R&D confirmation of capability and capacity process.

8.26 Record Keeping
The Principal/Chief Investigator must keep a comprehensive, accurate and up to date study file for each research project, containing all study related documents and correspondence.

Any data must be available for audit, and the handling of data must comply with the Data Protection Act. Research data collected from study participants should always be pseudo-anonymised to avoid unnecessary identification and wherever possible anonymised for confidentiality.

For clinical trials there is a comprehensive list of essential documents that must be held in an Investigator Site File or Trial Master File study file and be available for inspection by the MHRA. These documents are stipulated in the Guidelines for Good Clinical Practice issued by The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use and are available on:

https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q10/Concept_papers/Q10_Concept_Paper.pdf

At the end of a project, records should be kept until they are no longer required or the sponsor gives authorisation to destroy the records. Data verification may be requested after the study has closed during review of research findings and records must be available and accessible for this purpose. Clinical Trial data may need to be kept for a minimum of five years after the close of the project for review by the licensing authority, and the retention period should be clearly stated in the protocol.

The R&D Office has a duty to maintain accurate central records of all R&D projects and related activities conducted in the Trust. This information and all research related activity documentation, e.g. minutes of R&D group meetings etc., has to be available for auditing.

All adverse events relating to R&D being conducted within HUTH should be reported to the R&D Office of the Trust, as well as the routine Trust procedures for reporting such events. This includes both clinical adverse events and non-clinical adverse events such as issues concerned with gaining consent and record keeping.

Any praise or complaints or Health and Safety issues relating to R&D should be handled through the normal Trust mechanisms. The R&D Office should also be notified.

All research visits should be recorded in the patients' casenotes in accordance with the Trust Patient Documentation Policy: http://intranet/policies/policies/185.pdf

For HUTH Sponsored research (CTIMP and non-CTIMP) the following minimum requirements should be adhered to:

- Ensure patient study visits are clearly recorded in case notes as visits occur.
- The minimum details to record are:
    - Clearly written date, brief study title and visit number
    - Date patient given patient information sheet
    - Date of consent
    - Date of screening
    - Relevant results
    - Brief description of any AEs with onset & offset times/dates (including any change in blood/urine etc. test results)
    - Any changes in concomitant diseases and medication including study medication

- Any other relevant details.

File one copy of the signed informed consent form in the patients' case notes together with a copy of the patient information sheet, the letter sent to the patient's GP and the signed inclusion/exclusion criteria checklist.

Investigators should note that research that is externally sponsored may require additional information to be recorded in the patient case notes. Any such request should be made clear by the sponsor in its SOPs.

8.27 Storage and re-use of research data
All data shall be stored according to Ethical Committee and/or recognised good practice guidelines (such as from the Medical Research Council), and the Department of Health guidelines.

Appropriate ethical and Trust approval (and where appropriate informed consent from patient/client) must be obtained for sharing or reuse of data for any purpose other than for which it was originally collected.

The Trust's Policy Intellectual Property Rights (IPR) should also be adhered to in such cases. No data should be passed to any third parties unless the data transfer complies with the Trust Information and Storage Policy: (page 19, **3.6** of the Confidentiality and Information Security Policy http://intranet/policies/policies/134.pdf

Further information on records retention, storage and disposal can be found in the Trust Health Records Management Policy: (Sections 8 and 9
http://intranet/policies/policies/281.pdf

8.28 Research Steering Groups
All R&D projects should ideally be managed by a formal steering group, which will monitor progress. For clinical trials, it is best practice to constitute an independently led Trial Steering Group, and in some cases an Independent Data Monitoring Committee. For further information on best practice for the conduct of clinical trials, the appropriate Department of Health and Medical Research Council guidance should be referred to.

8.29 Employment Contracts
All persons conducting research at the Trust must have a substantive or honorary employment contract.

It is the responsibility of the Lead Researcher to ensure that all members of the research team are suitably qualified and hold appropriate contracts. In view of the time taken to perform pre-employment checks, early initiation of the honorary contract process is advised. Please contact the R&D office for further information or advice on local procedures.

Researchers are advised to consult the 'Research in the NHS - Human Resources (HR) Good Practice Resource Pack' (Version 1.1 January 2009):
http://www.rnhrd.nhs.uk/uploads/files/222/Research%20in%20the%20NHS_full%20resource%20pack.pdf

The resource pack describes the Research Passport system and other standardised procedures for handling the HR arrangements for researchers. There are links to example documents including honorary research contract, example letter of access for researchers who do not require an honorary research contract, occupational health assessment questionnaire and confidentiality code of conduct. The R&D Office will adhere to this resource pack and associated legislation and guidance in determining and issuing

appropriate research contracts. Researchers should also consult the Trust Honorary Contract Policy: http://intranet/policies/policies/212.pdf

Please note that research may only commence following NHS REC, MHRA (where applicable) and R&D Office confirmation of capability and capacity. Please contact the R&D Office for advice regarding Research Passports and HRCs.

8.30 Amendments to the protocol
All substantial amendments must be submitted to the HRA and REC, using the online amendment form in IRAS and studies involving a CTIMP must be submitted to the MHRA in the same amendment request.

All amendments received by the HRA are reviewed and classified (A, B or C). The classification code and implementation date (for the changes to take effect from) is communicated to the sponsor in an e-mail. The sponsor forwards the HRA classification e-mail and any associated amendment documentation to the local Trust R&D office to review with the research team to determine "Capability and Capacity" to adopt the changes. Trust confirmation of "Capability and Capacity" is always subject to receipt of copies of the relevant documentation and regulatory approvals from the sponsor prior to the implementation date stated within the HRA categorisation e-mail.

Further guidance and examples of substantial and non-substantial amendments can be found at www.hra.nhs.uk

8.31 Notification Requirements
For any ongoing study the CI or PI must inform the NHS REC and R&D Office if changes are made to any of the following:

- Research personnel or protocol;
- Start/finish dates;
- Funding arrangements;
- Contractual agreements
- Serious unexpected adverse events.

8.32 Deviation from approved protocol
Any deviation from the approved protocol should be notified to the R&D office and agreed with the appropriate Research Ethics Committee, the Sponsor, the Trust and the external Funder (if externally funded).

8.33 Reporting Requirements
Researchers are required to deliver progress and final reports, as stated in approval letters from funders, NHS REC and R&D Office. For clinical trials there is a legal requirement for the Sponsor to report the end of a trial to the MHRA and therefore the Chief Investigator must inform the Sponsor as soon as the trial finishes. It is a legal requirement to adhere to the timelines for notification of end of trial in the UK Clinical Trial Regulations.

8.34 Dissemination of Research Findings
Research is conducted to increase the knowledge base and improve health care. Research findings, should be critically received by accepted scientific and professional channels and made freely available. Findings should be presented at relevant scientific meetings and written up for publication in peer-reviewed journals,(Clinical Governance mechanisms for

Quality and Clinical Effectiveness should be utilised in the evaluation of the dissemination of research findings and their implementation into practice) - impact assessment process.

Researchers should Contact the R&D Office for advice on in-house dissemination methods.

8.35 Final reports of progress and research findings
The Trust will request final reports of progress made and a summary of the research findings according to specified formats. These reports will be used to ensure that the research has been conducted according to the approved protocol and ethical favourable opinion. In addition, the report will facilitate dissemination of any research findings within the Trust and wider.

Where appropriate, the Trust will request a financial reconciliation at the end of the project. This will include research where there has been specified Trust R&D funding and/or service support used to support an R&D project (either externally funded non-commercial or Trust sponsored). Commercially sponsored and funded research will also be subject to financial reconciliation during the course of the trial and at study close-out. Researchers are expected to keep the R&D Office informed of progress of all financial payments made to the Trust against the agreed total contract value.

All publications involving the Trust should acknowledge the Trust appropriately. For commercially sponsored and some commercially funded research, the investigators must check all contracts and agreements prior to publication to ensure that there are no breaches of contract.

The Committee on Publication Ethics (COPE) was founded in 1997 to address breaches of research publication ethics. It is a voluntary body providing a discussion forum and advice for scientific editors and aims to find practical ways of dealing with the issues and developing good practice. Researchers are advised to visit the following link for further guidance: http://www.publicationethics.org.uk

8.36 Archiving
The Sponsor, in conjunction with the Chief/Principal investigator, is responsible for making sure that all essential documents are archived in accordance with the regulatory requirements.

The investigator is recommended to make the sponsor aware of the storage arrangements for their essential documents by contacting the HUTH R&D Office named archivist or nominated deputy. The ultimate responsibility for the documents to be retained by the investigator/institution resides with the sponsor. If the investigator becomes unable to be responsible for their essential documents (e.g. relocation, retirement etc.) the sponsor should be notified in writing of this change and informed as to whom the responsibility has been transferred.

The Chief/Principal investigator has a responsibility to allow the sponsor access to the archived data on request. The archived data can be audited by the sponsor or competent authority on request.

For HUTH sponsored CTIMPs, archiving logistics and all necessary arrangements should be made via the Chief/Principal investigator (or nominated deputy) and the HUTH R&D Office named archivist (or nominated deputy) following the process outlined in the HUTH Archiving SOP. https://www.hey.nhs.uk/wp/wp-content/uploads/2016/03/SOP14.pdf

8.37 Research Misconduct
Anyone suspecting research misconduct or fraud should report it immediately to the R&D Office.

The investigative process will be conducted in accordance with the procedure as laid down in the Trust's policy for dealing with Allegations of Misconduct or Fraud in Research: http://intranet/policies/policies/256.pdf

8.38 GCP training
In order to comply with the UK Clinical Trial Regulations, all researchers who are undertaking a Trust sponsored clinical trial of an investigational medicinal product (CTIMP) must have current GCP training (undertaken within the last two years) in order to undertake that trial. Evidence of compliance is sort prior to receipt of Trust approval.

8.39 Monitoring Arrangements and UK Policy Framework for Health and Social Care Research Compliance
Researchers are required to fully cooperate with the R&D Office should their research be audited. This audit will also check for compliance with this Policy.

Monitoring and auditing with regards to financial probity and governance adherence will focus on the projects which are not already subject to routine monitoring from external funders.

8.40 Auditing
All research taking place within the Trust must be subject to a monitoring procedure which includes an audit of projects in line with Department of Health requirements, and a final and interim reporting system. The frequency and number of audits to be undertaken will be determined by the volume and type of research being conducted and will be reviewed on an annual basis.

Monitoring of CTIMPs shall be undertaken on behalf of the Trust (where HUTH is sponsor) by the R&D Clinical Trials Monitor as per R&D GCP SOP15: https://www.hey.nhs.uk/wp/wp-content/uploads/2016/03/SOP15.pdf.

The 'Procedure for Auditing Research Conducted at HUTH' SOP https://www.hey.nhs.uk/wp/wp-content/uploads/2016/03/SOP20.pdf is designed to complement, and not replace, the Trust SOP on CTIMP monitoring.

Audit shall be undertaken, as outlined in this SOP, by a member of the HUTH R&D Office staff. The Trust will need to ensure that all staff undertaking the audits on its behalf are suitably qualified by training or experience. To this end, the auditor shall be responsible for:

- Collecting evidence to enable comparison of current practice with the requirements of research governance, GCP and, where applicable, UK Clinical Trials Regulations.
- Writing a final report detailing all required preventative and corrective actions to be taken (where necessary).

Further information on monitoring and reporting can be obtained by contacting the R&D Office.

9. HEALTH AND SAFETY

All researchers are to be aware of their responsibilities under the Health & Safety Act. When submitting projects for approval, researchers should identify the use of potentially dangerous or harmful equipment, substances or organisms.

All researchers should undertake to give priority to the safety of participants and staff and that Health & Safety regulations will be strictly observed.

The Trust has a mandatory programme of Health and Safety training for all employees. It is the responsibility of the researcher to attend such training as outlined in all job descriptions and employment contracts including honorary contracts issued to non NHS researchers.

10. IMPLEMENTATION INCLUDING TRAINING AND AWARENESS

Members of the R&D office will be available for advice and training, and will link researchers with wider training opportunities including those available externally.

The policy will be disseminated via the Trust intranet.

11. MONITORING OF THIS POLICY

The Director of the Research and Development will be the responsible person for monitoring this policy, ensuring it remains fit or purpose and that it is implemented appropriately within the Trust. These responsibilities include reviewing all protocols, procedures and guidelines referred to in the Policy and to advise the Chairs of relevant Committees.

12. ASSOCIATED POLICIES

All relevant policies are referenced throughout this policy and can be accessed via “Pattie”...

13. STAKEHOLDER CONSULTATION

Key stakeholders are members of or are represented on the Research and Development Committee and the Quality Committee/EMC.

Acknowledgements – some of the content of this policy has been adapted from the Kent and Medway NHS Trust R&D Operational Policy.

14. REFERENCES

- Department of Health http://www.dh.gov.uk
- HRA: Health Research Authority http://www.hra.nhs.uk
- The Department of Health website has a research governance index page which has direct links to many of the most relevant documents: https://www.gov.uk/government/organisations/department-of-health
- National Institute for Health Research: http://www.nihr.ac.uk
- NRES: National Research Ethics Service www.hra.nhs.uk/about-the-hra/our-committees/res/
- COPE: Committee on Publication Ethics https://publicationethics.org/
- MRC: Medical Research Council http://www.mrc.ac.uk
- AREC: Association of Research Ethics Committees http://www.arec.org.uk
- Administration of Radioactive Substances Advisory Committee (ARSAC) http://www.arsac.org.uk/ (application for ARSAC certificate by nuclear medicine professional administering radioactive exposure in research)
- Gene Therapy Advisory Committee (GTAC) https://www.gov.uk/government/organisations/department-of-health (application for ethical opinion on a trial of a gene therapy medicinal product)

- Medicines and Healthcare products Regulatory Agency (MHRA) http://www.mhra.gov.uk (Notification of a clinical investigation of a medical device)
- Ministry of Justice (National Offender Management Service) https://www.gov.uk/government/organisations/national-offender-management-service (Application to conduct health research involving prisoners (England & Wales only)
- NHS / HSC research offices www.hra.nhs.uk/research.../applying-for-approvals/nhs-management-permission (Application for NHS management permission)
- NRES, www.hra.nhs.uk/research-community/applying-for.../research-ethics-committee / NHS / HSC Research Ethics Committees http://www.orecni.org.uk (Application for ethical opinion on a research project, tissue bank or database)
- Research in the NHS - Human Resources (HR) Good Practice Resource Pack (Version 1.1 January 2009) www.rnhrd.nhs.uk/.../Research%20in%20the%20NHS_full%20resource%20pack.pdf
- European Commission – the EU Pharmacovigilance system https://ec.europa.eu/health/human-use_en https://ec.europa.eu › ... › Public health › Medicinal products for human use
- MHRA - Medicines & Healthcare Products Regulatory Agency http://www.mhra.gov.uk
- The Clinical Trials Tool Kit http://www.ct-toolkit.ac.uk
- The Medicines for Human Use (Clinical Trials) Regulations 2004 www.legislation.gov.uk/uksi/2004/1031/contents/made
- The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006 www.legislation.gov.uk/uksi/2006/1928/contents/made
- Is it a Clinical Trial? http://www.mhra.gov.uk/home/groups/l-unit1/documents/websiteresources/con009394.pdf
- Clinical Trial Authorisation http://www.ct-toolkit.ac.uk/_db/_documents/Applic_CTA.pdf
- HREA: Human Fertilisation & Embryology Authority http://www.hfea.gov.uk/
- ARSAC: Administration of Radioactive Substances Advisory Committee http://www.arsac.org.uk/
- GTAC: Gene Therapy Advisory Committee www.hra.nhs.uk/resources/applying-to-recs/gene-therapy-advisory-committee-gtac/
- CQC: Care Quality Commission http://webarchive.nationalarchives.gov.uk/20130513181011/http://www.cqc.org.uk/
- HTA – Human Tissue Authority http://www.hta.gov.uk/
- Data & Tissues Tool Kit http://www.dt-toolkit.ac.uk/home.cfm
- Human Fertilisation and Embryology Act (1990) www.legislation.gov.uk/ukpga/1990/37/section/28
- The NHS Act 2006 Health and Social Care Act (2001) www.legislation.gov.uk/ukpga/2001/15/pdfs/ukpga_20010015_en.pdf
- Human Rights Act 1998 www.legislation.gov.uk/ukpga/1998/42/contents
- Data Protection Act 1998 www.legislation.gov.uk/ukpga/1998/29/contents
- The Ionising Radiation (Medical Exposure) Regulations 2000 http://www.opsi.gov.uk/si/si2000/20001059.htm
- Ionising Radiation (Medical Exposure) (Amendment) Regulations 2006 http://www.opsi.gov.uk/si/si2006/20062523.htm
- NHS R&D Forum guidance: Approval for research involving ionising radiation (2006) www.hra.nhs.uk/documents/.../approval-of-research-involving-ionising-radiation.pdf
- Control of Substances Hazardous to Health Regulations (2002) www.hse.gov.uk/nanotechnology/coshh.htm
- Human Tissue Act 2004 www.legislation.gov.uk/ukpga/2004/30/contents
- UK Medicines for Human Use (Clinical Trials) Regulations (2004) www.legislation.gov.uk/uksi/2004/1031/contents/made

- Mental Capacity Act 2005 http://www.legislation.gov.uk/ukpga/2005/9/contents
- NHS R&D Forum – HTA Guidance http://www.rdforum.nhs.uk/htact.htm
- ABPI – Association of the British Pharmaceutical Industry http://www.abpi.org.uk/
- NHSLA: NHS Litigation Authority www.nhsla.com/
- Research in the NHS – Indemnity Arrangements (December 2005) http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4125281
- NHS Indemnity: Arrangements for Clinical Negligence Claims in the NHS www.nhsla.com/claims/Documents/NHS%20Indemnity.pdf
- The NHS as an Innovative Organisation – A Framework and Guidance on the Management of Intellectual Property in the NHS (2002) webarchive.nationalarchives.gov.uk/+/.../PublicationsPolicyAndGuidance/DH_40026.
- NHS Innovation Hubs knowledge.nic.nhs.uk/orgDetails.aspx?orgId=4
- MHRA Good Pharmacovigilance Practice http://www.mhra.gov.uk/Howweregulate/Medicines/Inspectionandstandards/GoodPharmacovigilancePractice/index.htm
- MRC Policy and Guidance on Ethics and Research Governance https://www.mrc.ac.uk/research/policies-and-guidance-for-researchers/

1 APPENDICES – DEFINITIONS

Definitions adapted from:
http://www.dt-toolkit.ac.uk/glossary.cfm
http://www.ct-toolkit.ac.uk/glossary.cfm
http://www.em-toolkit.ac.uk/glossary.cfm

Adverse Event (AE)

An adverse event is any undesirable occurrence on a particular study. For clinical trials of investigational medicinal products (CTIMP's) adverse events is defined by ICH GCP as any unfavourable and unintended sign, symptom or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to that product. For other research that does not use investigational products, it may be any unfavourable and unintended sign, symptom or disease temporally associated with participation in the research project. The term has also been used to describe unfortunate events that may have serious consequences for the research project, e.g. breaking down of a freezer and loss of tissue samples. Alternative terms: Adverse Outcome, Adverse Incident.

Amendment

A change made to the terms of the Research Ethics Committee (REC) application, the protocol or any supporting documentation after the study has started. A study is normally considered to start after the commencement of any protocol procedures. Amendments can be 'substantial' or 'non-substantial'.

- **Substantial amendments**

These require the issue of a favorable opinion from the main REC and NHS R&D departments. If the amendment has implications for study in terms of the scientific peer review, the funding body should also be consulted.

- **Non-substantial amendments**

The HRA, REC, NHS R&D departments (if appropriate) and sponsor(s) may require notification of non-substantial amendments. NHS RECs do not require notification of non-substantial amendments.

For more information please see the Protocol amendments station in the Data and Tissues Tool Kit.

Anonymised data / information

Anonymised data are data prepared from information from which the person to whom is relates cannot be identified. The term is used when referring to robustly pseudonymised / linked data or unlinked anonymised data.

- **Pseudonymised data, also referred to as linked anonymised**

This is anonymous to the people who receive and hold it (e.g. a research team), but contains information or codes that would allow others (e.g. those responsible for the individual's care) to identify an individual from it.

- **Unlinked anonymised data, or truly anonymised data**

This contains no information that could reasonably be used, by anyone, to identify the individual or study participant.

Anonymised tissue

The Human Tissue Authority consider that tissue is anonymised if the researcher is not in possession, and is not likely to come into possession, of information from which the individual can be identified. This does not mean that samples must be permanently unlinked, and coding samples meets these requirements.

Archiving

The retention of valuable research data which may have secondary use, or may be analysed further to verify results or as part of a meta-study; and the retention of study files which demonstrate the compliance of the investigator and sponsor with GCP and regulatory requirements.

During archiving it should be ensured that data are properly selected, stored, can be accessed and that logical and physical integrity are maintained over time, including security and authenticity.

Periods of retention will depend on the nature of the research and sponsor's and funder's requirements. Please see the Research Scenarios section of the Data and Tissues Tool Kit for more guidance on this area.

ARSAC

Administration of Radioactive Substances Advisory Committee advises the Health Departments on written applications from practitioners for certificates which will enable them to use specific radioactive medicinal products in diagnosis, therapy or research.

ATMP

Advanced therapy medicinal products: include gene therapy, stem cell therapy and tissue engineered products (containing some viable cells) exhibiting medicinal function.

Audit

A systematic and independent examination of study-related activities and documents, to determine whether the evaluated study-related activities were conducted, and the data were recorded, analysed and accurately reported according to the protocol, sponsor's standard operating procedures (SOP's), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

The Department of Health's minimum standards for research governance state that at least 10% of projects should be routinely audited. Audit should look at areas such as: protocol amendments, start and stop dates, changes to inclusion/exclusion criteria, changes to the consent procedure, changes to recruitment, funding, research team or the patient information sheet, approvals for amendments, adverse events, health and safety, intellectual property, subject logs, recruitment, consent, and changes to data management.

A distinction should be made between monitoring and auditing. All research activity should be monitored routinely. In addition, an organisation should conduct formal audit of a selection of research projects/activity.

Authorisation

The Human Tissue Act 2004 uses the term 'consent', whereas the Human Tissue (Scotland) Act 2006 uses the term 'authorisation'.

Bodily material

The Human Tissue Authority defines bodily material in the context of DNA analysis as: Material that has come from the human body (living or deceased) and which consists of or includes human cells. This includes hair, nails and gametes, and does not specifically exclude gametes.

Under the Human Tissue Act 2004, it is an offence to have bodily material with the intent of analysing its DNA without qualifying consent, subject to certain exceptions, which are outlined in the Consent Code of Practice. This applies UK-wide.

Chief Investigator (CI)

The Investigator with overall responsibility for the research, who is accountable to their employer and through them to the sponsor. In a multi-site study the CI has responsibility for design, management and reporting of the study, coordinating investigators who take the lead at each site.

All applications for ethical review should be submitted by the CI.

Clinical trial

With the advent of the Clinical Trial Regulations, the term clinical trial is used to describe a trial that tests the safety or efficacy of an investigational medicinal product, i.e. a clinical trial that is within the scope of the UK Medicines for Human Use (Clinical Trials) Regulations 2004. To avoid confusion we recommend that the term Clinical Trials of an Investigation Medicinal Product or CTIMP is used for this definition.

In the academic sector the term clinical trial is commonly used more loosely to describe:

Any prospective evaluation of a health care intervention, which involves the administration of a treatment or type of management, including diagnosis or the provision of lifestyle (e.g. dietary) advice.

Clinical Trial of an Investigational Medicinal Product (CTIMP)

A clinical trial that is within the scope of the UK Medicines for Human Use (Clinical Trials) Regulations 2004, i.e. a trial that tests the safety or efficacy of an investigational medicinal product. For more information, please see is the trial within the scope of the UK Regulations? section in the Clinical Trials Tool Kit.

Clinical Trial Regulations

The Medicines for Human Use (Clinical Trials) Regulations (2004) is the law within the UK that applies to research into the safety and/or efficacy of investigational medicinal products. These Regulations are how the EU Clinical Trials Directive was transposed into UK legislation. Further information can be found in the Clinical Trials Tool Kit.

Coded

Coded samples or data have a coded identification to protect the confidentiality of the individual during routine use, but it is possible for the code to be broken, and thus identify the individual from whom they were obtained. The key should not be freely accessible but held by senior individuals with a strict duty of confidentiality.

Competence

The ability of a person, given the necessary information, to understand the nature and the consequences of the proposed procedure or treatment, and to use that information to make a valid choice in accordance with their own fundamental values.

In relation to research this would be the ability to understand the research project and their proposed role within that project. And to make a decision as to whether they would like to participate or not, based on this information.

Competent Authority (CA)

An organisation (usually a governmental body) that has a statutory role to ensure compliance with relevant current legislation. This can involve licensing specific activities, performing inspections, granting approvals and/or developing codes of practice.

Confidential information

Any information obtained by a person on the understanding that they will not disclose it to others, or obtained in circumstances where it is expected that they will not disclose it. The law assumes that whenever people give personal information to health professionals caring for them, it is confidential as long as it remains personally identifiable. See also 'Personal data'.

Confidentiality

The duty of persons to whom personal information has been given not to share the information with any unauthorised person.

Consent

The voluntary agreement of an adult or competent child to participate in research, based on adequate knowledge and understanding of the relevant information.

Consent is often recorded by a signature on a consent form, but is simply a record of the dialogue and thought which has taken place. Consent can be verbal; the person seeking consent should record this.

Consent form

A written record of the study participant's decision to take part in the research study.

Custodian

The custodian is responsible for the safekeeping of data or tissue samples and control of their use, and eventual disposal (if required), all in accordance with legislation and the terms of the consent given by the donor.

Custodianship implies some rights to decide how the data/samples are used and by whom, and also responsibility for safeguarding the interests of the donors.

CRF

Clinical Record Form/Case Report Form, also used in a different context to mean Clinical Research Facility.

CTA

Clinical Trial Authorisation - statutory approval from the MHRA for a Clinical Trial of an Investigational Medicinal Product. Is also used to describe a Clinical Trial Agreement: a legal agreement drawn up between parties to define roles and responsibilities in the initiation, conduct and management of a clinical trial.

CTIMP

Clinical Trial of an Investigational Medicinal Product, i.e. a clinical trial that is within the scope of the UK Medicines for Human Use (Clinical Trials) Regulations 2004. The European Commission have developed an algorithm to enable you to determine whether

or not your study falls within the scope of the regulations (available from the Clinical Trials Tool Kit)

Data curation

The actions needed to maintain research data from point of creation to ensure they are fit for contemporary purpose and available for discovery and re-use. Implicit to this are the processes of archiving and preservation. Higher levels of curation will involve maintaining links between datasets, annotation, published materials and other information resources.

Database (research database)

A collection of research data that is organised and allows its contents to be easily accessed, managed and updated. The types of database depend on the requirements of each study. A common type is the relational database, where data are related to each other in a systematic manner so that they can be reorganised and accessed in a number of different ways.

A database may house one or many datasets.

Dataset

An organised collection of data that have a common theme, source or format; usually considered as a discrete entity.

Direct Costs

Direct costs are those associated with equipment, personnel, travel, and other expenses necessary to carry out a research application. Directly Incurred Costs: costs that are explicitly identifiable as arising from the conduct of a project, are charged as the cash value actually spent and are supported by an audit record. Directly Allocated Costs: the costs of resources used by a project that are shared by other activities. They are charged to projects on the basis of estimates rather than actual costs and do not represent actual costs on a project-by-project basis.

DNA analysis

The Human Tissue Act 2004 uses the term DNA analysis. This is not defined in the Codes of Practice, it could be interpreted as the investigation of variation in the nuclear or mitochondrial DNA that forms the genome of an individual and may be inherited from parent to child.

Under the Human Tissue Act 2004, it is an offence to have bodily material with the intent of analysing its DNA without qualifying consent, subject to certain exceptions, which are outlined in the Consent Code of Practice. This applies UK-wide.

EC

European Commission

EMEA

European Agency for the Evaluation of Medicinal Products is responsible for the scientific evaluation of applications for European marketing authorisation for medicinal products (centralised procedure). Under the centralised procedure, companies submit one single marketing authorisation application to the EMEA, which cover the whole of the European Economic Area. Its main responsibility is the protection and promotion of public and animal health, through the evaluation and supervision of medicines for human and veterinary use across the European Economic Area.

Exclusion Criteria

Specific criteria which are defined within the study protocol that expressly exclude specific individuals from participating in a study. The reasons for considering exclusion can range from safety issues, potential difficulties in management of particular participants or the need to control variables within the study. Exclusion criteria must always be defended ethically to guard against discrimination and uphold the concept of justice (or words to that effect).

Expedited Reporting

Reporting in a specified period of time: e.g. the reporting of SUSARs on CTIMPs

Experimental Medicine (EM)

Investigations undertaken in humans, relating where appropriate to model systems, to identify mechanisms of pathophysiology or disease, or to demonstrate proof-of-concept evidence of the validity and importance of new discoveries or treatments.

FDA

Food and Drug Administration is the competent authority for the regulation of food and drugs in the United States of America

Fraud

The fabrication, falsification, plagiarism or deception in proposing, carrying out or reporting results of research or deliberate, dangerous or negligent deviations from accepted practices in carrying out research. It does not include honest error or honest differences in the design, execution, interpretation or judgement in evaluating research methods or results or misconduct unrelated to the research process. Similarly it does not include poor research unless this encompasses the intention to deceive.

Full Economic Costing (fEC)

fEC is a governmental system to ensure research institution income covers not only the direct costs of research, teaching, administrative and support services, but also the ongoing investment in maintaining and renewing its infrastructure (e.g. buildings, equipment and systems).

GCP (Good Clinical Practice)

Good Clinical Practice (GCP) is an ethical and scientific quality standard for designing, conducting and reporting trials that involve the participation of human subjects. The International Conference on Harmonisation (ICH) standardised practice across Europe, Japan and the USA.

The relevant principles of GCP should be applied to any research that involves human participants, their tissues or data. The principles of GCP are listed in https://www.nihr.ac.uk/our-faculty/documents/GCP%20Reference%20Guide.pdf

Gene Therapy

The deliberate introduction of genetic material into human somatic cells for therapeutic, prophylactic or diagnostic purposes. This includes techniques for delivering synthetic or recombinant nucleic acids into humans and also involves (in the UK definition):genetically modified biological vectors (such as viruses or plasmids) genetically modified stem cells oncolytic viruses nucleic acids associated with delivery vehicles naked nucleic acids antisense techniques (for example, gene silencing, gene correction or gene modification) Genetic vaccines DNA or RNA technologies such as RNA interference Xenotransplantation of animal cells (but not solid organs).

GMP

Good Manufacturing Practice is that part of quality assurance which ensures that medicinal products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorisation (MA) or product specification. GMP is concerned with both production and quality control.

GTAC (Gene Therapy Advisory Committee)

GTAC is the ethics committee for clinical trials of gene therapies. They define gene therapy as the deliberate introduction of genetic material into human somatic cells for therapeutic, prophylactic or diagnostic purposes.

Harm

That which adversely affects the interests or welfare of an individual. This may be physical harm, discomfort, anxiety, pain, and psychological disturbance or social disadvantage as well as damage to reputation.

Hazard

Anything that could cause harm. Risk assessment requires identification of potential hazards and assessing the likelihood and possible impact of each hazard.

Health and Safety

Health and Safety is a discipline concerned with ensuring that the risks in the changing workplace are properly controlled. In the UK it is the role of the Health & Safety Executive to inspect, investigate and enforce H & S legislation.

Healthy volunteers

Persons recruited to and consenting to participate in research not by virtue of the fact they are an NHS patient suffering from a specific condition, but rather as they represent normal, non-diseased physiology.

HFEA (Human Fertilisation and Embryology Authority)

The HFEA is the UK's independent regulator overseeing safe and appropriate practice in fertility treatment and embryo research. The HFEA license and monitor centres carrying out IVF, donor insemination and human embryo research. They provide a range of detailed information for patients, professionals and Government.

HRA (Health Research Authority)

The HRA was established in December 2011. Its main purposes in accordance with the Care Act 2014, is to protect and promote the interest of patients and the public in health and social care research, co-ordinate and standardise practices relating to regulation, recognise and establish Research Ethics Committees (RECs), be a member of UK Ethics Committee Authority (UKECA), promote transparency in research and provide approvals for the processing of confidential information relating to patients.

Many members of the public want the opportunity to participate in research. The HRA make sure that health and social care research involving them is ethically reviewed and approved, that people are provided with the information they need to help them decide whether they wish to take part, and that their opportunity to do so is maximised by simplifying the processes by which high quality research is assessed. In doing this, the HRA help to build both public confidence and participation in health research, and so improve the nation's health.

- See more at: http://www.hra.nhs.uk/about-the-hra/#sthash.d0uYnnO4.dpuf

HTA (Human Tissue Authority)

The Human Tissue Authority (HTA) regulates the removal, storage, use and disposal of human bodies, organs and tissue from the living and deceased.

Under the Human Tissue Act 2004, the HTA has jurisdiction in England, Wales and Northern Ireland. For human application (under the EU Tissue and Cells Directive), the HTA has a UK-wide role.

HTA license

The HTA license premises for storage of relevant material for research purposes in England, Wales and Northern Ireland. There are many exemptions to the need for an HTA licence for research, best described in HTA Licence [insert link] station of the Data and Tissues Tool Kit.

The HTA also issues licences for human application under the EU Tissues and Cells Directive, in the whole of the UK.

Human tissue or samples

Generic term used to encompass human organs, tissues and biological samples. Depending on the context, human tissues or samples may be used in this Tool Kit to describe relevant material; this is likely when used in reference to the Human Tissue Act 2004. Strictly speaking relevant material is a more specific term.

ICH

International Conference on Harmonisation - often used in combination with GCP or Good Clinical Practice (i.e. ICH GCP).

IMP

Investigational Medicinal Product is a pharmaceutical form of an active substance or placebo being tested or used as a reference in a CTIMP. This includes products already with a marketing authorisation: when used or assembled (formulated or packaged) in a way different from the authorised form, when used for an unauthorised indication, or when used to gain further information about the authorised form.

Inclusion criteria

Specific criteria which are defined within the study protocol that expressly include specific individuals to participate in a study. E.g. individuals within a certain age range, with a specific condition, etc.

Indirect Costs

Non-specific costs charged across all projects based on estimates that are not otherwise included as Directly Allocated Costs. They include the costs of the Research Organisation's administration such as personnel, finance, library and some departmental services.

Identifiable information

See ‘Personal Data’.

Infrastructure Costs

The cost of rent, maintenance, electricity, water and other overheads considered in determining the full economic cost of conducting a research study.

Information Commissioner's Office (ICO)

The Information Commissioner’s Office is the UK’s independent authority set up to promote access to official information and to protect personal information under the Data Protection Act 1998. Also the authority that deals with Freedom of Information in England, Wales and N. Ireland.

Information sheets

See 'Participant / Patient information sheets' and https://www.hra.nhs.uk/planning-and-improving-research/research-planning/prepare-study-documentation/

Inspection

Inspection is a statutory activity, undertaken by government agencies or those acting on their behalf. It is a systematic investigation into systems and processes to measure compliance with legal frameworks.

IP

Intellectual property is the novel or previously undescribed tangible output of any intellectual activity. It has an owner, it can be bought, sold or licensed and must be adequately protected. It can include inventions, industrial processes, software, data, written work, designs and images.

IRAS

IRAS is a single system for applying for the permissions and approvals required for health and social care / community care research in the UK.
https://www.myresearchproject.org.uk/

IRMER

Ionising Radiation (Medical Exposure) Regulations 2000 lays down basic measures for the health protection of individuals against dangers of ionising radiation in relation to medical exposure. The Regulations impose duties on those responsible for administering ionising radiation to protect persons undergoing medical exposure whether as part of their own medical diagnosis or treatment or as part of occupational health surveillance, health screening, voluntary participation in research or medico-legal procedures

ISRCTN

The International Standard Randomised Controlled Trial Number is a simple numeric system for the unique identification of randomised controlled trials worldwide. The ISRCTN Register also accepts registration of other forms of studies designed to assess the efficacy of health-care interventions.

Medical Device

The term 'medical device' covers all products, except medicines, used in healthcare for the diagnosis, prevention, monitoring or treatment of illness or disability. The range of products is very wide: it includes contact lenses and condoms; heart valves and hospital beds; resuscitators and radiotherapy machines; surgical instruments and syringes; wheelchairs and walking frames or other assistive technology products - many thousands of items used each and every day by healthcare providers and patients. For more information, see the MHRA devices webpages

Medicinal Product

Article 1 of Directive 2001/83/EC as amended defines a "medicinal product" as: "Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological,

immunological or metabolic action, or to making a medical diagnosis" More information is available from the MHRA Borderline Medicines webpages

Medicines for Human Use (Clinical Trials) Regulations

The Medicines for Human Use (Clinical Trials) Regulations (2004) apply to research into the safety and/or efficacy of investigational medicinal products. Further information can be found in CTIMP, IMP and the Clinical Trials Tool Kit.

MHRA (Medicines and Healthcare products Regulatory Agency)

The MHRA is the UK government agency which is responsible for ensuring that medicines and medical devices work, and are acceptably safe.

They have statutory powers both in the approval of drug / devices for licence and in approving Clinical Trials of Investigational Medicinal Products, and clinical investigations involving devices. https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency

Monitoring

The process of monitoring a study should ensure that the rights and wellbeing of any participants are protected, the reported data are accurate and complete, and that the conduct of the study is in compliance with the approved protocol/amendments and with applicable regulatory/governance requirements.

Monitoring should be built into the conduct of the study as a means to minimise risk, and should be ongoing and performed by members of the research team and people independent to it.

MRC

Medical Research Council

NHS REC

NHS Research Ethics Committee

NHS R&D Forum

The NHS R&D Forum is a network for those involved in planning and managing research in health and social care.

NHS UK Policy Framework for Health and Social Care Research

The UK Health Departments' UK Policy Framework for Health and Social Care Research documents a set of standards and principles for carrying-out health related or social/community care research in the UK. It is mandatory for all research taking place in the NHS and using NHS resources. It aims to improve research and safeguard the public by:

- Enhancing ethical awareness and scientific quality
- Promoting good practice

- Reducing adverse incidents and ensuring lessons are learned
- Forestalling poor performance and misconduct

NIHR

National Institute for Health Research

NIHR Clinical Research Network Coordinating Centre (NIHR CRN CC)

The National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC), formerly known as UKCRN Coordinating Centre (UKCRN CC), was established to support clinical research and to facilitate the conduct of trials and other well-designed studies within the NHS. As part of the UK Clinical Research Collaboration (UKCRC), it works towards the development of a world class infrastructure to support clinical research in the UK.

RES (Research Ethics Service) – Now part of the HRA (Health Research Authority)

The Research Ethics Service (RES) Head Office is a directorate within the National Patient Safety Agency and provides help and leadership for NHS Research Ethics Committee's (RECs) by coordinating the development of operational and infrastructure arrangements in support of their work. This includes implementing standards to ensure national consistency, providing training for REC members and Co-coordinators, identifying IT solutions for procedural management and establishing regional REC centres to manage REC's.

Formerly (Central Office for Research Ethics Committees) COREC.

Participant

A person who takes part in a research study or allows their tissue samples or information to be used in research, following appropriate consent, e.g. a patient or a healthy volunteer.

Participant / Patient information sheet (PIS)

The participant information sheet, in a form appropriate for the study population, explains what the research involves and how the research study will affect the participant. It is usually accompanied by a consent form.

Peer review

A system whereby research, or research proposals, are reviewed by independent experts to assure the quality of the research (e.g. can the research design answer the question? Does the research add to existing knowledge?).

Personal data

In the context of the Data Protection Act 1998 personal data comprise information about living people who can be identified from that data, or from combinations of data and other information which the person in control of the data has, or is likely to have in future.

This includes written and electronic records, opinions, images, recordings and information obtained from samples, from which the person can be identified.

The terms: confidential personal/patient data/information; identifiable personal/patient information/data; or identifiable confidential information, are used interchangeably and mean the same as personal data.

Phase I

Phase I or Healthy Volunteers studies are often non-placebo controlled, small studies, and the first test of a drug in humans. To establish safe/tolerable levels to establish initial pharacology in humans usually carried out on volunteers who may be paid.

PI (Principal Investigator)

The UK Policy Framework for Health and Social Care Research defines the Principal Investigator as the leader responsible for a team of individuals conducting a study at a site. In a single site study the PI and the CI are likely to be the same person. (To avoid confusion the term Principal Applicant is being increasingly used to describe the lead investigator on a funding application.)

CAG (Confidentiality Advisory Group)

CAG was established to provide advice on issues of national significance involving the use of patient information and to oversee arrangements created under Section 60 of the Health and Social Care Act 2001. Its membership is drawn from patient groups, healthcare professionals and regulatory bodies. This group was formerly known as National Information Governance Board (NIGB).

Proposal

A proposal details the scientific and ethical reasons for research and should demonstrate conceptual innovation, methodological rigor and substantive content. The term is used to refer to a document produced to apply for funding.

Protocol

A research protocol is a written document demonstrating the necessity and feasibility of a particular study, as well as giving a detailed plan of how the study will be conducted, analysed and disseminated. In CTIMPs, the protocol should contain specific information (see HUTH Trust sponsored CTIMP template) or visit https://www.hra.nhs.uk/planning-and-improving-research/research-planning/protocol/

Pseudonymised data / information

Described under the Data Protection Act 1998 to mean where the normal personal identifiers have been replaced by an artificially-created identifier so as to conceal the identity of the patient. The links between the artificial and normal identifiers are stored separately and securely, and so the data may still qualify under the Data Protection Act as personal data. Also referred to as linked anonymous data or coded data.

Quality Assurance (QA)

A planned and systematic pattern of all actions necessary to provide adequate confidence that the research data output collected was done so consistently and in accordance with established methods.

RCT

A Randomised Controlled Trial is a scientific procedure in which treatments are allocated to subjects at random, in order to eliminate bias. It is considered the most reliable form of scientific evidence because it ensures that different treatment groups are statistically equivalent.

REC

Research Ethics Committees are independent committees that review the ethical issues within research projects that involve people as participants or their data or tissues. Research Ethics Committees (REC) is established throughout the UK within the NHS, in particular universities as well as independent Phase 1 committees.

Recognised Research Ethics Committee

A Research Ethics Committee (REC) recognised by UKECA (UK Ethics Committee Authority) under the Medicines for Human Use (Clinical Trials) Regulations 2004. A list of all recognised RECs is available on the NRES website

Regulators

Organisations that ensure research is conducted in line with the law, e.g. such as the Human Tissue Authority, Medicines and Healthcare products Regulatory Agency.

Reproducible

A reproducible measurement is one that is repeatable, but not necessarily valid.

R&D office / department

This term is used generically to describe Research and Development offices or departments within either NHS organisations or universities. Meaning the office or department that has responsibility for research governance in that organisation.

Regulators or Regulatory Authorities / Agencies / Bodies

A body that has a statutory role to ensure compliance with regulation. Their role is usually described within the relevant primary legislation or associated regulations. They may issues licences (e.g. Human Tissue Authority), approvals (e.g. HFEA) and usually will have an Inspection role.

Related and unexpected serious adverse events

NRES define this term as:

A serious adverse event (SAE) occurring to a research participant should be reported to the REC that gave a favorable opinion of the study (the 'main REC') where in the opinion of the chief 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.

A serious adverse event is an untoward and unexpected occurrence that:

results in death;

is life-threatening;

requires hospitalisation or prolongation of existing hospitalisation;

results in persistent or significant disability or incapacity;

consists of a congenital anomaly or birth defect.

Relevant material

In the Human Tissue Act 2004, "relevant material" is defined as material, other than gametes, which consists of or includes human cells. In the HT Act, references to relevant material from a human body do not include:

(a) embryos outside the human body, or

(b) hair and nail from the body of a living person.

The HTA has a more detailed definition of relevant material.

Relevant material is different to Bodily material.

Research Ethics committee (REC)

RECs are independent committees that review the ethical issues within research projects that involve people as participants or their data or tissues. See Ethical approval station in the Data and Tissues Tool Kit for more information on the remit of REC's.

Research Governance

Research governance is a term that is used in the UK Health Departments' UK Policy Framework for Health and Social Care Research. See 'NHS UK Policy Framework for Health and Social Care Research'.

It is commonly used in a generic way to encompass the UK Policy Framework for Health and Social Care Research standards and principles, including all applicable regulatory requirements.

Research passport

A streamlined system for issuing honorary research contracts to researchers who do not have a contractual relationship with the NHS in the UK. The system enables existing pre-engagement checks and assurances from substantial employers to be used by other organisations wishing to issue honorary research contracts to investigators. More information is available on the R&D website at https://www.hey.nhs.uk/research/researchers/research-passport/

Research tissue bank

The HTA define a Tissue Establishment as a tissue bank or unit of a hospital or another body where activities of processing, preservation, storage or distribution of human tissue and cells are undertaken. It may also be responsible for procurement or testing or tissue and cells.

A research tissue bank could be described as organised entities that procure, store and distribute tissues samples for research purposes.

Risk

The likelihood of harm being caused by a hazard. The characteristics of risk include the probability of its occurrence, as well as the magnitude and duration. Harm may be to a research participant, a researcher or to the research itself.

Risk management

The process of identifying possible risks associated with a study and planning how to reduce the risk, or contingency plans should the risk occur.

Screening

Screening is a process, usually preceded by consent, in which members of a population are tested to identify those individuals who are suitable for inclusion in a study.

Sensitive information

Information that when used incurs a need for extra care, e.g. about mental health, sexuality and other areas where revealing confidential information is especially likely to cause embarrassment or discrimination. According to the Data Protection Act 1998 “sensitive personal data” includes all information about physical as well as mental health or condition, or sexual life.

Serious advise event (SAE)

The HTA describe a serious adverse event as any untoward occurrence associated with the procurement, testing, processing, storage and distribution of tissue and cells that might lead to the transmission of a communicable disease, to death or life-threatening, disabling or incapacitating conditions for patients, or which might result in, or prolong, hospitalisation or morbidity.

RES define a serious adverse event as an untoward and unexpected occurrence that:

results in death;

is life-threatening;

requires hospitalisation or prolongation of existing hospitalisation;

results in persistent or significant disability or incapacity;

consists of a congenital anomaly or birth defect.

Significance

There is a difference between statistical and clinical significance. Statistical significance means that a discovered difference between populations could not have occurred by chance alone. Clinical significance is largely a matter of judgement e.g. the difference between populations may be statistically significant but, if the difference isn't worth achieving, not clinically significant. Differences may be found to be statistically significant, but of no clinical significance.

SmPC

Summary of Product Characteristics (associated with a marketing licence for a drug)

Source data verification

Source data verification (SDV) is a check that the data collected on a research study (e.g. on a case report form or in a database) can be verified by looking at a primary source (e.g. medical record). In essence, checking for consistency and accuracy in transcribing data from one place to another. Auditors will often wish to see SDV documented when the risks involved indicate it should be used.

Sometimes the research record will be the source data, e.g. for electronic questionnaire-based studies. In these situations mechanisms should be built in to ensure that checks are in place to minimise the chances of error when completing the questionnaire.

Sponsor

The sponsor is the individual, or organisation (or group of individuals or organisations) that takes on responsibility for confirming there are proper arrangements to initiate, manage and monitor, and finance a study. Responsibilities are defined by the UK Policy Framework for Health and Social Care Research and by the Clinical Trial Regulations.

Support departments

Departments, often service departments with the NHS, which provide input into the conduct of a research project by providing a specific service i.e. Pharmacy, as opposed to a collaborating department which provide intellectual input into study design and /or interpretation.

Suspected Unexpected Serious Adverse Reaction (SUSAR)

All suspected adverse reactions related to an investigational medicinal product (the tested investigational medicinal products and comparators) which occur in the concerned

trial, and that are both unexpected and serious. For more detailed guidance please see Clinical Trials Tool Kit.

Tissue bank

See 'Research tissue bank'.

Tissue sample

See 'Human tissue sample'.

UKCRC

The UK Clinical Research Collaboration (UKCRC) is a partnership of organisations working to establish the UK as a world leader in clinical research. The UKCRC brings together key organisations in the UK clinical research environment. This includes the main funding bodies, academia, the NHS regulatory bodies, industry and patients.

UKCRN – now CRN (see NIHR CRN CC)

Urgent Safety Measure

The sponsor and investigator may take appropriate urgent safety measures in order to protect the subjects of study against any immediate hazard to their health or safety. If such measures are taken, the sponsor shall immediately and in any event no later than 3 days from the date the measures are taken, give written notice to the relevant ethics committee of the measures taken and the circumstances giving rise to those measures

Validity

Validity indicates that a measurement truly reflects the size or extent of a particular parameter. For data to be ‘truthful' the measurements used must be both valid and reproducible.

Version control

Version control is the management of multiple revisions to the same document. Version control enables users to tell one version of a document from another. Usually the latest approved version of a document is the one that should be used.

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