

# Clinical Research in Oxford

A guide for Research Nurses,  
Midwives and other Research  
Health Professionals



The amount of information in this booklet may seem daunting right now; please be assured that it is meant to support you on your journey into research for as long as you need it, and there is no expectation that you read it from cover to cover on your first day or week.

Reference is frequently made to 'research nurses' who are currently the largest single staff group in clinical research, but the information is intended to be useful to all research practitioners

Compiled by Sally Beer updated by Karen Bell, Oxford Biomedical Research Centre – Education and Training Coordinator, based on *West Yorkshire/Bradford Teaching Hospitals NHS Trust Induction Pack*, *Leeds Teaching Hospitals NHS Trust Clinical Research Nurse Induction Pack & Competency Framework* and *Yorkshire Cancer Research Network's Induction Handbook*.

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## Welcome to your post in Research

Welcome to the NIHR Oxford Biomedical Research Centre (BRC), a partnership between Oxford University Hospitals NHS Trust and Oxford University.

We hope you will find that your role in clinical research is varied and interesting. Research nurses take part in studies from start to finish. They play a vital role in supporting patients throughout the course of the research, ensuring clinical studies run smoothly and that participants are safe and fully informed. They may be responsible for recruiting patients, gaining consent, collecting data, carrying out study-related clinical procedures and much more.

As a Clinical Research Nurse you will be providing specialist care that will have a potential benefit to your patients as well as a benefit to future patients. The role of a Clinical Research Nurse is diverse, covers many specialties and is increasingly becoming recognised as a specialty in its own right. It can be a challenging role but is an opportunity to use the skills you have gained in clinical practice, combined with new research skills that you will acquire that will establish your career as a Clinical Research Nurse.

You will be responsible for ensuring that your clinical trials are completed according to the study protocol, that you perform any tasks which are delegated to you and that you have sufficient experience and training to complete these tasks.

The most important elements of your role will be to provide a **high standard of care and ensure patient safety** and to **collect good quality data**. The safety of your patients remains as important as it would in a non-research role and poor data quality can affect the quality of the entire study.

This booklet is designed to be a practical and informative resource for you. Take every opportunity to obtain advice and support from your research colleagues and R&D Department.

*"I can genuinely say that I feel I have the best job in the world! I feel privileged to be in a profession which is fundamental to the process of ensuring that patient care is based on the best available evidence."* Research Nurse, Milton Keynes

Your move into research will allow you the opportunity to consider your career progression. You will be presented with many opportunities to develop yourself: make the most of every opportunity!



# Research and the NHS

## Why engage in research

Studies suggest that patients who receive care in research-active institutions may have better health outcomes than patients who are treated in a non-research environment. By joining the research community you are actively helping to drive up the standard of healthcare for your patients. By investigating the cause and course of diseases and how best to treat them, you are also helping to establish 'what works' and build the body of evidence that can lead to a positive change in future care.

## The importance of Research within the NHS

The Department of Health's strategy to improve the health of the nation continues to place research at the forefront of the NHS. The White Paper *Equity and Excellence: Liberating the NHS* (DH 2010) highlights research in terms of quality, transparency and value for money, with the aim of achieving health outcomes as good as anywhere else in the world. It aims to deliver quality care from evidence based practice which is thoroughly researched. The NHS has a constant challenge to provide a service that is up to date and efficient. Health research plays a key role in this service by using the evidence from studies to support health strategies and changes in medical practice.

The NHS has the potential to provide one of the best health research environments in the world. However, before 2000, although research was taking place across the UK, it was being carried out by a wide range of researchers and organisations: government, academia, pharmaceutical industries, charities etc. with a lack of an overall strategy and coordination. Resources were being allocated in an *ad hoc* way and there was dissatisfaction with the lengthy bureaucratic procedures.

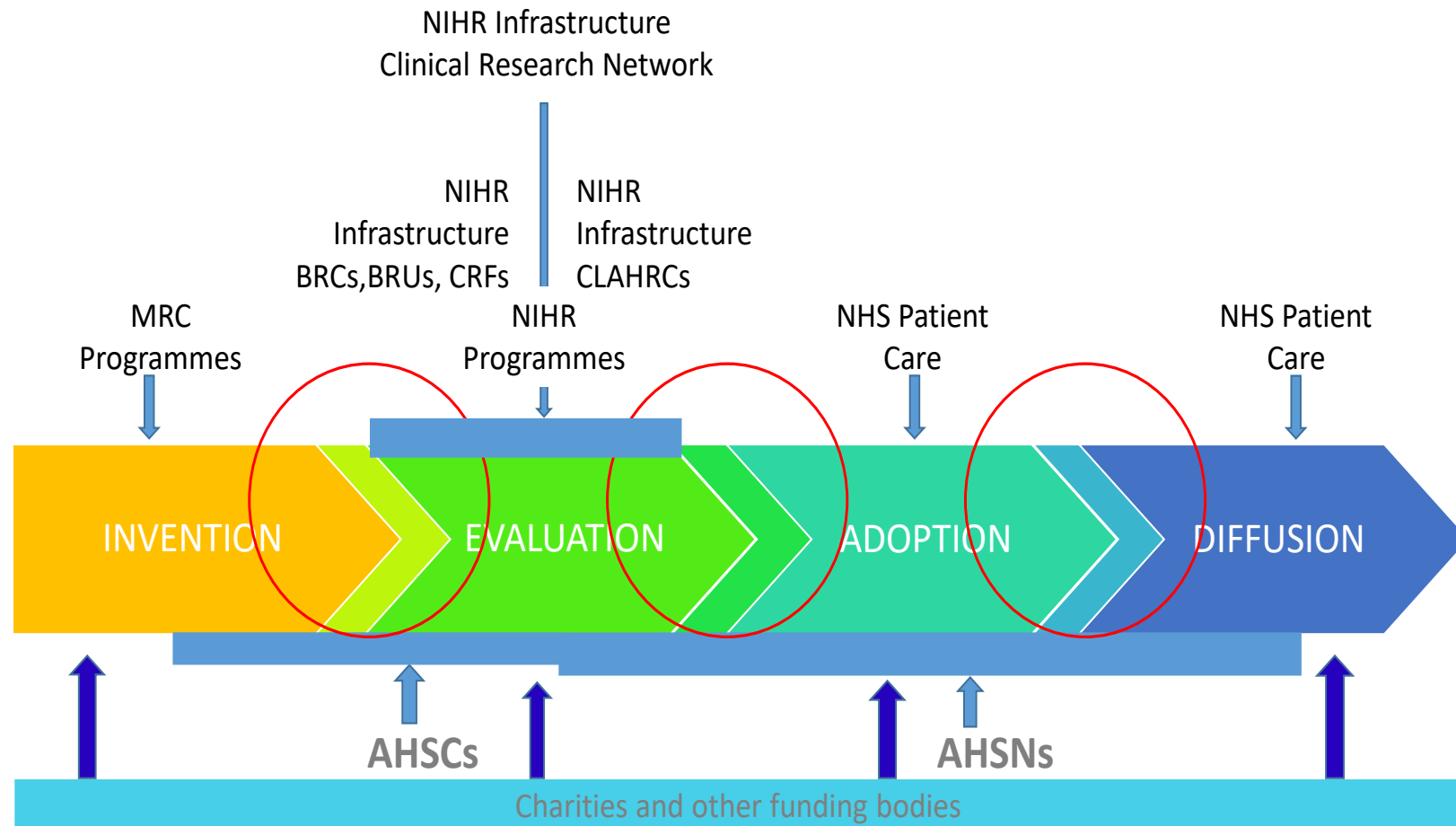
The NHS Constitution published in January 2009, commits to innovation and to the promotion and conduct of research to improve the current and future health and care of the population. The commitment features in one of seven key principles - the principle that the NHS aspires to high standards of excellence and professionalism.

*"Research is a core part of the NHS. Research enables the NHS to improve the current and future health of the people it serves. The NHS will do all it can to ensure that patients, from every part of England, are made aware of research that is of particular relevance to them. The NHS is therefore putting in place procedures to ensure that patients are notified of opportunities to join in relevant ethically approved research and will be free to choose whether they wish to do so."* (Handbook to the NHS Constitution, January 2009).

The Health and Social Care Act (2012) went on to further embed research in the NHS and enable a greater voice for patients. Through the National Institute for Health Research (NIHR) the NHS now has a thriving research culture. As a member of a clinical research team you will play a key role in contributing to this research culture through clinical trials and/or health related research, therefore continually improving the quality and choices available for patients and healthcare as a whole.

You will also be supported and encouraged to work with patients as equal partners in this research endeavour through numerous Patient and Public Involvement (PPI) activities that are underway in Oxford. PPI is not about recruiting patients as participants in trials and studies (although good PPI can make this much easier) – it is about working with those outside the professional world of medicine, who may have extensive expertise through experience, to identify what research matters, how best to do it and to communicate its results to other patients and the public. The overall aim is to make sure research is truly responsive to patients' needs and wishes.

# Research and Innovation landscape



# Research across Oxford University Hospitals NHS Foundation Trust and University of Oxford Partnership

## Funders of Research

NIHR

MRC,  
Wellcome Trust

Charities

University

### Oxford Biomedical Research Centre

#### Themes

- Antimicrobial Resistance and Modernising Microbiology
- Cardiovascular
- Clinical Informatics and Big Data
- Diabetes and Metabolism
- Gastroenterology and Mucosal Immunity
- Genomic Medicine
- Haematology and Stem Cells
- Imaging
- Molecular Diagnostics
- Multi-modal Cancer Therapies
- Multimorbidity and Long Term conditions
- Musculoskeletal
- Neurological conditions
- Obesity, diet and lifestyle
- Partnerships for Health, Wealth and Innovation
- Respiratory
- Stroke and Vascular Dementia
- Surgical Innovation and Evaluation
- Technology and Digital Health
- Vaccines for Emerging and Endemic Diseases

### CRN -Thames Valley and South Midlands (hosted by OUH)

#### Divisions

1. Cancer
2. Diabetes, stroke, cardiovascular, metabolic and endocrine, renal
3. Children, genetics, haematology, reproductive health and childbirth
4. DENDRON, mental health and neurological disorders
5. Primary care, aging, health service and delivery, oral health and dentistry, public health, musculoskeletal disorders and dermatology
6. Anaesthetics/peri-operative medicine and pain management, critical care, injuries and emergencies, surgery, infectious diseases/microbiology, ophthalmology, respiratory disorders, gastroenterology, hepatology

**The Cross Divisional and Support Services team offer support with governance; study support; cost attribution; finance: IT**

### Clinical Trials Units

- Diabetes Trials Unit
- Primary Care and Vaccines Collaborative
- National Perinatal Epidemiology Unit
- Oxford Cognitive Health and Neurosciences
- Clinical Trials Services Unit and Epidemiological Studies Unit
- Oxford Clinical Trials Research Unit which integrates the following trials groups
  - Centre for Statistics in Medicine
  - Critical Care, Trauma and Rehabilitation Trials Group
  - Gastroenterology Trials Group
  - Oncology Clinical Trials Office (all phases)
  - Respiratory Trials Unit
  - Rheumatology
  - Surgical Intervention Trials

### Departments

- Department of Biochemistry
- Nuffield Department of Clinical Medicine
- Nuffield Department of Clinical Neurosciences
- Department of Experimental Psychology
- Radcliffe Department of Medicine
- Nuffield Department of Obstetrics and Gynaecology
- Department of Oncology
- Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences
- Department of Paediatrics
- Sir William Dunn School of Pathology
- Department of Physiology, Anatomy and Genetics
- Nuffield Department of Population Health
- Nuffield Department of Primary Care Health Sciences
- Department of Psychiatry
- Nuffield Department of

### Also in Oxford

Oxford Health BRC for Mental Health, Oxford Academic Health Science Centre (OxAHSC), Oxford Academic Health Science Network (OxAHSN), Oxford Collaborations for Applied Health Research and Care (OxCLAHRC)



## National Institute for Health Research (NIHR)

<https://www.nihr.ac.uk/>

The National Institute for Health Research (NIHR) is funded through the Department of Health to improve the health and wealth of the nation through research. The NIHR provides the framework through which the Department of Health can position, maintain and manage the research, research staff and research infrastructure of the NHS in England as a national research facility. The NIHR systems represent the most integrated clinical research system in the world, driving research from bench to bedside for the benefit of patients and the economy.

Since its establishment, the NIHR has transformed research in the NHS. It has increased the volume of applied health research for the benefit of patients and the public, driven faster translation of basic science discoveries into tangible benefits for patients and the economy, and developed and supported the people who conduct and contribute to applied health research.

### Aims

- Establish the NHS as an internationally recognised centre of research excellence.
- Attract, develop and retain the best research professionals to conduct people-based research.
- Commission research focused on improving health and social care.
- Increase the opportunities for patients and the public to participate in, and benefit from, research.
- Promote and protect the interests of patients and the public in health research.
- Drive faster translation of scientific discoveries into tangible benefits for patients.
- Maximise the research potential of the NHS to contribute to the economic growth of the country through the life sciences industry.
- Act as a sound custodian of public money for the public good.

The NIHR works in partnership with many sectors including the public and service users, the NHS, public health, other Government funders, the academic and third sectors and industry.

### Structure

The NIHR manages its health research activities through four main work strands:

- **Infrastructure:** providing the facilities and people for a thriving research environment.
- **Faculty:** supporting the individuals carrying out and participating in research.
- **Research:** commissioning and funding research.
- **Systems:** promoting faster, easier clinical research through unified, streamlined and simple systems for managing ethical research and its outputs.

## **NIHR Oxford Biomedical Research Centre (OxBRC)**

<http://oxfordbrc.nihr.ac.uk/about-us-intro/>

The Oxford BRC is based at the Oxford University Hospitals and run in partnership with the University of Oxford. It was one of the first BRCs set up by the National Institute for Health Research (NIHR) in 2007 and is one of the largest today. In its third round of funding, it was awarded £113.7m to support translational research from 2017 to 2022 across 20 research themes, including cancer, heart disease, stroke and other conditions, diabetes, microbiology and infections, musculoskeletal, neurological conditions, gastroenterology and immune conditions, vaccines, respiratory conditions, haematology, obesity, genomics, imaging, digital technology and the use of clinical data. The Oxford BRC's aim is to translate basic scientific developments into tangible clinical benefits for NHS patients.

## **Clinical Research Network – Thames Valley and South Midlands (CRN)**

<https://www.nihr.ac.uk/nihr-in-your-area/thames-valley-and-south-midlands/>

The NIHR Clinical Research Network is the clinical research delivery arm of the NHS. It operates across England through a national coordinating centre and 15 local branches delivering research in the NHS across all disease areas. The NIHR Clinical Research Network Thames Valley and South Midlands is hosted by Oxford University Hospitals NHS Foundation Trust and covers Berkshire, Buckinghamshire, Milton Keynes and Oxfordshire.

It provides funding, training and other support to local qualified NHS providers (such as local hospitals and GP surgeries) so that they are able to improve healthcare by running clinical research studies. They also offer a comprehensive training programme for NHS professionals who want to get involved with clinical research.

## **Patients Active in Research (PAIR)**

<https://patientsactiveinresearch.org.uk/>

The main purpose of this site is to enable patients, carers or other members of the public to get involved with planning research and how it is carried out, and to put researchers in touch with people who want to do this. Researchers can post a project, and members of the public can register interest on this site.

In addition, this site also promotes opportunities for people to join research studies, and enable those who want to take part in clinical trials to find out about any that are currently recruiting in the Thames Valley.

The PPI working group is guided by the PAIR group which has equal numbers of patient and professional members (approx. 16 in total) with a lay co-chair alongside a researcher.

## **Oxford Collaboration for Leadership in Applied Health Research and Care (CLAHRC)**

<http://www.clahrc-oxford.nihr.ac.uk/>

The NIHR CLAHRC Oxford is a partnership between universities, healthcare commissioners and healthcare providers in the region of Oxford and the Thames Valley, hosted by Oxford Health NHS Foundation Trust. They identify local and national health and social care priorities and fund and support projects which address these.

## **Oxford Academic Health Science Centre (OxAHSC)**

<https://www.oxfordahsc.org.uk/>

OxAHSC is the partnership and close alliance between Oxford Health NHS Foundation Trust, Oxford University Hospitals NHS Foundation Trust, Oxford Brookes University and the University of Oxford. They coordinate clinical and academic research which can be translated, applied and evaluated for patient benefit.

## **Oxford Academic Health Science Network (AHSN)**

<http://www.oxfordahsn.org/>

The Oxford AHSN is one of 15 AHSNs across England. They aim to turn innovation into mainstream clinical practice quickly and widely, improving health and creating wealth through better connections between the NHS, research and business.

## **Joint Research Office (JRO)**

The Joint Research Office brings together all aspects of research governance, finance, contract and support services, spanning both Oxford University Hospitals NHS Trust and the University of Oxford. The Research Governance Team supports and advises researchers in meeting the requirements of local and UK regulatory frameworks.

The Finance Team offers advice and support in costing studies and has a role in managing accounts for commercial and non-commercial trials. Contracts are negotiated with external organisations for commercial and non-commercial trials. The team also has an ongoing monitoring responsibility for clinical trials and other studies sponsored by Oxford University Hospitals and for audit of research hosted by the Trust.

## **Research Design Service (RDS)**

The RDS supports researchers to develop and design high quality research proposals for submission to NIHR funding programmes and other open, national, peer reviewed funding competitions for applied health or social care research. They provide support on all aspects of developing a grant application including, research design, research methods, identifying funding sources and involving patients and the public. Their advice is confidential and free of charge.

<https://www.nihr.ac.uk/about-us/how-we-are-managed/our-structure/research/research-design-service/rds-new.htm>

## Attributing the costs of health and social care research (AcoRD)

<https://www.gov.uk/government/publications/guidance-on-attributing-the-costs-of-health-and-social-care-research>

Research studies comprise a number of component activities, which, for the purpose of agreeing funding arrangements, are attributed to one of three broad cost categories

- **Research Costs** - the costs of the R&D itself that end when the research ends. They relate to activities that are being undertaken to answer the research questions.
- **NHS Treatment Costs** - the patient care costs, which would continue to be incurred if the patient care service in question continued to be provided after the R&D study had stopped.
- **NHS Support Costs** - the additional patient care costs associated with the research, which would end once the R&D study in question had stopped, even if the patient care involved continued to be provided.

The funding arrangements for non-commercial NHS research can be complex, often involving a number of partner organisations. It is essential that both the NHS and its partner organisations identify and quantify the full cost of research and reach a shared understanding of how these costs are recovered through appropriate funding arrangements.

NIHR has established a network of AcoRD specialists based in your Local CRN to:

- Signpost researchers to resources and training to understand the principles of AcoRD
- Provide specialist advice and support for activity attribution
- Support resolution of attribution queries

<https://www.nihr.ac.uk/funding-and-support/study-support-service/early-contact-and-engagement/acord/>

## Competencies

A set of practical competencies has been developed by a team of experienced NHS R&D managers who understand what an effective research support team needs to know, understand and be able to do, in order to provide an effective service for health research in an organisation. Each competency has five levels to reflect a range of abilities from a new or inexperienced team member to a proactive leader of activity.

[www.nihr.ac.uk/systems/Pages/Research\\_Support\\_Services.aspx](http://www.nihr.ac.uk/systems/Pages/Research_Support_Services.aspx)

## Research Governance

<https://www.ouh.nhs.uk/researchers/about/default.aspx>

Research governance applies to everyone connected to clinical research, whether as a chief investigator, care professional, researcher, their employer(s) or support staff. Clinical research is any health-related research that involves humans, their tissue and/or data.

- Research governance is needed to:
- safeguard participants in research
- protect researchers/investigators (by providing a clear framework within which to work)
- enhance ethical and scientific quality
- mitigate risk
- monitor practice and performance
- promote good practice and ensure that lessons are learned

## Research Drop-in Sessions

The Joint Research Office offers bi-monthly drop-in sessions for researchers requiring advice and support about their research study including guidance on:

- Sponsorship process
- Ethics applications
- Research versus audit/service evaluation
- IRAS system
- Regulatory approvals
- NHS permission (Trust approval)

All sessions 12.30-13.30 and held in the meeting room of the Joint Research Office at the Churchill Hospital. The sessions are informal with no need to book a space - just turn up! Email: [debbie.franklin@ouh.nhs.uk](mailto:debbie.franklin@ouh.nhs.uk)

## Research Bulletin

R+D publish a regular bulletin of updates and events. To join the mailing list contact [foteini.mavrommati@ouh.nhs.uk](mailto:foteini.mavrommati@ouh.nhs.uk)

## The Oxford Research Network Committee

This is a forum for research nurses, co-ordinators, data managers and others working in clinical research and meets four times a year to discuss a variety of topics across the OUH site. If you would like to be included on the Research Network mailing list contact [research.network@nhs.net](mailto:research.network@nhs.net)

## Section 1: Your first week

Whether you are new to the Trust or University, or moving into research for the first time, you will be meeting many new people, going places you didn't even know existed and encountering a whole new world of abbreviations, acronyms, protocols, SOPs (Standard Operating Procedures) and legislation. (Find a list of commonly used acronyms and terms on page 19)

Your line manager will introduce you to many of these, and we have included some important information below to help you on your path.

### Induction

It is important that you meet with your line manager to discuss the scope of your role, your previous experience and ensure your induction programme covers all aspects of your role.

Your Induction Programme should include the following:

- Familiarisation with working areas and the building(s) as appropriate
- Fire and evacuation procedures (Trust mandatory Fire Awareness Training)
- Trust induction programme if new to the Trust
- ID badge and access procurement
- Introduction to and access to electronic information management systems
- Absence policy and arranging of annual leave
- Clear understanding of line management and reporting
- Information gathering around specialty area of practice, advice on key learning and sources of appropriate information/courses
- Allocation of a mentor or buddy for supervision and guidance
- Date to set objectives to be reviewed after three months

Introduction to key staff:

- Relevant consultants and wider medical team
- Matron (or appropriate AHP line manager)
- Directorate manager/faculty or R&D lead at University
- R&D lead for specialty
- Business Manager
- Nursing and other local research colleagues
- Outpatient or other patient areas to be utilised when conducting research
- Administrative team and or wider research support staff as appropriate/available to your area

## Information Governance

As a member of a research team you will have access to confidential data almost daily. It is a requirement for all staff in the Trust to complete Information Governance training annually. This is available as e-learning or drop in sessions via the OUHT Learning Management System (LMS).

If you have a Honorary Trust contract, please contact [recruitment.administrator@ouh.nhs.uk](mailto:recruitment.administrator@ouh.nhs.uk) to request a payroll/assignment number, and then register for an LMS account at <http://ouh.oxnet.nhs.uk/Pages/Home.aspx> or [New E-LMS Users register here](#)

## Informed Consent

If you will be consenting participants into studies, it is advisable to attend a Valid Informed Consent course before taking on this responsibility. Further information in **Appendix 3**.

## Good Clinical Practice (GCP) training

A key requirement for anyone involved in the conduct of clinical research is Good Clinical Practice (GCP) training. GCP is the ethical and practical standard to which all clinical research is conducted.

To get started, it is advisable to complete an online course, but to then attend a face-to-face session, where there is the opportunity to ask questions and learn from others experiences.

<https://www.nihr.ac.uk/our-research-community/clinical-research-staff/learning-and-development/national-directory/good-clinical-practice/>

<https://researchsupport.admin.ox.ac.uk/ctrq>

Compliance with GCP provides public assurance that the rights, safety and wellbeing of research participants are protected and that research data are reliable. Everyone involved in the conduct of clinical research must be competent to perform their tasks, qualified by education, training and experience. This is a requirement of the UK Policy Framework for Health and Social Care Research, the policy covering all research in the NHS in England, and in law (SI 2004/1031, Schedule 1, Part 2, 8) for those people working on clinical trials.

The OUH Trust expectation is that GCP training will be renewed every three years, and strictly enforced for those involved in CTIMPS. See **Appendix 2** for further information on GCP Training.

## Section 2: Your first month

You will be required to comply with mandatory training as required by the Trust, University and research, dependent on your role and clinical area.

Continue to explore the following:

- Familiarisation with data protection legislation and institutional policies
- Internal governance procedures and quality assurance
- Understanding the roles of RECs and R&D, and the statutory legislation for research governance
- Understanding of research methods
- Patient and Public Involvement (PPI) in research
- How to describe randomisation and equipoise to potential subjects
- Other trial related procedures, clinical and non-clinical
- Introduction to multi-disciplinary team and attendance at MDT meetings where appropriate
- Shadowing colleagues in clinical areas and for peer learning re research trial conduct
- Introduction to blood sampling handling, processing, shipment
- Dry ice handling and legislation/guidance
- Familiarisation with departmental SOPs
- Participate in a monitoring visit
- Pathway Co-ordinators (oncology)

## Training Opportunities

- Oxford BRC Education and Training  
<http://oxfordbrc.nihr.ac.uk/professional/education-and-training/>
- NIHR Learning Management System <https://learn.nihr.ac.uk> or contact CRN Training [training.crnthamesvalley@nihr.ac.uk](mailto:training.crnthamesvalley@nihr.ac.uk) 01865 223292
- Oxford Brookes offers a module on managing clinical trials  
<https://www.brookes.ac.uk/hls/cpd/course-list/planning-and-managing-clinical-trials-distance-learning/>
- University of Oxford offers various courses. These courses give preference to University employed staff, but others will be considered  
<https://www.learning.ox.ac.uk/>  
<https://www.medsci.ox.ac.uk/study/skillstraining>  
<https://www.conted.ox.ac.uk/>
- University of Birmingham offers research methods in clinical trials courses  
<https://www.birmingham.ac.uk/research/activity/mds/trials/bctu/research-methods-course/index.aspx>



## Library Services

The Bodleian Health Care Libraries provide a range of services to support the information needs of staff and students working for the Oxford University Hospital NHS Trust. The librarians can offer training and help with literature searches, help you to find the evidence you need to support your research and healthcare practice, management, education, and continuing professional development.

Their outreach librarians provide these services from our libraries or in your department at a time to suit you.

<http://www.bodleian.ox.ac.uk/hcl>

## Help with Searching & Keeping Up-to-Date

Your Outreach Librarian is an expert searcher and can help you develop your literature searches in support of activities such as systematic reviews, research bids or project bids. They can help you find the full text of the article you need, help you track down that obscure conference paper and advice on the best ways of keeping up-to-date in your subject area.

## Group & One-to-One Training

We offer free training sessions to help you develop your search skills from beginner to advanced level. Most sessions include hands-on practice covering topics such as Essential and Advanced Search Skills, NHS OpenAthens Resources, Reference Management, Open Access, Impact Factors, Tracking your Citations and Impact, and many more

## Modern & Comfortable Spaces

Our libraries provide access to a wide range of IT facilities and software packages (24/7 at the Cairns and NOC libraries). You can borrow laptops and iPads and make use of our well-equipped group study rooms and training rooms. We also offer quiet study spaces with easy access to large collections of books and journals, WiFi, and breakout spaces. All of them have food and drink nearby.

## Support for Writing Articles & Theses

We can help you find relevant journals to publish in, help you run your literature search and help you manage your references (we run courses on Endnote, RefWorks, Mendeley and other packages). We can also provide advice on topics such as impact factors, altmetrics, and how best to comply with funding bodies' open access policies.

## Useful resources

- **Trial Managers Guide:**  
[http://c.ymcdn.com/sites/www.tmn.ac.uk/resource/resmgr/TMN\\_Guide/tmn\\_guidelines-web\\_amended\\_.pdf](http://c.ymcdn.com/sites/www.tmn.ac.uk/resource/resmgr/TMN_Guide/tmn_guidelines-web_amended_.pdf)
- For **radiographers** in research <http://www.sor.org/career-progression/researchers/research-resource-pack>

## Glossary of Research Related Acronyms

These are some of the many acronyms you will come across

Acronym	Description
<b>ABPI</b>	Association of British Pharmaceutical Industry
<b>ACFs</b>	Academic Clinical Fellowships
<b>ADR</b>	Adverse Drug Reaction (also known as AR)
<b>AE</b>	Adverse event
<b>AHPs</b>	Allied Health Professionals
<b>AMRC</b>	Association of Medical Research Charities
<b>AR</b>	Adverse reaction
<b>ARSAC</b>	Administration of Radioactive Substances Advisory Committee: Research studies wishing to administer radioactive medicinal products to human subjects need to obtain ARSAC approval before NHS R&D approval
<b>ASR</b>	Annual Safety Report: For studies involving the use of an Investigational Medicinal Product, this is the annual report which must be submitted to the MHRA detailing all SUSARs and SARs that have occurred in subjects on that study in the past year
<b>BRC</b>	Biomedical Research Centre
<b>BRU</b>	Biomedical Research Unit
<b>CA</b>	Competent Authority - organisation approving the testing of new drugs/devices or approving the marketing licences, in the UK this is the MHRA
<b>CAG</b>	Confidentiality Advisory Group – function of the HRA to reviewed applications for use of identifiable data where consent was not practicable
<b>CAT</b>	Clinical Academic Training Programme
<b>CE</b>	Conformité Européenne
<b>CI</b>	Chief Investigator - The lead investigator with overall responsibility for the research. In a multi-site study, the CI has coordinating responsibility for research at all sites.
<b>CL</b>	Clinical Lectureships
<b>CLAHRCs</b>	Collaborations for Leadership in Applied Health Research and Care
<b>CQC</b>	Care Quality Commission
<b>CRA</b>	Clinical Research Associate (Monitor)
<b>CRF</b>	Case Report Form - data collection tools provided by a sponsor on which the clinical data is recorded for each participant, such as weight, lab results, symptoms
<b>CRFs</b>	Clinical Research Facilities for Experimental Medicine - hospital-like facility with consulting rooms, standard patient beds, ward medical equipment, research nurses supporting only research
<b>CRN</b>	Clinical Research Network
<b>CRN TV+SM</b>	Clinical Research Network – Thames Valley and South Midlands
<b>CRNCC</b>	Clinical Research Network Coordination Centre
<b>CRO</b>	Contract Research Organisation - A person or an organisation (commercial, academic or other) contracted by the sponsor to perform one or more of a sponsor's trial- related duties and functions
<b>CSP</b>	Coordinated System for gaining NHS Permission
<b>CSAG</b>	Clinical Studies Advisory Group
<b>CSP</b>	Coordinated System for gaining NHS Permissions: Standard process for adoption onto NIHR Portfolio of Studies in order to access NIHR CRN Support and funding; streamlines the process

	for gaining NHS permissions by collating the information for global and local approvals; researchers initiate this in IRAS by completing and submitting CSP Application Form
<b>CT</b>	Clinical Trials
<b>CT Toolkit</b>	Clinical Trials Toolkit
<b>CTA</b>	Clinical Trials Agreement: contract between the legal Sponsor and the hosting research sites
<b>CTIMP</b>	Clinical Trial of an Investigational Medicinal Product
<b>CTRG</b>	Clinical Trials and Research Governance
<b>CTUs</b>	Clinical Trials Units - Design and manage CTIMPs, sometimes in specialist clinical areas, such as Cancer, or types of trial, such as RCTs
<b>CUREC</b>	Central University Research Ethics Committee
<b>CV</b>	Curriculum Vitae
<b>Dementia TRC</b>	Dementia Translational Research Collaboration
<b>DeNDRoN</b>	Dementias and Neurodegenerative Diseases Research Network
<b>DH</b>	Department of Health
<b>DIPEx</b>	Database of Individual Patient Experience – the DIPEx website has a range of open source videos of real patient experiences <a href="http://www.healthtalkonline.org">www.healthtalkonline.org</a>
<b>DMC/DMSC</b>	Data Monitoring Committee / Data Monitoring and Safety Committee
<b>DPA</b>	Data Protection Act
<b>DRFs</b>	Doctoral Research Fellowships
<b>DSUR</b>	Development Safety Update Report
<b>ECMCs</b>	Experimental Cancer Medicine Centres
<b>EMA</b>	The European Medicines Agency: A body of the European Union which has responsibility for the protection and promotion of public health through the evaluation and supervision of medicines for human use EU European Union
<b>ENRICH</b>	Enabling Research in Care Homes
<b>EQUATOR</b>	Enhancing the Quality and Transparency of Health Research Network
<b>EUCTD</b>	European Union Clinical Trials Directive
<b>EUDRACT</b>	European Union Drug Regulating Authorities Clinical Trials - A database of all clinical trials in Europe, held since 1994 in accordance with EU directive 2001/20/EC
<b>FAQs</b>	Frequently Asked Questions
<b>FDA</b>	Food and Drug Administration: the Competent Authority in the United States, giving authorisation to conduct clinical trials and issuing marketing licences
<b>GCP</b>	Good Clinical Practice
<b>GLP</b>	Good Laboratory Practice - standard for laboratories involved in pre-clinical analyses (e.g. animal, in vitro); does not apply to Laboratories analysing samples from clinical trials involving humans
<b>GMP</b>	Good Manufacturing Practice - quality assurance standard for producing IMP, medicinal products
<b>GP</b>	General Practitioner
<b>GTAC</b>	Gene Therapy Advisory Committee: the ethics committee for clinical studies using genetically modified products; usually no REC approval required
<b>HEE</b>	Health Education England
<b>HETV</b>	Health Education Thames Valley

<b>HEI</b>	Higher Education Institution
<b>HFEA</b>	Human Fertilisation and Embryological Authority
<b>HRA</b>	Health Research Authority
<b>HS&amp;DR</b>	Health Services and Delivery Research Programme
<b>HTA</b>	Health Technology Assessment Programme
<b>HTA</b>	Human Tissue Act/Authority
<b>HTCs</b>	Healthcare Technology Co-operatives
<b>IAT</b>	Integrated Academic Training Programme
<b>IB</b>	Investigators Brochure: A compilation of clinical and pre-clinical pharmacological/biological data relevant to the use of that IMP(s) in human subjects (one single IB for all trials using the same IMP)
<b>ICF</b>	Informed Consent Form
<b>ICH</b>	International Conference on Harmonisation (Europe, USA, Japan): Defined standards for the terminology, design, conduct, monitoring, recording, analysis and reporting of a study. These standards give assurance that the reported results are accurate and credible and that the rights, integrity and confidentiality of all study participants have been protected throughout the study.
<b>ICMJE</b>	International Committee of Medical Journal Editors
<b>IDMC</b>	Independent Data Monitoring Committee
<b>IEC</b>	Independent Ethics Committee
<b>IMP</b>	Investigational Medicinal Product - an unlicensed new drug, or an existing drug tested outside its licence, or existing drugs tested against each other for their efficacy/safety.
<b>INVOLVE</b>	INVOLVE national advisory group
<b>IRAS</b>	Integrated Research Application System
<b>IRB</b>	Independent Review Board - US equivalent of authorised REC
<b>IRMER</b>	Ionising Radiation Medical Exposure Regulations
<b>IS</b>	Information Systems Programme
<b>ISF</b>	Investigator Site File - A file designed for use in organising and collating all essential documentation required to conduct a study in accordance with the principles of GCP and the applicable regulatory requirements (e.g. REC approval letter/correspondence, MHRA approval, blank CRF, staff CVs, delegation of duties log etc.)
<b>ISRCTN</b>	International Standard Randomised Controlled Trial Number Register - A simple numeric system for the identification of randomised controlled clinical trials worldwide. Allows the identification of trials and provides a unique number that can be used to track all publications and reports resulting from each trial; can be obtained from <a href="http://www.isrctn.org">www.isrctn.org</a>
<b>JLA</b>	James Lind Alliance
<b>JLA PSPs</b>	James Lind Alliance Priority Setting Partnerships
<b>JRO</b>	Joint Research Office
<b>KMFs</b>	Knowledge Mobilisation Fellowships- NIHR
<b>MCA</b>	Mental Capacity Act
<b>mCIA</b>	model Clinical Investigation Agreement
<b>mCTA</b>	model Clinical Trial Agreement - for IMP studies with commercial sponsor/CRO conducted
<b>MHRA</b>	Medicines and Healthcare products Regulatory Agency - The UK Competent Authority (CA) and licensing authority for medicines and medical devices. It replaced both the Medical Devices Agency (MDA) and the Medicines Control Agency (MCA) in April 2003

<b>MfHU (CT)</b>	Medicines for Human Use (Clinical Trials) Regulations: SI 2004:1031 and subsequent amendments 2006:1928, 2006:2984 ,2008:941 , 2009:1164 and 2010:1882 are the UK Statutory Instruments translating EU directives 2001/20/EC and 2005/28/EC into UK law, laying down the legal requirements for conducting CTIMPs in the UK
<b>mNCA</b>	model Non-Commercial Agreement
<b>MRC</b>	Medical Research Council
<b>MRC-NIHR NPC</b>	MRC-NIHR National Phenome Centre
<b>MRP</b>	Methodology Research Programme
<b>ND</b>	Not done
<b>NETS CC</b>	NIHR Evaluation, Trials and Studies Coordinating Centre
<b>NHS</b>	National Health Service
<b>NHS EED</b>	NHS Economic Evaluation Database
<b>NICE</b>	National Institute of Health Care Excellence
<b>NIHR</b>	National Institute for Health Research
<b>NK</b>	Not known
<b>NOCRI</b>	NIHR Office for Clinical Research Infrastructure
<b>NRES</b>	National Research Ethics Service - umbrella organisation responsible for all REC across the UK
<b>OHSRC</b>	Oxfordshire Health Services Research Committee
<b>OSCHR</b>	Office for Strategic Co-ordination of Health Research
<b>OUHT</b>	Oxford University Hospitals NHS Trust
<b>OXTREC</b>	Oxford Tropical Research Ethics Committee
<b>PCPIE</b>	Patient, Carer, Public Involvement and Engagement
<b>PDAs</b>	Product Development Awards
<b>PDGs</b>	Programme Development Grants
<b>PGfAR</b>	Programme Grants for Applied Research Programme
<b>PHR</b>	Public Health Research Programme
<b>PI</b>	Principal Investigator
<b>PIC</b>	Participant Identification Centre: NHS or other organisation which only identifies participants from a database etc, but recruitment /receiving consent and study conduct are managed elsewhere
<b>PIS</b>	Participant or Patient Information Sheet: An information leaflet given to those who have been invited to participate in a research study. The sheet is provides the potential participant with sufficient information to allow that person to make an informed decision on whether or not they want to take part
<b>PIL</b>	Participant/ Patient Information Leaflet
<b>PIS</b>	Participant/ Patient Information Sheet
<b>PPI</b>	Patient and Public Involvement
<b>PROSPERO</b>	Database of Prospectively Registered Systematic Reviews
<b>PSTRC</b>	Patient Safety Translational Research Centre
<b>QA</b>	Quality Assurance
<b>QC</b>	Quality Control
<b>QOL</b>	Quality of Life Questionnaire
<b>R&amp;D</b>	Research and Development - often name of Department within NHS hospitals giving permission to conduct projects on those facilities with patients/staff
<b>R&amp;G</b>	Regulation and Governance
<b>RAE</b>	Research Assessment Exercise
<b>RCF</b>	Research Capability Funding
<b>RCGP</b>	Royal College of General Practitioners
<b>RCTs</b>	Randomised Controlled Trials - A RCT is a clinical study in which two (or more) forms of care are compared; the participants are

	allocated to one of the forms of care in the study, in an unbiased way
<b>RDS</b>	Research Design Services - organisation with a number of experts who can help write the protocol/documents for NIHR grant applications
<b>REC</b>	Research Ethics Committee - authorised by NRES to review study documents for research taking place in the NHS, or social services. Some REC specialise in Clinical Trials, or topics such as research in children, MCA.
<b>RETG</b>	Research Education and Training Group, Oxford Biomedical Research Centre
<b>RFPB</b>	Research for Patient Benefit Programme
<b>RGF</b>	Research Governance Framework
<b>RM&amp;G</b>	Research Management and Governance
<b>RP</b>	Research Passport
<b>RSS</b>	Research Support Services
<b>SAE</b>	Serious Adverse Event
<b>SAR</b>	Serious Adverse Reaction
<b>SDV</b>	Source Data Verification - checking the original data record, such as lab reports, patient medical notes against what was transferred onto the CRF/into a database
<b>Serious-ADR</b>	Adverse drug reaction which falls in to one of the serious criteria and therefore warrants expedited reporting (serious = resulting in hospitalisation, prolonged hospitalisation, death, life-threatening, congenital anomaly/birth defect or persistent or significant disability/incapacity)
<b>SLA</b>	Service Level Agreement
<b>SmPC</b>	Summary of Medicinal Product Characteristics - : smaller version of Investigator Brochure with details on pharmacological effects, side effects, but issued for a product that already holds a marketing licence
<b>SOP</b>	Standard Operating Procedure - detailed written instructions designed to achieve uniformity of the performance of a specific function
<b>SSI</b>	Site Specific Information - local detail to inform SSA including qualifications/expertise of the PI and wider research team, study procedures, departmental capacity to absorb project (includes Pharmacy, Pathology, Radiology) and departmental leads signatures; The SSI form is completed in IRAS
<b>SUSAR</b>	Suspected Unexpected Serious Adverse Reactions - A Serious Adverse Reaction (SAR) which is Unexpected (i.e. its nature and severity is not consistent with the known information about that product from the Investigator's Brochure or the SmPC) and suspected, as it is not possible to be certain of causal relationship with the IMP
<b>TCC</b>	NIHR Trainees Coordinating Centre
<b>TMF</b>	Trial Master File - file with essential documents held by the Chief Investigator/Sponsor organisation
<b>TSG</b>	Oxford University Hospitals Trust / University of Oxford Trials Safety Group
<b>UKCRC</b>	UK Clinical Research Collaboration
<b>UKCRN</b>	UK Clinical Research Network
<b>UKCTG</b>	UK Clinical Trials Gateway



## Dictionary of Research Related Terms

<b>Amendment</b>	A written description of a change or formal clarification. Substantial amendments to protocol, participant information/consent require REC, R&D, MHRA approval, Non-substantial amendments should be 'notified' to REC, R&D, MHRA.
<b>Allocation concealment</b>	A technique used to prevent selection bias by concealing the allocation sequence from those assigning participants to intervention groups, until the moment of assignment. Allocation concealment prevents researchers from (unconsciously or otherwise) influencing which participants are assigned to a given intervention group.
<b>Arm</b>	A group or subgroup of participants in a clinical trial that receives specific interventions, or no intervention, according to the study protocol. This is decided before the trial begins.
<b>Bias</b>	A loss of balance and accuracy in the use of research methods. It can appear in research via the sampling frame, random sampling, or non-response. It can also occur at other stages in research, such as while interviewing, in the design of questions, or in the way data are analysed and presented.
<b>Blinding</b>	A clinical trial design strategy in which one or more parties involved with the trial, such as the investigator or participant, do not know which participants have been assigned which interventions. Types of masking include none, open label, single blind masking, and double blind masking.
<b>Collaborator</b>	An organization other than the sponsor that provides support for a clinical study. This may include funding, design, implementation, data analysis, or reporting.
<b>Comparison arm</b>	A grouping of participants in a clinical study that is used in summarizing the data collected during the study. This grouping may be the same as or different from a study arm.
<b>Data monitoring committee</b>	A group of independent scientists who monitor the safety and scientific integrity of a clinical trial. The group can recommend to the study sponsor that the study be stopped if it is not effective, if it is causing harm to participants, or if it is not likely to serve its scientific purpose. Committee members are chosen based on the scientific skills and knowledge needed to monitor the particular study. Also referred to as a data safety and monitoring board (DSMB).
<b>Delegation log</b>	A list of appropriately qualified persons to whom the investigator has delegated significant trial related duties.
<b>Double blind</b>	A trial where the investigators and the subjects included in the trial (healthy volunteers or patients) do not know which interventions or treatments have been assigned.
<b>Efficacy</b>	A measure of whether the medicinal product has its intended effect.
<b>Eligibility criteria</b>	The key standards that people who want to participate in a clinical study must meet or the characteristics they must have. These include inclusion criteria and exclusion criteria. For example, a study might only accept participants who are above or below certain ages.
<b>Enrolment</b>	The act of admitting a participant into a trial. Participants should be enrolled only after study personnel have confirmed that all the

	eligibility criteria have been met. Formal enrolment must occur before randomised assignment.
<b>Exclusion criteria</b>	The factors (or reasons) that prevent a person from participating in a clinical study.
<b>Experimental Arm</b>	A group of participants that receives the intervention that is the focus of the study – sometimes called 'treatment arm'.
<b>Follow up</b>	A process of periodic contact with participants enrolled in the trial for the purpose of administering the assigned intervention(s), modifying the course of intervention(s), observing the effects of the intervention(s), or for data collection.
<b>Generalisability</b>	The extent to which the findings of a clinical trial can be reliably extrapolated from the subjects who participated in the trial to a broader patient population and a broader range of clinical settings.
<b>Hypothesis</b>	In a trial, a statement relating to the possible different effect of the interventions on an outcome. E.g. the null hypothesis predicts no effect, can be tested by statistical analysis.
<b>Incapacitated Adult</b>	An adult unable by virtue of physical or mental incapacity to give informed consent.
<b>Inclusion criteria</b>	The factors (or reasons) that allow a person to participate in a clinical study.
<b>Indemnity</b>	Compensation for damage, loss or injury.
<b>Intellectual Property (IP)</b>	IP can be described as the novel or previously un-described tangible output of any intellectual activity. It has an owner and can be bought, sold or licensed and must be adequately protected. It can include inventions, industrial processes, software, data, written works, designs and images.
<b>Interim Analysis</b>	<p>An analysis comparing intervention groups undertaken at any time before the formal completion of the trial, usually before recruitment is complete.</p> <p>Often used with "stopping rules" so that a trial can be stopped if participants are being put at risk unnecessarily. Timing and frequency of interim analyses should be specified in the protocol.</p>
<b>Interventional study</b>	A clinical study in which participants are assigned to receive one or more interventions (or no intervention) so that researchers can evaluate the effects of the interventions on biomedical or health-related outcomes. The assignments are determined by the study protocol. Participants may receive diagnostic, therapeutic, or other types of interventions.
<b>Investigator</b>	A researcher involved in a clinical study. Related terms include Site Principal Investigator, Site Sub-Investigator, Study Chair, Study Director, and Study Principal Investigator.
<b>Legal Representative</b>	A person who gives written informed consent on behalf of a vulnerable subject in a CTIMP as defined in Schedule 1, Part 1 (2) of The Medicines for Human Use (Clinical Trials) Regulations, as amended.
<b>Minor</b>	In relation to a CTIMP, defined in 'The Medicines for Human Use (Clinical Trials) Regulations' as a person under the age of 16.



<b>Monitor</b>	The person designated by the sponsor to perform site visits and conduct the monitoring process; eg check whether there are any deviations from the protocol and that all source data was transferred into the Case Report Forms correctly.
<b>Monitoring</b>	The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted and recorded in accordance with the protocol, Standard Operating Guidelines (SOP's), Good Clinical Practice (GCP) and the applicable regulatory requirement(s).
<b>Multi Centre Study</b>	A study conducted according to a single protocol but carried out at more than one site and by more than one investigator; one CI oversees several local PIs.
<b>Non Interventional Trial</b>	<p>A study of one or more medicinal products which <b>have a marketing authorisation</b>, where the following conditions are met:</p> <p>a) The products are prescribed in the usual manner in accordance with the terms of that authorisation</p> <p>b) The assignment of any patient involved in the study to a particular therapeutic strategy is not decided in advance by a protocol but falls within current practice</p> <p>c) The decision to prescribe a particular medicinal product is clearly separated from the decision to include the patient in the study</p> <p>d) No diagnostic or monitoring procedures are applied to the patients included in the study, other than those which are ordinarily applied in the course of the particular therapeutic strategy in question, and</p> <p>e) Epidemiological methods are to be used for the analysis of the data arising from the study.</p>
<b>Nonsubstantial amendments</b>	<p>Changes to the details of a study that have no significant implications for the subjects, the conduct, the management or the scientific value of the study (sometimes referred to as administrative amendments). Examples may be as follows:</p> <ul style="list-style-type: none"> <li>• Correction of typographical errors in the protocol or other study documentation</li> <li>• Amended contact details for the sponsor or project staff</li> <li>• Changes in funding arrangements</li> <li>• Appointment of new support staff</li> <li>• Changes in the documentation used to record study data</li> <li>• Changes in the logistical arrangements for transporting or storing samples.</li> </ul>
<b>Observational study</b>	A clinical study in which participants identified as belonging to study groups are assessed for biomedical or health outcomes. Participants may receive diagnostic, therapeutic, or other types of interventions, but the investigator does not assign participants to specific interventions.
<b>Open label</b>	Describes a clinical trial in which masking is not used. This means that all parties involved with the trial know which participants have been assigned which interventions.
<b>Outcome measure</b>	A planned measurement described in the protocol that is used to determine the effect of interventions on participants in a clinical trial.

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For observational studies, a measurement or observation that is used to describe patterns of diseases or traits, or associations with exposures, risk factors, or treatment. Types of outcome measures include Primary Outcome Measure and Secondary Outcome Measure.

**Patient and Public Involvement**

PPI is an active partnership between patients and the public and researchers in the research process, rather than the use of people as 'subjects' of research. PPI in research is often defined as doing research 'with' or 'by' people who use services rather than 'to', 'about' or 'for' them. This would include, for example, involvement in the choice of research topics, assisting in the design, advising on the research project or in carrying out the research.

**Peer review**

An appropriate process of independent expert review has demonstrated that the research proposal is worthwhile, of high scientific quality and represents good value for money.

**Phase**

- Phase 0: Exploratory study involving very limited human exposure to the drug, with no therapeutic or diagnostic goals (for example, screening studies, microdose studies)
- Phase 1: Studies that are usually conducted with healthy volunteers and that emphasise safety. The goal is to find out what the drug's most frequent and serious adverse events are and, often, how the drug is metabolized and excreted.
- Phase 2: Studies that gather preliminary data on effectiveness (whether the drug works in people who have a certain disease or condition). For example, participants receiving the drug may be compared with similar participants receiving a different treatment, usually an inactive substance (called a placebo) or a different drug. Safety continues to be evaluated, and short-term adverse events are studied.
- Phase 3: Studies that gather more information about safety and effectiveness by studying different populations and different dosages and by using the drug in combination with other drugs.
- Phase 4: Studies occurring after FDA has approved a drug for marketing. These including postmarket requirement and commitment studies that are required of or agreed to by the sponsor. These studies gather additional information about a drug's safety, efficacy, or optimal use.

**Placebo**

A substance that does not contain active ingredients and is made to be physically indistinguishable (that is, it looks and tastes identical) from the actual drug being studied.

**Protocol**

The written description of a clinical study. It includes the study's objectives, design, and methods. It may also include relevant scientific background and statistical information.

**Qualified Person**

All manufacturing activities will need to be conducted in a unit which has an IMP manufacturing authorisation with a named Qualified Person (QP).

This person ensures that an investigation medicinal product (IMP) batch is only released if there is documentation to confirm compliance with Good manufacturing Practice (or equivalent).

<b>Quality Assurance</b>	All those planned and systematic actions that are established to ensure that the trial is performed and the data is generated, documented (recorded), and reported in compliance with Good Clinical Practice (GCP) and the applicable regulatory requirement(s).
<b>Quality control</b>	The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled.
<b>Randomisation</b>	The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.
<b>Research Design Service (RDS)</b>	The NIHR has established a network of Research Design Service in England to help researchers develop and design high quality research proposals for submission to national, peer-reviewed funding competitions for applied health or social care research.
<b>Research Ethics Committee (REC)</b>	Committee established to provide participants, researchers, funders, sponsors, employers, care organisations and professionals with an independent opinion on the extent to which proposals for a study comply with recognised ethical standards. For CTIMPs, the ethics committee must be one recognised by the United Kingdom Ethics Committee Authority. The REC undertaking the ethical review of an application is also known as the Main REC.
<b>Research Passport</b>	A system for HEI employed researchers/postgraduate students who need to undertake their research within NHS organisations, which provides evidence of the pre-engagement checks undertaken on that person in line with NHS Employment Check Standards (among them CRB and occupational health checks).
<b>Sample Size</b>	The number of participants in the trial. The intended sample size is the number of participants planned to be included in the trial, usually determined using a statistical power calculation. The sample size should be adequate to provide a high probability of detecting as significant an effect size of a given magnitude if such an effect actually exists. The achieved sample size is the number of participants enrolled, treated or analysed in the study.
<b>Service Level Agreement (SLA)</b>	A communication document that makes clear what the supplier will deliver and what the organisation will ensure. It is based on the conditions of contract and specification and does not in any way replace them.
<b>Site</b>	The NHS organisation in which study activities and assessment are performed or the location(s) where trial-related activities are actually conducted. Each site/Trust needs to give R&D approval.
<b>Source Data</b>	All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies). Source data may be in hard copy or electronic format.
<b>Source documents</b>	Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after

verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).

### **Substantial Amendment**

A substantial amendment can be defined as an amendment to the protocol or any other study specific documentation, the terms of the REC application or the terms of the CTA application (as applicable) that is likely to affect to a significant degree the:

- The safety or physical or mental integrity of the subjects of the trial;
- The scientific value of the trial;
- Clinical Research Network
- The conduct or management of the trial; or
- The quality or safety of any investigational medicinal product used in the trial.
- Other changes to the particulars of a study that qualify as substantial amendments include:
  - A change of sponsor(s)
  - Appointment of a new Chief Investigator and
  - Extension of the research beyond the planned closing date for recruitment

A substantial amendment may not be made to a research study without the favourable opinion from the REC that gave a favourable opinion for the study (the main REC) and as applicable the MHRA. The only exceptions to this rule are:

- The Inclusion of a new research site or
- The Appointment of a new PI at an individual site

Both of these qualify as substantial amendments but as they require further SSA and approval from the REC there is no requirement for notice of amendment to the REC. These changes do still however need to be notified to the MHRA (as applicable).

### **Trial Management Group (TMG)**

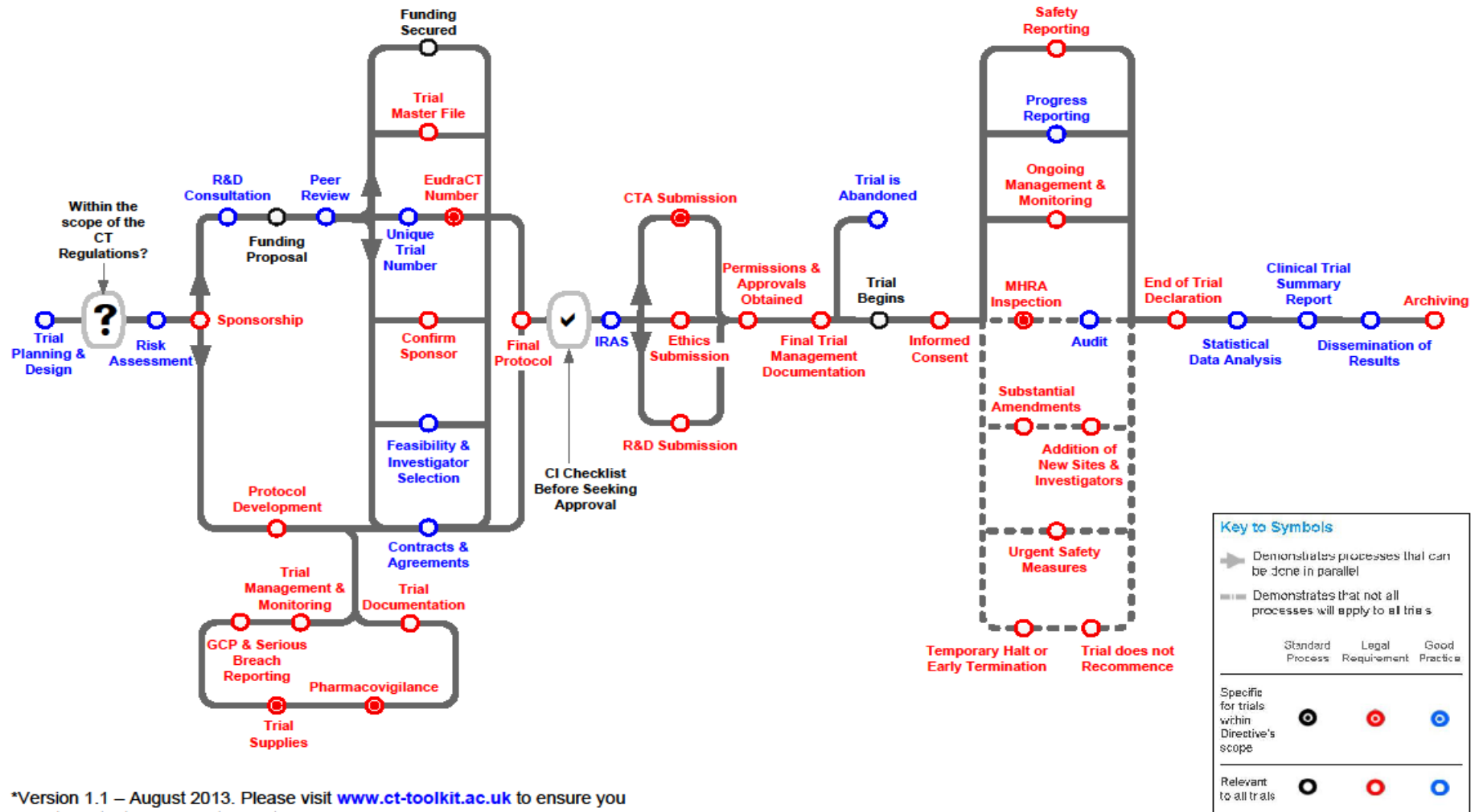
The Trial Management Group normally includes those individuals responsible for the day-to-day management of the trial, such as the Chief Investigator, statistician, trial manager, research nurse, data manager. The role of the group is to monitor all aspects of the conduct and progress of the trial, ensure that the protocol is adhered to and take appropriate action to safeguard participants and the quality of the trial itself.

### **Trial Steering Committee**

The role of the Trial Steering Committee (TSC) is to provide the overall supervision of the trial. Ideally, the TSC should include members who are independent of the investigators, their employing organisations, funders and sponsors. The TSC should monitor trial progress and conduct and advice on scientific credibility. The TSC will consider and act, as appropriate, upon the recommendations of the Data Monitoring Committee (DMC) or equivalent and ultimately carries the responsibility for deciding whether a trial needs to be stopped on grounds of safety or efficacy.

Please see [www.ct-toolkit.ac.uk](http://www.ct-toolkit.ac.uk) for an interactive version, with links to extensive further information

# The Clinical Trials Toolkit - Routemap



\*Version 1.1 – August 2013. Please visit [www.ct-toolkit.ac.uk](http://www.ct-toolkit.ac.uk) to ensure you have the latest version of the routemap.

## **Appendix 1: 'Role Transition' when becoming a Research Nurse\***

**Blog post on Jan 10, 2011 by Kelly Gleason, Senior Research Nurse, Imperial College Healthcare NHS Trust, London**

*Although this blog is written about research nurses, it is equally applicable to anyone entering a research post for the first time.*

Following the decision to become a research nurse, the first few months can be quite difficult and can really make you wonder whether or not you have made the right decision. You miss the routine of the ward, the camaraderie of your peers and feeling like you actually know what you are doing!

You arrive in clinical research equipped with your years of clinical experience, feeling like a competent healthcare professional able to answer your patients' questions, make decisions about their care, and enjoy the well-established and trusting relationships you have developed with your medical colleagues. Suddenly you are in a sea of unfamiliar acronyms, being asked to steer several ships to dock – and all this without a life jacket and the usual support, guidance and knowledge upon which you had come to rely. While navigating this new sea we have all also found it difficult to ask for help in fear that we will look incompetent and that our new employers might question their decision to recruit us in the first place!

I would like to take this opportunity to say: 'it's okay and it's normal'...we ALL go through the same process...and it does end...and you do, once again, find yourself feeling like the professional you once were.

Spilbury et al 2007, describe this period as 'role transition': a time when a research nurse experiences a loss of role confidence while acquiring new skills, knowledge and competence – in order to function in a new role and to adapt to working more autonomously than one did on the wards.

It is much easier, I think – once you accept that this is going to be a period of transition and that your role during this time is to learn – not to have all the answers. As Earl Gray Stevens once said, "Confidence, like art, never comes from having all the answers, it comes from being open to all the questions."

I also think it is important to accept that not everything can be learned straight away, and rather that the first 6 months is a good time to learn the systems and processes of your particular place of employment, and become familiar with the regulations that govern clinical research, your assigned trial portfolio, your patient pathway to optimise recruitment, and get to know the multidisciplinary team you will be working with.

In my experience it takes most people 6 months to start feeling more 'at home' in this new chosen field. This of course will depend on what you are exposed to in this first 6 months, and who you have supporting you. Support in the role of the research nurse is also essential for survival, so make links where you can – even if it is with research nurses in other disease areas. The 'peer group' for research nurses is growing and there is now greater awareness of the role – so if you have not come into a team but instead work more in isolation, then try to speak to

management or your nursing directorate, as they will likely know other research nurses in your organisation who can provide you with support and understanding when you need it.

I believe that for most of us, persistence through this initial transition period is well worth it. The field of clinical research is growing and beginning to offer nurses wonderful opportunities to develop themselves professionally. The anticipated changes in the NHS over the foreseeable future will undoubtedly affect how we deliver care and how we support research. Let's be ready to offer solutions. Solutions that will benefit the healthcare system, and solutions that will support research nurses in developing themselves as advanced practitioners, committing themselves to innovation and the highest standards of care – all of which can only be achieved if research fully integrates itself in the service we deliver.

So if you like to be challenged, have a passion for leadership and for making things better, maybe research nursing really is for you...the initial change can be a little uncomfortable – but with a little understanding that this is likely only to be temporary and that you are allowed this time to learn, you will hopefully come out 'the other side' to see many opportunities that this new and growing field has to offer.

Spilbury K, Petherick E, Cullum N, Nelson A, Nixon H & Mason S, (2007) 'The role and potential contribution of clinical research nurses to clinical trials' *Journal of Clinical Nursing* **17**(4), 549-57.

## Appendix 2: The Principles of GCP

Good clinical practice is the quality standard by which clinical trials must be performed, by detailing the processes required in the conduct of clinical trials. If not followed, clinical trial data can be rejected and found to be unreliable, therefore it is vital that all involved in clinical trials have a thorough working knowledge of GCP requirements and adhere to them.

1. Clinical trials shall be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with good clinical practice and the requirements of the UK Regulations of Medicines for Human Use.
2. Before the trial is initiated, foreseeable risks and inconveniences have been weighed against the anticipated benefit for the individual trial participant and other present and future patients. A trial should be initiated and continued only if the anticipated benefits justify the risks.
3. The rights, safety, and wellbeing of the trial subjects are the most important considerations and shall prevail over interests of science and society.
4. The available non-clinical and clinical information on an investigational medicinal product shall be adequate to support the clinical trial.
5. Clinical trials shall be scientifically sound, and described in a clear, detailed protocol.
6. A trial shall be conducted in compliance with the protocol that has a favourable opinion from an ethics committee.
7. The medical care given to, and medical decisions made on behalf of, subjects shall always be the responsibility of an appropriately qualified doctor or, when appropriate, of a qualified dentist.
8. Each individual involved in conducting a trial shall be qualified by education, training, and experience to perform his or her respective task(s).
9. Subject to the other provisions relating to consent, freely given informed consent shall be obtained from every subject before clinical trial participation.
10. All clinical trial information shall be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.
11. The confidentiality of records that could identify subjects shall be protected, respecting the privacy and confidentiality rules in accordance with the requirements of the Data Protection Act 1998 and the law relating to confidentiality.
12. Investigational medicinal products used in the trial shall be:
  - a) manufactured or imported, and handled and stored, in accordance with the principles and guidelines of good manufacturing practice
  - b) used in accordance with the approved protocol.
13. Systems with procedures that assure the quality of every aspect of the trial shall be implemented
14. A trial shall be initiated only if an ethics committee and the competent authority comes to the conclusion that the anticipated therapeutic and public health benefits justify the risks and may be continued only if compliance with this requirement is permanently monitored.
15. The rights of each subject to physical and mental integrity, to privacy and to the protection of the data concerning him or her in accordance with the Data Protection Act 1998 are safeguarded.
16. Provision has been made for insurance or indemnity to cover the liability of the investigator and sponsor that may arise in relation to the clinical trial.



## Appendix 3: Informed Consent

Freely given informed consent is central to ethical research involving human participants or the use of human tissues or genetic material. It is essential to ensure that those who participate in research understand exactly what it will involve for them. It is morally and professionally unacceptable to perform any research related procedure on someone without first obtaining their fully informed consent. It is also important to remember that after a consent form has been signed, a participant can still withdraw from the trial at any time without giving a reason. It is the duty of the investigator to reiterate this and to reassure participants that they will not compromise their future medical care if they decide to withdraw.

### What is informed consent?

Informed consent is an ongoing agreement by a person to participate in research, after risks, benefits and alternatives have been adequately explained to them. It helps to ensure that people are not deceived or coerced into participating in research. In order to give fully informed consent, potential participants need to understand the following:

- the purpose of the research
- the practicalities and procedures involved in participating
- the benefits and risks of participation and, if appropriate, the alternative therapies
- how data about them will be managed and used
- the consent form
- their role if they agree to participate in the research
- how information will be provided to them throughout the study
- that their participation is voluntary
- that they can withdraw from the study at any time, without giving any reason and without compromising their future treatment
- the insurance indemnity arrangements for the conduct of the research where appropriate
- that the research has been approved by a research ethics committee.

In addition, they should be given the contact details of the Principal Investigator and research nurse/practitioner, should they have further questions or should they wish to withdraw from the study

### Maintaining Informed consent

Informed consent is not a one-off process, it is an ongoing requirement. The participant's condition may change; there could be difficulties with compliance, or side effects from trial treatments. New information may emerge which could be relevant to the trial.

Researchers must ensure that participants:

- Are kept fully informed about any changes to the information that they have been given
- Understand the information and any changes in that information.
- Continue to consent to participate throughout the study.

### Who should receive informed consent?

It has been widely acknowledged that research nurses/practitioners in the study team frequently play a major role in obtaining and maintaining informed consent. They may have excellent communication skills and patients often consider them to be more approachable than the investigator.

At local level, there will be a Standard Operating Procedure (SOP) which all research staff should adhere to. Although others may play a major role in the consent process explaining procedures, answering questions etc, for studies involving medical intervention, ultimate

responsibility for enrolling the subject usually lies with the investigator. (In non-intervention studies the investigator may not necessarily be a physician) The investigator should ensure that subjects have fully understood what they are consenting to and sign and date the consent form accordingly. Any other research personnel involved in giving information during the informed consent procedure should also sign the informed consent form.

Overall responsibility for all elements of research activity, including gaining informed consent, rests with the lead researcher. They may delegate the task of obtaining informed consent to another appropriately qualified and experienced member of the research team, but this delegation must be clearly documented, and the person gaining informed consent must sign and date the consent form. Individual members of the research team remain responsible for their own specific actions. This approach meets the criteria of the key documents, and adheres to the Declaration of Helsinki

### **Guidelines for Research Nurses/Practitioners in obtaining consent**

The information to the patient should be given in oral and written form wherever possible and subjects must be allowed sufficient time to decide whether or not they wish to participate.

When discussing a research study with potential participants, it is important that you as a researcher understand the protocol sufficiently to explain it and to answer questions that the potential participant may have. If you cannot answer a question, you must allow time to seek the answer from a colleague before taking consent.

It is very important to understand and to explain in simple terms, the concept of equilibrium between the different research arms. This exists, despite any promise shown in early trials, or any expectation bias on the part of researchers or trial promoters. According to current evidence, standard treatment (which may mean supportive care only) remains the gold standard, until any new treatment or procedure has been proven to have benefits which outweigh its disadvantages.

You should ensure that any personal views you may have do not influence whether or not an individual consents to take part. You need to assess suitability and eligibility according to the protocol, and to give adequate information and then allow them to decide for themselves. If a patient wants someone to help them make their decision, recommend that they discuss it with a relative or friend, or a health care professional who is not involved in the research, such as a GP. However, you should emphasise that ultimately, they should only consent to participate if they are certain that they wish to do so. For various reasons a patient might find it difficult to decline participation. In this case it is your role to enable and empower them to say "no."

Potential participants should also understand that, if they agree to take part in research, they have a duty to the researchers. In giving informed consent they are agreeing to comply with the requirements of the research. If at any time they are unable or unwilling to do this they should consider withdrawing from the study. It is important to emphasise that withdrawal from a clinical study will not compromise the quality of care they receive, although their treatment may change.

For the purposes of audit and inspections, the whole process of obtaining consent should be documented in the patient's case notes. This should include who spoke to the patient, what was discussed and when.

Refer to your local SOP for informed consent and adhere to any additional local policies.

## **Respecting Diversity**

The core ethical principle in research is respect for every individual (Royal College of Nursing 2004) Researchers must therefore respect diversity when gaining informed consent (Department of Health, 2001 & 2005); Scottish Executive Health Department, 2001; Wales Office of Research and Development, 2001).

Researchers must take into account factors such as:

- age
- ethnicity
- gender
- disability
- religious beliefs
- culture
- language
- level of understanding.

Researchers need to be sensitive as to how any or all of these factors might affect a potential participant, taking care to avoid making stereotypical assumptions. Special rules apply in research involving minors and incapacitated adults. In assessing a person's capacity to understand, it is important to be aware of any reading, writing, or language difficulties, and that these might be hidden. They could have visual or hearing impairments, or emotional difficulties. Also a person may have capacity at the initial stage of consent, but lose it as treatment progresses. This may have been expected, for example if the patient is terminally ill, so it does not necessarily invalidate the consent. The

## **Legal framework**

Gaining informed consent in research which involves invasive procedures is a legal requirement. If a research activity proceeds without an individual's informed consent legal action could be taken against the chief investigator or researcher.

Case law on consent in the UK has established three requirements to be satisfied before a potential research participant can give informed consent:

- the consent should be given by someone with the mental capacity to do so
- sufficient information should be given to and understood by the participant
- the consent must be freely given

**Table 1: Informed consent for a minor as defined as < 16 years of age**

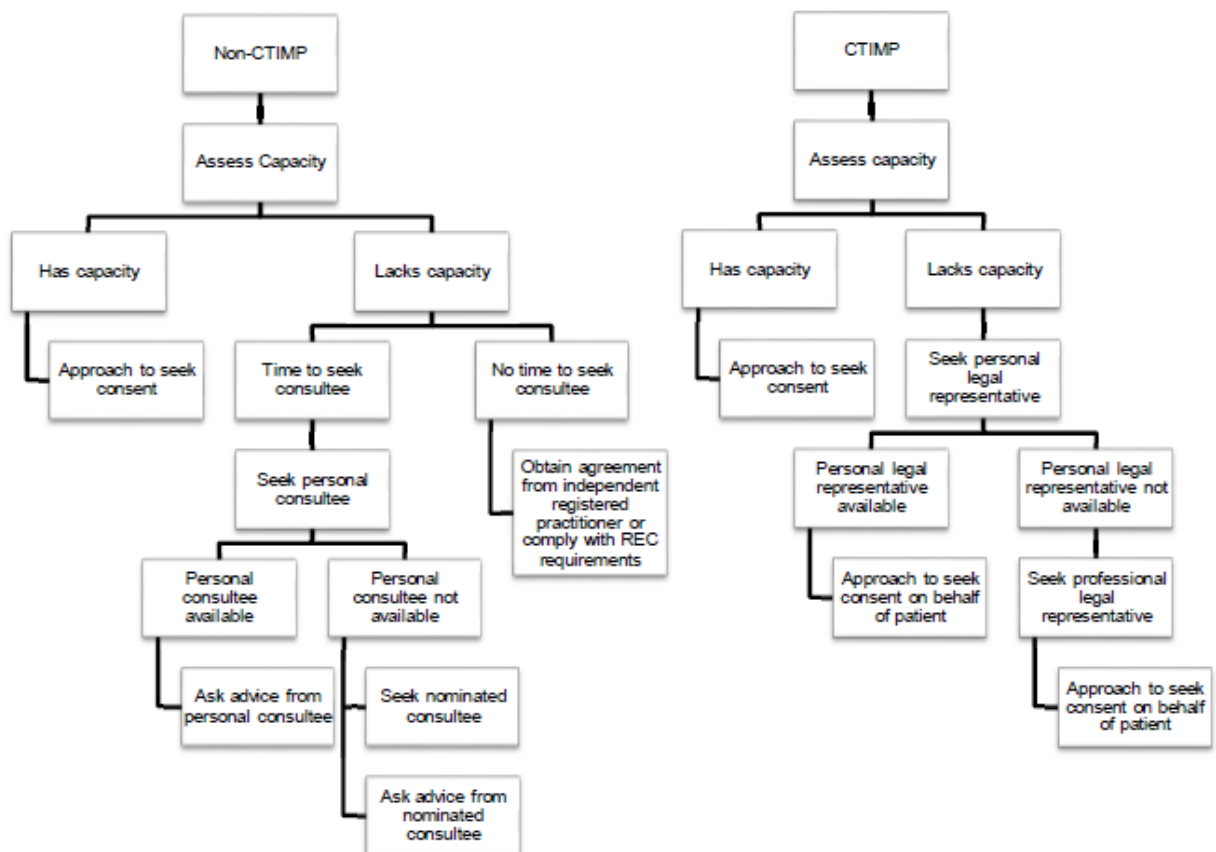
Person who may give consent		Definition	Commentary
1.	Parent	A parent or person with parental responsibility.	Should always be approached if available.
2.	Personal legal representative	A person not connected with the conduct of the trial who is: (a) suitable to act as the legal representative by virtue of their relationship with the minor, <b>and</b> (b) available and willing to do so.	May be approached if no person with parental responsibility can be contacted before the proposed inclusion of the minor, by reason of the emergency nature of the intervention provided as part of the trial.
3.	Professional legal representative	A person nominated by the relevant health care provider (e.g. an acute NHS Trust or Health Board) who is not connected with the conduct of the trial.	May be approached if no person suitable to act as a personal legal representative is available.

**Table 2. Informed consent for an incapacitated adult**

England, Wales and Northern Ireland	Scotland
<p>1. Personal legal representative</p> <p>A person not connected with the conduct of the trial who is:</p> <ul style="list-style-type: none"> <li>a. suitable to act as the legal representative by virtue of their relationship with the adult,</li> </ul> <p>and</p> <ul style="list-style-type: none"> <li>b. available and willing to do so.</li> </ul>	<p>1. Personal legal representative</p> <ul style="list-style-type: none"> <li>a. Any guardian or welfare attorney who has power (in law) to consent to the adult's participation in research.</li> <li>b. (b) If there is no such person, the adult's nearest relative as defined in section 87(1) of the Adults with Incapacity (Scotland) Act 2000.</li> </ul>
<p>2. Professional legal representative</p> <p>A person not connected with the conduct of the trial who is:</p> <ul style="list-style-type: none"> <li>(a) the doctor primarily responsible for the adult's medical care,</li> </ul> <p><b>or</b></p> <ul style="list-style-type: none"> <li>(b) a person nominated by the relevant health care provider (e.g. an acute NHS Trust)</li> </ul> <p>A professional legal representative may be approached if no suitable personal legal representative is available.</p>	<p>2. Professional legal representative</p> <p>A person not connected with the conduct of the trial who is:</p> <ul style="list-style-type: none"> <li>(a) the doctor primarily responsible for the adult's medical care,</li> </ul> <p><b>or</b></p> <ul style="list-style-type: none"> <li>(b) a person nominated by the relevant health care provider.</li> </ul> <p>A professional legal representative may be approached if it is not reasonably practicable to contact either 1A or 1B before the decision to enter the adult into the trial is made.</p>

## NRES Decision Tree: Adults lacking capacity to consent to research

This decision tree can be found in the NRES Adults lacking capacity on-line toolkit:  
<https://connect.le.ac.uk/alctoolkit/>



## Appendix 4: Roles & Responsibilities of Researchers and Organisations

### Review of research

- An independent expert review of protocols is required.
- A separate ethical review of the study is required.
- All data must be available to inspection and auditing bodies from both internal and external organisations.
- The protocol must not change without formal agreement from those who gave appropriate permission for the study.
- Funder of research
- Ensures quality and value for money, based on research costs and any care or treatment costs and makes arrangements for independent expert review.
- Ensures funding is conditional on identifying a sponsor (usually a university or NHS Trust).
- Provides assistance to any enquiry, audit or investigation of the funded work.

### Sponsor

All clinical trials and studies:

- Responsible for ensuring expert scientific and ethics reviews are carried out.
- Puts in place arrangements to adhere to GCP (if no other person is specified) and ensures arrangements are in place to be alerted to significant developments.
- Takes appropriate urgent safety measures (with investigator).
- Ensures arrangements are in place for compensation (indemnity/insurance arrangements).
- Keeps records of all adverse events reported by investigators.
- Ensures the Research Ethics Committee is notified when the trial has ended.

Clinical Trials involving investigational medicinal products (CTIMP):

- Ensures the EudraCT (European Clinical Trials Database) Number is obtained.
- Competent Authority Authorisation is obtained (Chief Investigator).
- Pharmacovigilance reporting and time frames are adhered to.
- EudraCT and the Competent Authority are notified when trial has ended.

### Chief Investigator

- Is responsible for the design, management and reporting of the study for all sites.
- Is responsible for ensuring that each investigator is aware of their legal duties and obligations.
- Is responsible for ensuring the protocol is approved by relevant bodies, any pre-conditions are acted upon, and that research follows the agreed protocol except in the case of urgent safety measures.
- Undertakes duties delegated by the sponsor (usually working in conjunction with a clinical research organisation CRO if it is a pharmaceutically funded trial).
- Publishes the clinical study results as soon as possible following study completion. In a multi-centre study, the chief investigator must ensure that the data from one centre is not published before the publication of the whole study without his/her consent, and must obtain Sponsor approval before to publication.

### Principal Investigator

It is the responsibility of the PI to conduct the study according to the protocol and to ensure that they have the necessary patient population available to conduct the study within the period defined in the study protocol. The investigator also holds additional responsibilities:

- To ensure that the study is performed in accordance with the International Good Clinical Practice standards (ICH-GCP) and conforms with the principles of the Declaration of Helsinki (revised version 1996), all local laws and regulations concerning clinical studies.
- To submit the protocol, patient information sheet and consent form for local Research Management & Governance approval (R&D approval).
- To ensure that all staff involved in the study have a full understanding of the protocol and its requirements, and that their roles are documented on a study delegation log.
- To confirm subject eligibility according to the inclusion/exclusion criteria stated in the protocol.
- To obtain and record subject consent.
- To withdraw a subject from the clinical trial for any reason should this be thought to be in their best interests.
- To perform protocol directed medical care including assessment, examination and prescription of study and support medication.
- To ensure subject anonymity is maintained.
- To ensure the completeness and accuracy of case report forms.
- To agree to allow the monitor/auditor/inspector to have access to any or all of the study materials needed for source data verification and proper review of study progress.
- To report all safety events: SAEs, SARs, SUSARs as outlined in the protocol, including prompt reporting to Sponsor to ensure further communication with MHRA/REC if applicable within the statutory timelines.
- To retain all essential documents as per NHS and Trust guidelines (usually a minimum of five years following the end of a study, at least two years after the approval of a marketing application, for a new drug, or longer if required by the regulator requirements).
- To comply with the study sponsor and regulatory authority requirements about the auditing of the study.

### **Co-investigator (Medical)**

The co-investigator is responsible for medical care of patients participating in research studies, working under the supervision of the principle investigator. The co-investigator is usually delegated the following responsibilities:

- To ensure that the study is performed in accordance with ICH-GCP and conforms with the principles of the Declaration of Helsinki (revised version 1996), all local laws and regulations concerning clinical studies.
- To confirm subject eligibility according to the inclusion/exclusion criteria stated in the protocol.
- To obtain and record patient consent.
- To withdraw a subject from the clinical trial for any reason should this be thought to be in their best interest.
- To perform protocol directed medical care including assessment, examination and prescription of study and support medication.
- To ensure subject anonymity is maintained.
- To ensure the completeness and accuracy of case report forms.
- To agree to allow the monitor/auditor/inspector to have access to any or all of the study materials needed for source data verification and review of study progress.
- To retain all essential documents as per NHS and Trust guidelines (usually a minimum of five years following the end of a study, at least two years after the approval of a marketing application, for a new drug, or longer if required by the regulator requirements).

- To comply with the study sponsor and regulatory authority requirements about the auditing of the study.

### **Trial Coordinator/Manager**

- To have a leading role in planning, co-ordinating and completing clinical trials, bringing project management and administrative expertise to the trial team.
- Provide administrative support for the allocated clinical trials, taking responsibility for the preparation and submission of relevant approvals and registration and organisation of TSC, DMEC and other meetings. This may involve supervision of clerical and support staff.
- Ensure that clinical trials adhere to the Standard Operating Procedures developed by the Clinical Trials Unit and Trust and University policies and procedures.
- Design, produce and regularly update trial materials, including clinical research forms and databases.
- Assist with trial set up and activation and establish procedures that ensure compliance with the protocol. This may involve travel to sites and providing training.
- Take overall responsibility for data management and quality assurance according to regulatory guidelines and requirements of individual trials (ICH GCP and Data Protection Act 1998). This may involve supervision of data entry clerks.
- Travel to centres involved in trials and undertake trial related duties as required.
- Establish good working relationships with local, national and international clinical networks as appropriate.
- Identify when protocol amendments become necessary and take action as appropriate.
- Maintain regular contact with the chief investigator and act as the main communication source between funding, regulatory agencies, clinical teams and investigators.
- Ensure that trials recruit at an acceptable level at each centre. Suggest and implement strategies for improving recruitment.
- Maintain up-to-date electronic and paper files for all participating centres / investigators, including comprehensive ethics and research governance documentation.
- Produce progress reports on trials as necessary, under the direction of Chief Investigator, Clinical Trials Unit Manager, TSC or DMEC.

### **Research Nurse/AHP/Midwife/Clinical Trials Officer/Practitioner**

The research nurse/AHP/Midwife/CTO is delegated responsibilities by the PI, these may include:

- Preparing and submitting local regulatory approval applications.
- Ensuring that they have attended an initiation meeting and received any appropriate training before the trial commences.
- Co-ordinating the clinical trial in terms of patient screening, recruitment, entry into the trial via randomisation if applicable and subsequent patient visits.
- Checking patient eligibility according to the inclusion/exclusion criteria stated in the protocol in collaboration with medical staff.
- Collaborating with clinicians to assess patients and making treatment decisions according protocol.
- Delivery of investigational agents/treatments and protocol directed care.
- Handling, spinning, labelling, storage and shipping of blood and urine pharmacokinetic samples.
- Ensuring that source documentation is a true reflection of decisions and actions taken for each individual patient.



- Completion of case report forms and ensuring relevant follow up data is collected (eg QoL data).
- Monitoring and reporting all safety events: SAEs, SARs, SUSARs as outlined in the protocol, including prompt reporting to Sponsor to ensure further communication with MHRA/REC if applicable within the statutory timelines.
- Liaising with the study sponsor about the conduct of the trial.
- Educating patients/subjects and dissemination of trial related information to staff.

### **Data Managers/Research Assistants**

Non Clinical research support staff work closely with the research nurses and other members of the clinical team to ensure accurate and appropriate data collection. Their delegated responsibilities may include:

- Ensuring that they have attended a site initiation meeting and received any appropriate training necessary in order to conduct the trial safely and efficiently.
- Entering subjects into clinical trials, utilising appropriate randomisation procedures when necessary.
- Completing case report forms and other research records.
- Ensuring that all data is available for monitoring visits.
- Assisting with or completing submissions to Ethics/Research and Development.
- Archiving all clinical trial related documents according to regulatory requirements.
- Shipping blood and urine pharmacokinetic samples.
- Entering data and updating fields/information within databases.

### **Clinical Trials Pharmacist**

As the number and variety of trials continues to increase it is vital that there is a good communication between the sponsor, the research team and the trials pharmacist. This will ensure issues are raised and resolved at an early stage, allowing the trial to run smoothly and effectively. Early input from pharmacy in the planning of a clinical trial enables early recognition of potential pharmaceutical issues; pharmacy should be given a copy of the protocol at the earliest opportunity.

The Clinical Trials Pharmacist will review:

- The design of prescriptions so the correct trial supplies are ensured.
- How the blinding of trial medication is to be achieved and maintained.
- The requirement for documentation and record keeping.
- Labelling requirements.
- Drug receipt, delivery, reordering and stock checks.
- The mechanism for continuation of supplies, if appropriate, once the trial period has finished.
- Storage conditions for the trial medication.
- Size of packaging, which has implications for storage space.
- For parenterally administered products there may be a requirement for aseptic preparation.

### **Organisations providing care**

- Must ensure the sponsor has assumed responsibility, research has been reviewed by appropriate bodies, and that an authorised person has given written permission on behalf of the care organisation for the research to begin.
- Must arrange for researchers not employed by any NHS organisation to hold an NHS honorary contract.
- Must ensure adverse incidents are reported.

## Appendix 5: Joint Research Office Handbook

The Oxford Joint Research Office provides an integrated specialist support service to world-leading medical research teams at the University of Oxford and Oxford University Hospitals NHS Foundation Trust.

Heads of the Oxford Joint Research Office

Dr Heather House

Head of Clinical Trials & Research Governance, University of Oxford

[heather.house@admin.ox.ac.uk](mailto:heather.house@admin.ox.ac.uk)

Dr Chris Bray

Head of Research & Development Operations at OUH NHS Foundation Trust

[christopher.bray@ouh.nhs.uk](mailto:christopher.bray@ouh.nhs.uk)

The Oxford Joint Research Office (JRO) provides comprehensive support throughout the research process, from pre- set up through to contract and commercialisation expertise and communications advice. The office, currently based at the Churchill Hospital site in Oxford, supports more than 1800 studies and clinical trials and a research investment of more than £200m.

### Business Development (OU/OUH)

The principal role of the Business Development team is to promote joint working between external companies and the University/OUH partnership. We facilitate collaborations via a variety of models, from clinical trials to fundamental research and with a range of partners, from multi-national pharmaceutical companies to smaller biotech and medical device industries.

#### Team Contact

Dr Maxine Allen

Head of Business Development and Partnering

[maxine.allen@medsci.ox.ac.uk](mailto:maxine.allen@medsci.ox.ac.uk) 01865 572217

<https://www.medsci.ox.ac.uk/divisional-services/support-services-1/business-development>

### Contracts and Grants Team (OU)

Research Services Medical Sciences Divisional team provides comprehensive support to researchers in the University's clinical departments. Our services include

- (a) assistance with the submission of research grants by providing information and advice on costing and pricing, reviewing and approving complete applications and facilitating their submission
- (b) negotiation of research-related contracts with other Universities, governmental agencies and industry to ensure terms are consistent with University policies and academic mission
- (c) undertaking the first steps in the establishment of research expenditure budgets.

We have a close working relationship with other departments in the JRO to ensure responsible conduct of research and compliance with regulatory and sponsor specific requirements.

#### Team Contact

Carly Banner, Head of Medical Sciences Team

[carly.banner@admin.ox.ac.uk](mailto:carly.banner@admin.ox.ac.uk)

<https://researchsupport.admin.ox.ac.uk/contacts/medsci>

## **Clinical Trials Research Governance (CTRG) (OU)**

CTRG takes on the role of Sponsor on behalf of the University where relevant to clinical research studies. This includes ensuring that the study is funded, reviewed and managed appropriately and that they are compliant with the relevant legislation, both before regulatory and ethics submission and throughout its conduct. All studies are subject to pre-submission checks and progress is monitored according to a risk-based approach. Clinical Trials of Investigational Medicinal Products (CTIMP) and device trials have additional regulatory requirements and need more intensive oversight, through monitoring of data. CTRG also provide training courses in Good Clinical Practice and other relevant areas for research teams working within the University and OUH.

### **Team Contact**

Karl Shepherd

Clinical Research Advisor CTRG

[karl.shepherd@admin.ox.ac.uk](mailto:karl.shepherd@admin.ox.ac.uk)

<https://researchsupport.admin.ox.ac.uk/ctrg>

## **IP and Research Contracts (OUH)**

The OUH's IP and Research Contracts Team provides dedicated support to draft, review, negotiate and finalise research and intellectual property related contracts on behalf of OUH and in accordance with OUH policies. It also provides assistance with the submission of research grants. The team works in conjunction with OUH Investigators, Research teams, the R & D Governance team, R & D Finance Team, Business Development and Legal Services. The team also works closely with the University of Oxford's Medical Sciences Contracts and Grants team, Research Services' IP Rights team and Oxford University Innovation Ltd. The team also assists Oxford Health NHS Foundation Trust and the Oxford AHSN.

### **Team Contact**

Charles A Lescott

Head of IP and Research Contracts

charles.lescott@ouh.nhs.uk 01865 572202

<http://orh.oxnet.nhs.uk/IPResearchContracts/>

## **NIHR Oxford Biomedical Research Centre (OUH)**

Biomedical Research Centres are part of the Government's initiative to improve the translation of basic scientific developments into clinical benefits. The BRC Management team office forms part of the Joint Research Office. In addition to project and research staff funding, the BRC provides administrative support for the JRO, its staff and its research portfolio. This includes:

- Research co-ordination and funding
- Business development
- Legal, IP and contract services
- Systems and informatics support
- Patient and public involvement advice
- Media, events and communication
- NIHR research performance metrics
- Training and Education

### **Team Contact**

Dr Lorna Henderson

Clinical Research Manager

Lorna.henderson@ouh.nhs.uk

<http://oxfordbrc.nihr.ac.uk/>**R&D Finance (OUH)**

The Finance team manages and facilitates financial processes to ensure that the NHS resources used in research are fully identified, funded appropriately and also ensure that costs are recovered from the funding bodies. In undertaking the role, the team engage with a large number of stakeholders. The team support and provide financial information to support R&D developments.

There are 3 Teams:

- 1) The Costing team are responsible for the accurate and timely costing of all research grants and studies, ensuring that the costs to the NHS are identified and funded.
- 2) The Study Finance team provides comprehensive support to researchers to manage funding flows relating to all research projects, in line with contract agreements.
- 3) The Management Accounts team provide on-going financial support in the management of funding streams from the NIHR. The team works with research teams to ensure the monies granted to support Research infrastructure are managed effectively.

The teams also work closely with the OUH Trust Clinical delivery staff and engage with them concerning research related spend.

#### **Team Contact**

[study.finance@nhs.net](mailto:study.finance@nhs.net)

<http://www.ouh.nhs.uk/researchers/>

### **R&D Governance (OUH)**

The Research Governance team's role is to ensure that research which is using OUH NHS resources including NHS patients:

- is compliant with the relevant regulations (e.g. GDPR)
- follows Clinical Research Principles (e.g. Good Clinical Practice (GCP) and DH Research Governance Framework for Health and Social Care)
- has relevant approvals in place (e.g. Research Ethics Committee, Health Research Authority, Medicines and Healthcare Products Regulatory Authority)
- is of a high scientific standard.

The Research Governance Team provides support throughout the research journey, from acting as sponsor for certain studies to providing local Trust Management Approval and GCP compliant training.

#### **Team Contact**

[ouhtma@ouh.nhs.uk](mailto:ouhtma@ouh.nhs.uk)

[ouh.sponsorship@ouh.nhs.uk](mailto:ouh.sponsorship@ouh.nhs.uk)

<https://www.ouh.nhs.uk/researchers/about/default.aspx>

### **Risk and Insurance (Research) (OU)**

Graham is responsible for assessing projects from a risk and insurance angle. This requires an understanding of the evolving legal and financial services regulations of research conducted beyond the UK, and an appreciation of major risk transfer mechanisms which are distinct from commercial policies of insurance, particularly those comprising the suite of schemes administered by the NHS Litigation Authority.

#### **Team Contact**

Graham Waite

Risk and Insurance (Research) Manager

[graham.waite@admin.ox.ac.uk](mailto:graham.waite@admin.ox.ac.uk)

<https://www.admin.ox.ac.uk/researchsupport/>

## Appendix 6: Access to Participants Medical Records

If a researcher is part of a Research Participants Clinical Care Team and would normally and appropriately have access to those records, then no additional authorisation is required.

If however, as a member of a research team you would not normally have such access you need to get permission to access those records, and depending on your employer follow one of two routes:

Either:

1. Employed by another organisation – Oxford University / Other University / Other NHS Trust – contact R&D [OUHTMA@nhs.net](mailto:OUHTMA@nhs.net) to discuss whether you require an Honorary Research Contract or a Letter of Access.
2. In addition complete a Research Access to Notes Registration Form (RANR form) and send to R&D for verification, if this is required, for each project.
3. Once approved – take the RANR with you **every time** you wish to request research participant's medical records.

Or:

1. Employed by the OUH Trust – complete a Research Access to Notes Registration Form and send to R&D for verification.
2. Once approved – take with you **every time** you wish to request research participant's medical records.

The Research Access to Notes Registration (RANR) form can be downloaded from the R&D Website or will be sent to you on request by the R&D team at [OUHTMA@nhs.net](mailto:OUHTMA@nhs.net).

The Medical Records Library staff will request to see the RANR form before retrieving notes for researchers or allow staff to retrieve notes themselves on each occasion the research attends the Medical Records Library.

Where new staff join the research team the RANR form should be updated with their names through contact with R&D. [If staff are conducting a study and they do not have a research number a signed letter from the head of the study and a list of patients should be given to the library staff.]

All staff using the library are required to attend Library & HIM Tracker training. This is to ensure that staff are able to 'track' medical notes and how to look for notes within the libraries. Researchers can contact the Medical Records Training Team via email [medrecstraining@ouh.nhs.uk](mailto:medrecstraining@ouh.nhs.uk)

## Appendix 7: Key documents and regulations T

### The Declaration of Helsinki 1964

The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects which includes research on identifiable human material or identifiable data.

Recent modifications include clarification on the ethical use of placebos, issues surrounding vulnerable groups, and a requirement that research participants should be informed about the outcomes of the research that they have participated in. They should also have post study access to new interventions which have proved to be beneficial and protocols must include arrangements for how this will be achieved. Similarly, researchers are under greater pressure to publish any disbenefits as they accrue and protocols should clearly state in advance any expected unwanted side effects, and what arrangements there are to compensate participants for any harm that may occur as a result of their research

The declaration was previously not legally binding, but the principles have now been incorporated into the EU Directive (2001) and into UK law (2004) as described below.

### The EU Directive of 2001

The EU Directive aims to harmonise and streamline clinical trials procedures throughout the member states, and relates to all trials, except non-intervention studies. It covers all trials involving medicinal products, and encompasses all personnel involved with the clinical trial procedures. The EU Directive is applicable to all centres performing interventional research trials. These include academic institutions and those trial units supported by charities.

### Medicines for Human Use Act Clinical Trials Regulations 2004

This Act ensured that the ICH GCP guidelines were enshrined into UK Law and compels all parties practicing research to adhere to them.

### Mental Capacity Act 2005

The Mental Capacity Act 2005 (MCA) provides a statutory framework for people who may not be able to make their own decisions, for example because of learning difficulties, brain injury or mental health problems. It sets out who can take decisions, in which situations, and how they should go about this. The Act applies to England and Wales only.

For further information see: <http://www.legislation.gov.uk/ukpga/2005/9/contents>

A patient facing website simplifies the legislation <http://www.nhs.uk/Conditions/social-care-and-support-guide/Pages/mental-capacity.aspx>

### UK Policy Framework for Health and Social Care Research 2017

Previously the Research Governance Framework 2005, updated 2008

<https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/>

The policy framework applies to health and social care research involving patients, service users or their relatives or carers. This includes research involving them indirectly, for

example using information that the NHS or social care services have collected about them.

The Health Research Authority and the health departments in Northern Ireland, Scotland and Wales have developed the policy framework following public consultation. It replaces the separate Research Governance Frameworks in each UK country with a single, modern set of principles for the whole UK.

This policy framework sets out principles of good practice in the management and conduct of health and social care research in the UK.

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.

It is for organisations and individuals that have responsibilities for health and social care research. This includes funders, sponsors, researchers and their employers, research sites and care providers.

## General Data Protection Regulation 2016

Under the GDPR, the data protection principles set out the main responsibilities for organisations.

GDPR requires that personal data shall be:

- a) processed lawfully, fairly and in a transparent manner in relation to individuals;
- b) collected for specified, explicit and legitimate purposes and not further processed in a manner that is incompatible with those purposes; further processing for archiving purposes in the public interest, scientific or historical research purposes or statistical purposes shall not be considered to be incompatible with the initial purposes;
- c) adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed;
- d) accurate and, where necessary, kept up to date; every reasonable step must be taken to ensure that personal data that are inaccurate, having regard to the purposes for which they are processed, are erased or rectified without delay;
- e) kept in a form which permits identification of data subjects for no longer than is necessary for the purposes for which the personal data are processed; personal data may be stored for longer periods insofar as the personal data will be processed solely for archiving purposes in the public interest, scientific or historical research purposes or statistical purposes subject to implementation of the appropriate technical and organisational measures required by the GDPR in order to safeguard the rights and freedoms of individuals; and
- f) processed in a manner that ensures appropriate security of the personal data, including protection against unauthorised or unlawful processing and against accidental loss, destruction or damage, using appropriate technical or organisational measures.

For more information visit: <https://www.gov.uk/government/publications/guide-to-the-general-data-protection-regulation>



## The Human Tissue Act 2004

This was introduced to regulate the removal, storage and use of Human Organs and Tissue.

The Act:

- streamlines and updates current law on organs and tissue so that current gaps and anomalies are put right and the system is made fit for the 21st century
- provides safeguards and penalties to prevent a recurrence of the distress caused by retention of tissue and organs without proper consent. Tissue or organs cannot be taken or kept without consent other than for a Coroner to establish the cause of death
- sets up an overarching authority which will rationalise existing regulation and will introduce regulation of post mortems and the retention of tissue for purposes like education and research
- provides for the Human Tissue Authority to issue Codes of practice giving practical guidance on the conduct of activities within its remit
- will help improve public confidence so that people will be more willing to agree to valuable uses of tissue and organs like research and transplantation
- will improve professional confidence so that properly authorised supplies of tissue for research, education and transplantation can be maintained or improved.

Further information can be found on the Human Tissue Authority website.

<https://www.hta.gov.uk/>

## IRMER Regulations: The Ionising Radiation (Medical Exposure) (Amendment) Regulations (2000,2006)

Trial patients are often exposed to higher levels of radiation than non trial patients as they undergo more tests and imaging to monitor progress and response to trial treatments. This Act (amended in 2006) requires staff involved in undertaking medical exposures to establish diagnostic reference levels (DRLs) and to undertake appropriate reviews if these are consistently exceeded. DH has issued guidance on national DRLs which is available from the link below:- <https://www.gov.uk/government/publications/the-ionising-radiation-medical-exposure-regulations-2000>

## Administration of Radioactive Substances Advisory Committee ARSAC

Trial patients are often exposed to higher levels of radiation exposure than is necessary for routine diagnosis and treatment. This is allowed but an ARSAC research certificate must first be obtained for each research project which exposes patients to these higher levels. ARSAC assesses each application on its own merits and while it is important to keep doses as low as reasonably practicable, the activity administered (and the resulting dose) should be that necessary to provide the information required. All ARSAC certificates are site-specific, therefore in the case of multicentre studies; each study site requires its own certificate.

<https://www.gov.uk/government/organisations/administration-of-radioactive-substances-advisory-committee>



## Appendix 8: Health Research Authority

<https://www.hra.nhs.uk>

HRA approval is the new process for the NHS in England that brings together the assessment of governance and legal compliance, undertaken by dedicated HRA staff, with the independent REC opinion provided through the UK Health Departments' Research Ethics Service

### Ethics and NHS Approvals

All studies carried out in NHS organisations require before approval by:

- an ethics committee
- Health Research Authority (replaces the need for local checks of legal compliance and related matters by each participating organisation in England)
- local trust R&D (assess, arrange and confirm their capacity and capability to deliver the study )

### Ethics committee approval

Any health-related research project which involves humans, their tissue and/or data must be reviewed by a Research Ethics Committee (REC) before starting. This applies whether the project is to be externally or internally funded, and/or whether the project is to be conducted in the UK or overseas. The researcher must submit a protocol and supporting information to the committee for review, in accordance with the ethical principles developed by the World Medical Association in its Declaration of Helsinki (1964, latest revision 2008) This states:

*The design and performance of each research study involving human subjects must be clearly described in a research protocol. The protocol should contain a statement of the ethical principles involved and indicate how the principles in this Declaration have been addressed. The protocol should contain information about funding, sponsors, institutional affiliations, and other potential conflicts of interest, incentives for subjects and provisions for treating and/or compensating subjects who are harmed as a consequence of participating in the research study. The protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits. (2008 - see appendix)*

The primary function of a REC when considering a proposed study, is to protect the rights, safety, dignity and well-being of all actual or potential participants. The REC also has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events.

In the UK it is against the law, under the Medicines for Human Use (Clinical Trials) Regulations 2004, to start recruiting for a clinical trial of an investigational medicinal product (CTIMP) until there is a favourable opinion from a recognised REC (and authorisation from the licensing authority – the Medicines and Healthcare Products Regulatory Agency, MHRA).

### Ethics Committees

NHS Research Ethics Committees (RECs) have been established throughout the UK for many years with the purpose of safeguarding the rights, dignity and welfare of people participating in research in the NHS. Potential research participants at NHS organization in the UK will come under the protection of a REC. The REC is entirely independent of the researcher and the organisations funding and hosting the research. Ethics committees are guided by the Declaration of Helsinki.

The members of a REC are specially trained in research ethics and often have the type of experience which will be useful in scrutinizing the ethical aspects of a research proposal.

These include patients, members of the public, nurses, GPs, hospital doctors, statisticians, pharmacists and academics, as well as people with specific ethical expertise gained through a legal, philosophical or theological background. There are currently 155 NHS RECs in the UK (02/01/2008).

## **The National Research Ethics Service**

The National Research Ethics Service (NRES) was launched on 1 April 2007. NRES comprises the former Central Office for Research Ethics Committees and Research Ethics Committees (RECs) in England. The aim of NRES is to protect the rights, safety, dignity and well-being of research participants, whilst facilitating and promoting ethical research. It does this by:

- Providing ethical guidance and management support to Research Ethics Committees in England
- Delivering a quality assurance framework for the Research Ethics Service
- Working with colleagues in the UK to maintain a UK-wide framework
- Working with colleagues in the wider regulatory environment to streamline the processes

NRES is a core function of the Health Research Authority 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. We 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.

More information: <http://www.hra.nhs.uk/about-the-hra/our-committees/nres/>

## **Ethics Applications through the National Research Ethics Service (NRES)**

All applications to Research Ethics Committees must be made through the Integrated Research Application System (IRAS), which can be found on-line at <https://www.myresearchproject.org.uk/>

This is a new system for applying for all of the approvals required to run a research project, and is designed to enable the applicant to enter the information about their project once instead of duplicating information in separate application forms.

Researchers need to register on the IRAS website in order to create an application form.

Full guidance for applying to Research Ethics Committees is given on the main HRA website: <http://www.hra.nhs.uk/research-community/applying-for-approvals/>

## **Local Trust Approval**

Each hospital Trust or study site will have a named person who is responsible for ensuring that approvals have been obtained. S/he will also be responsible for raising any other issues which are pertinent to the local site. When all checks and local issues have been satisfactorily completed, an approval letter will be issued. Only then can a study commence at that site.

Contact Research and Development, based in the Joint Research Offices, Churchill Hospital, for further information <http://www.ouh.nhs.uk/researchers/>

## Appendix 9: Pharmacovigilance in trials of Investigational Medicinal Products and Safety Reporting

Pharmacovigilance is defined as watchfulness in guarding against danger from drugs or providing for safety of drugs. A joint medical research council and department of health work stream on pharmacovigilance aims to develop workable operating procedures for the publicly funded research community for reporting, monitoring and managing adverse reactions and events that will satisfy the requirements of the Medicines for Human Use (Clinical Trials) Regulations. To comply with this act organisations taking on pharmacovigilance responsibilities need to make arrangements to record, notify, assess, report, analyse and manage adverse events in those trials.

The regulations distinguish between Adverse Events (AEs), Serious Adverse Events (SAEs), Serious Adverse Reactions (SARs) and Suspected Unexpected Serious Adverse Reactions (SUSARs). It is the responsibility of the research team to notify the trials unit/ study sponsor of SAEs, SARs and SUSARS within the time specified in the protocol. Systems must be in place to ensure that adverse events are assessed for:

- Causality (is it a reaction to a trial medicine or not?)
- Expectedness (is the reaction a recognised adverse effect of the medication or is it unexpected?)

The regulations allow the Sponsor/Chief Investigator to specify in the protocol SAEs that do not need to be notified immediately, for example if the event is one of the main expected outcomes in the trial. Sponsors have to make sure that SUSARS are reported promptly to both the regulatory authorities and the relevant Ethics Committee. The Regulations set the following time limits.

**Fatal or life threatening SUSARS:** not later than 7 days after the person responsible for pharmacovigilance received information that the case fulfilled the criteria for a fatal or life threatening SUSAR.

**All other SUSARS:** not later than 15 days after the sponsor had information that the case fulfilled the criteria for a SUSAR.

At the clinical level, there will be a local SOP for the reporting of SAEs which must be adhered to. In order to meet the tight reporting deadlines above, the clinical research team must report any SAE to the trials office as soon as possible and not later than 24 hours after first discovering that the event has occurred.

An annual safety report must be sent by the trials office to the regulatory authorities and relevant Ethics Committee. The report should include adverse events (AE) explicitly detailed in the protocol; all reported Serious Adverse Events, Serious Adverse Reactions and SUSARS.

For more information visit: [https://ec.europa.eu/health/documents/eudralex\\_en](https://ec.europa.eu/health/documents/eudralex_en) or <http://www.ct-toolkit.ac.uk/>

## Medicines and Healthcare products Regulatory Agency (MHRA)

The MHRA was set up in April 2003 from a merger of the Medicines Control Agency and the Medical Devices Agency. The MHRA is the government agency which is responsible for ensuring that medicines and medical devices work, and are acceptably safe.

The MHRA is an executive agency of the Department of Health.

### Aims

The MHRA aims:

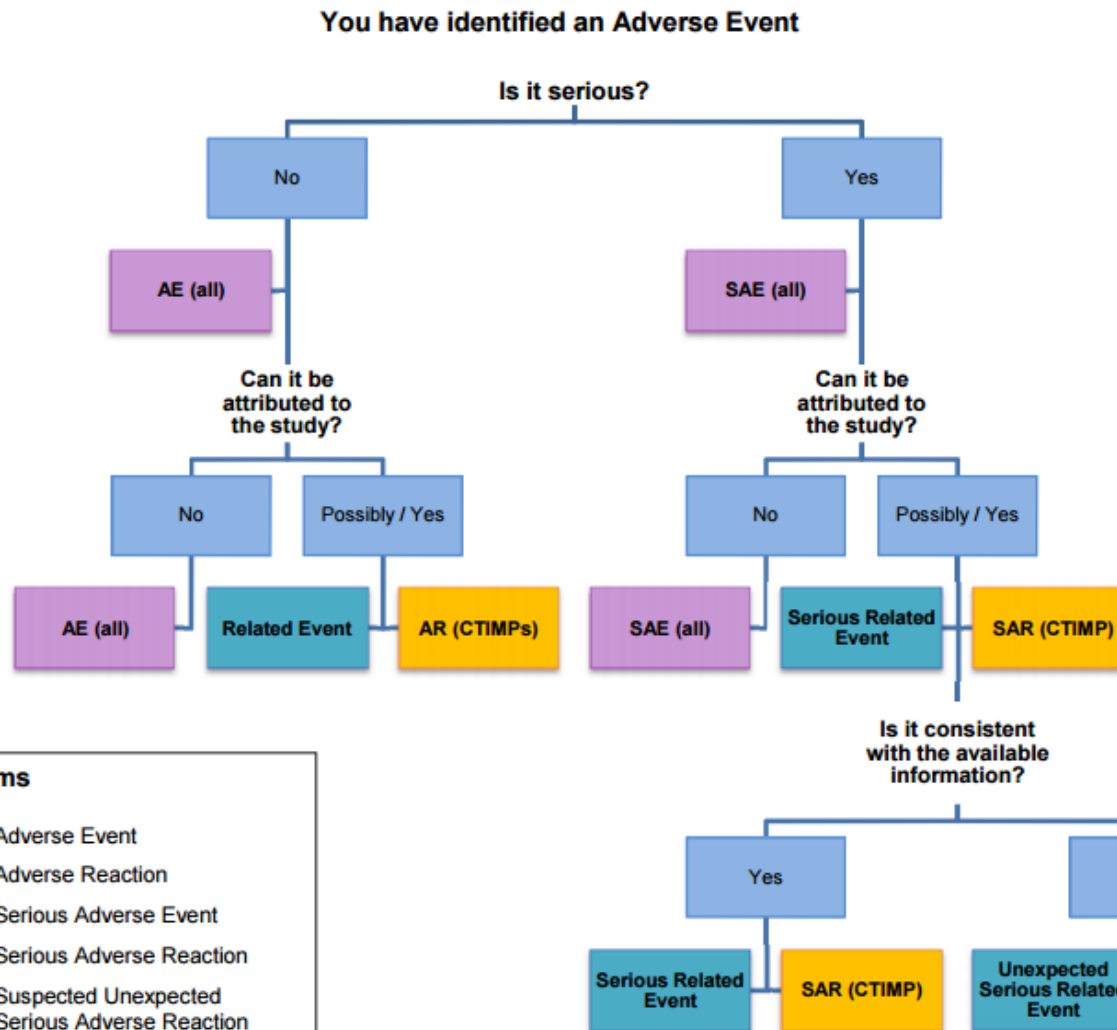
- To protect public health through regulation, including the development of benefit and risk profiles for medicines and devices.
- To promote public health by helping people to understand the risks and benefits of the products they use.
- To improve public health by facilitating the development of products that will benefit people.

### Key activities:

- To assess the safety, quality and efficacy of medicines, including to authorise their sale or supply in the UK for human use.
- To operate rigorous surveillance and inspection systems for the investigation of adverse reactions to medicines or incidents involving medical devices and taking any necessary action to safeguard public health <https://yellowcard.mhra.gov.uk/>
- To operate a quality surveillance system to sample and test medicines and to address quality defects, monitoring the safety and quality of imported unlicensed medicines and investigating internet sales and potential counterfeiting of medicines.
- To regulate clinical trials for medicines and medical devices. <https://www.gov.uk/government/collections/clinical-trials-for-medicines>
- To monitor and ensure compliance with statutory obligations relating to medicines and medical devices through inspection, taking enforcement action where necessary.
- To promote good practice in the safe use of medicines and medical devices.
- To provide the public and professions with authoritative information to enable informed dialogue on treatment choices

For more information visit: <http://www.mhra.gov.uk>

# Decision Tree for Adverse Event Reporting



**KEY**

- Definition for CTIMPs and non-CTIMPs
- Definition for non-CTIMPs only
- Definition for CTIMPs only

**CTIMP Acronyms**

AE	Adverse Event
AR	Adverse Reaction
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SUSAR	Suspected Unexpected Serious Adverse Reaction

## Appendix 10: Case Report Form Completion Guide

A CRF is a record of all the data and other information on each subject required by the research protocol. The ICH-GCP guidelines include strict guidance relating to CRF completion, as they are the official documentation of the trial for the authorities. The CRFs, along with source documentation are closely examined in the event of audit and inspection.

The CRF should collect necessary information about:

- The enrolled subject.
- Administration of the study drug or intervention.
- Study specific procedures.
- The outcome of any assessments.
- Details of any adverse events, serious adverse events and SUSARs.

Only those personnel identified by the principal investigator should complete CRFs. These can include:

- Co-investigators
- Clinical trial practitioners
- Research nurses/AHP

Anyone completing a CRF should have completed the signature delegation log in the Investigator file, and provided a signed and dated copy of their CV.

CRFs should be completed as soon as possible after the associated visit/patient assessment to ensure that the information is up to date and accurate. Before any monitoring or audit visits, it is essential to ensure that CRFs are as up to date as possible.

There are guidelines to CRF completion with each study protocol. Some general points are given here for reference.

### Paper CRF

- Always use a black ball point pen to complete paper CRFs.
- If the CRF is on carbonless duplication paper, ensure that an appropriate separator is inserted.
- Never leave blank spaces. If a section cannot be completed write, as appropriate, not known, not certain, test not done.
- All entries must be legible:
  - o Cross out incorrect entry with a single line, so that the original entry is still legible
  - o Enter the correct data
  - o Initial and data correction
  - o If it is not obvious, then give an explanation for alterations
- The CRF for each patient **MUST** be signed off by the principle investigator to indicate that they believe that they are complete and correct.

## Electronic CRF

- Adequate online training with the system to be used is required and will be facilitated by the study sponsor.
- A password will be issued to each individual authorised to access the system to enter data and should be kept safe and never shared with others.
- Data should be entered as soon as possible after the subjects scheduled visit.
- Corrections and query resolution is auditable through the electronic system.
- Provision is required at site to facilitate monitoring visits. And access to the electronic system.
- Computers should not be left unattended with patient data on screen even though anonymised. Adherence to the relevant data protection legislation is mandatory.

CRF completion is one of the most important roles of the clinical trials co-ordinator, as it is the only source of data that will be received by the sponsor company. Therefore, accurate and thorough completion is essential.

### Source documentation

Many items of data generated during routine and study related care episodes constitute source documentation. For example, blood results, radiology reports, pharmacy prescriptions, letters in medical notes, hand written notes in the patients record all constitute primary source data.

The development of study related source data sheets to capture relevant data items at designated study visit time-points are helpful in ensuring that items are not overlooked or missed in error and can significantly improve data quality overall. Such source sheets then also become primary source data and should be retained with the subject's medical notes for monitoring and data verification. If source data sheets are created they need to be version controlled and signed and data on completion of primary data entry.

## Appendix 11: Introduction to Research Methodology

Health research methodology is a complex area of study and only a very brief outline of the most relevant information will be discussed in this section.

There are a number of different research methods, which use differing rules and are underpinned by different philosophies. Each have their strengths and weaknesses and when research needs to be carried out, the type or combination of methods chosen will depend on the type of research question to be answered, as well as the skills, knowledge and preferences of the researchers.

### Epidemiology

This is the study of factors that might affect the health and illness of populations. It is used in public health research, identifying risk factors for disease and can sometimes demonstrate optimal treatment approaches to maintain public health.

### Observational studies

These include individual case studies, case control studies, and cohort studies (using a particular group of people e.g. participants with a strong family history of cancer). There is no active intervention in these studies. Investigators observe their participants and measure outcomes. They are looking for correlations (associations) between different factors e.g. various risk factors such as lifestyle, diet, environment, family history and genetic predisposition, and health status or outcomes of disease and treatment.

### Clinical Trials

These are medical research studies involving patients. Carrying out clinical trials is the only reliable way to find out if a new approach to cancer care is better than the standard cancer treatments that are currently available. Without trials, there is a risk that patients could be given treatments, which have no advantage, waste resources and might even be harmful to them. New treatments for cancer are evaluated in a number of stages or phases.

It is not only new treatments that are evaluated in trials. Other interventions can be studied, such as changing the timing, or the duration of existing treatments, combining existing treatments, or examining the effects of stopping a standard treatment completely, or introducing another type of intervention such as giving a psychological or supportive therapy.

### Phases of clinical trials

Clinical trials are usually conducted in phases. The trials at each phase have a different purpose and help scientists answer different questions:

**Phase I** trials are initial clinical tests of new potential treatments. They are used to determine whether or not a treatment is safe and to define a maximum tolerated dose. They generally are at the laboratory phase and use very few human subjects (typically 3-6). Often these are healthy volunteers, but in the case of cancer treatments this would be unethical as the treatments are often toxic. Therefore phase 1 trials tend to be offered to patients with advanced cancer who have exhausted all other treatment options. These trials can be expected to detect common side effects.

**Phase II** trials involve larger numbers of patients, starting with about 15 and continuing to approximately 40. They are designed to start to test the efficacy of the new treatment. Information on side effects and tolerability continues to be collected, so that some less common side effects and cumulative effects might become visible in phase II.



All phase and non-randomised (see below) phase II trials fall under the heading of **translational** research. This is a term used to define experimental research of new treatments and diagnostic procedures for all diseases, including cancer. It covers all experimentation to develop new treatments, rather than comparing them against a standard treatment. Many trials do not proceed to the next phase.

**Phase III** trials are large national or international trials involving hundreds or thousands of patients. They are comparative studies designed to compare the effects of new drugs, treatment methods, or other interventions (which could mean no intervention) with the standard treatment. Patients are usually divided at random into either the treatment intervention group, or a control group. Patients in both groups will be as similar as possible. Further and more reliable information can be gathered about efficacy: how well the treatment works and how long the benefits last on average. Less common side effects and possibly any longer term problems will be revealed at this stage.

Statisticians estimate how many research participants will be required to prove, with an acceptable degree of confidence (usually described as 95% confidence interval) that any results are not due to chance alone. Generally, if the expected improvements from the trial treatment are large, the differences will be measurable after a relatively smaller number of patients have been treated. If only a small improvement is expected, a larger number will need to be treated before the measured effect can be classed as significant (meaning the change is not due to chance alone).

**Phase IV** trials are post-marketing studies, carried out after a treatment has been shown to work and a license has been granted. Further information is gained about the effects of wider participation, longer-term risks and benefits, and more about possible rare side effects so that optimal use can be decided.

## **Trial design**

Clinical trials are designed in many different ways according to the research question. Many of the trials that you will be involved with are comparing new treatments with the tried and tested or "gold standard" treatment. The most effective way of comparing treatments in this way is through randomised controlled trials

### **Randomised Controlled Trials (RCTs)**

Across the world, RCTs are now seen as the most reliable way to test new treatments and to compare two (or more) existing treatments, to see which one works best.

An RCT is a study in which people are allocated at random to receive one of two or more clinical interventions. One of these interventions is the standard of comparison or control. The control may be a standard practice, a placebo, or no intervention at all. RCTs seek to measure and compare the outcomes after the participants receive the interventions. RCTs typically follow a prescribed series of study phases, which may last up to twenty years, although the timeframes associated with development, are increasing.

Ethically, equipoise should exist for a randomised trial to be undertaken: that is, there should be genuine uncertainty about the additional benefits and risks of the new intervention over the current standard intervention.

## **Quantitative Research**

Quantitative Research methods are based on measuring and counting observed phenomena and use mathematical models and statistics, usually with large numbers of subjects. RCTs are usually quantitative studies because the outcomes are measured.

### **Randomisation methods**

Randomisation is not always a simple case of randomly allocating patients to one of two or more groups. The following techniques can be applied to the randomisation process

Simple randomisation allocation is now usually decided by a computer programme, (previously used methods included tossing a coin, or using a random number table.)

Minimisation improves the balance between groups in terms of important characteristics, especially in small samples. It is based on the idea that the next participant to enter the trial is more likely to be allocated the intervention that would minimise the overall imbalance of selected characteristics between the groups at that stage.

Blocked/restricted randomisations are assigned randomly within blocks to ensure balance within the blocks. Blocks can be of any size but a multiple of the number of trial groups is logical. The block size should be small and variable, and unknown to the investigators, to prevent predictability and maintain concealment.

Stratified randomisation gives a balance within sub-groups defined by important variables such as centre/country in a multi-centre trial. Blocked randomisation must be used within each strata. Stratification is not feasible for small studies or for many variables. NCRN Induction Manual September 2009 60

Cluster randomisation is when the unit of randomisation is not the individual participant being studied but groups of participants (clusters) such as GP practice or village community.

### **Blinding**

Sometimes in clinical trials it is necessary to disguise the identity of the treatment to limit conscious and unconscious potential bias. This is achieved through a technique called "blinding".

Blinding is used in combination with randomisation to limit the occurrence of conscious and unconscious bias in the conduct of clinical trials (performance bias) and interpretation of outcomes (ascertainment bias).

There are two types of blinding:

Double Blind: Both investigator and participant are ignorant of the intervention allocation

Single Blind: Either the participant or the investigator is unaware of the intervention allocated. Usually it is the participant who is "blind".

### **Placebos**

If there is no standard treatment, patients taking part in a trial may be given a dummy drug, which looks like the drug being tested. This dummy drug is called a placebo. Placebos are used because sometimes people get better without treatment.

In some trials where a new treatment is being compared with the standard treatment, placebos are also used. This is usually because the treatments can be easily distinguished by the appearance of the drug being supplied and the patient could become aware of what they are taking. In this case two placebos are used, one made to look like each of the drugs and each person receives one of these placebos and one real drug.

In summary, RCTs are quantitative, comparative, controlled experiments in which investigators study two or more interventions in a series of individuals who receive them in random order. Randomised controlled trials are the most rigorous way of determining whether a cause-effect relation exists between treatment and outcome and for assessing the cost effectiveness of a treatment.

## **Qualitative Research**

Deriving a simple definition of qualitative research is difficult due to a lack of consensus on the fundamental tenets of qualitative research methods. It is usually based on a more in depth study of the subject matter, using a smaller number of participants. There are certain principles of qualitative research that separate it from quantitative approaches. Firstly, that this approach to research is constructed within and is not removed from social processes. Secondly, that the researcher is part of the research process and is not removed from it. Thirdly that qualitative research involves description rather than measurement. NCRN Induction Manual September 2009 61

Although RCTs are considered to be the “gold standard” method when trying to measure the effects of a discrete medical intervention, qualitative methods might be better when a deeper analysis is required, for example when trying to understand human behaviour or complex social phenomena. Qualitative methods can be used to evaluate the effects of more complex health or social interventions. Some health and social studies will use a mixed methods approach.

## **Systematic Reviews**

A systematic review is classed as secondary research. This is the analysis of published or recorded data from previously conducted research projects. Systematic and explicit criteria are adopted to identify select and critically appraise research studies to establish where the effects and effectiveness of healthcare interventions are consistent and where they vary.

## **Meta-analyses**

Meta-analyses occurs when statistical methods are applied to the review and analysis of combined data from studies included in a systematic review

## **Outcome measures in clinical trials**

An outcome measures is the means by which we measure the impact of an intervention on patients. Outcome measures are also known as response variables, events or endpoints. The outcome measure/s selected for a trial will depend on the phase of trial, stage of disease and the intervention being tested.

Early phase trials commonly use outcome measures of tumour response whilst late phase trials use outcome measures that include survival (disease free or overall survival). Almost all cancer trials will include some measure of toxicity and treatment compliance.

For information and a 'process map' of planning a research study, see <https://processmap.tghn.org/>

## Appendix 12: Why did you become a research nurse?

POSTED ON MAR 9, 2015 BY KELLY GLEASON IN RESEARCH

Like many of you I 'fell' into research nursing. Some are scouted by a professor with a project and a grant or a senior research nurse who spotted your 'talent' while working alongside you in out-patient clinic. Today even scientists are drawn to clinical research exchanging petri dishes for patients.

Whatever it was that brought you to clinical research you were likely looking for something: a change, a challenge, an adventure, a desire to grow and expand. In those first few months, you began to piece together a picture of what clinical research was 'really' about, all you needed to learn, who you needed to become, who you would now consider your 'colleagues' and that not everybody was going to see research as important as you did.

But if after learning all that, you stayed:

- It is likely because you felt you found *something* you liked.
- It felt good to learn new things.
- It felt good to be challenged – even if it was daily.
- It felt good to contribute to making things better.
- It felt good to work more autonomously.
- It felt good to be part of a motivated team.

When I ask people attending 'Developing Yourself in Clinical Research' what they feel the benefits of their role are, they usually say:

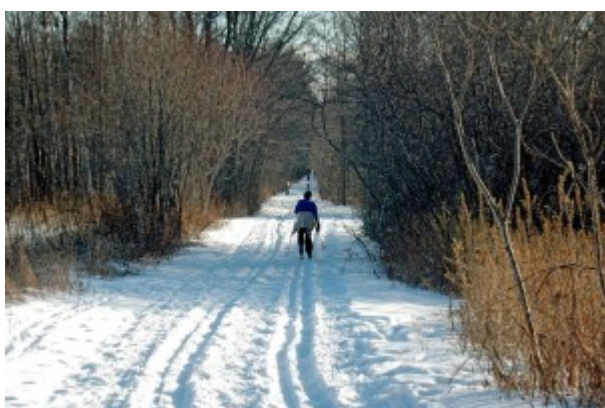
- Autonomy
- Innovation
- Creating change
- More time with patients
- Variety

Jobs in clinical research definitely give people the opportunity to experience all of the above. Just think back for a moment to all you have learnt since taking on your first role in research:

- You learnt about TMFs, ISFs, CRFs and SVDs. Things you likely knew nothing about before entering into research.
- You learnt new laws and regulations.
- You learnt some science.
- You learnt the real meaning of informed consent and that robust informed consent takes time, more time than we usually cost for.
- You probably thought deeply about the ethical principles of research.
- You learnt to balance a centrifuge, pipette with no air bubbles, and some may even have become familiar with the 'buffy coat'.
- You learnt to package dry ice without putting your courier's life at risk.
- You learnt to use encrypted USB sticks.
- You learnt to ask nicely...and sometimes desperately for an urgent MRI or PET scan.

- After your first inspection, you learnt to take pride in maintaining site files. To the MHRA, that file is a reflection of your work.
- You've probably learnt to have your voice heard in meetings and circles where you may not have ever spoken before.
- You have developed your PR, your marketing & your public speaking skills.
- You have redefined assertiveness.
- Mapped patient pathways from parts of the service you didn't even know existed.
- You've learnt to work with different personalities, stakeholders and agendas.
- You created recruitment strategies.
- You established yourself as the 'hub' of the team.
- You learnt how far a 'can-do' attitude gets you.

You have likely grown in ways you never thought possible. You are a trail blazer.



Roles in the field of clinical research are still 'new'. You are creating new pathways for others to follow. This is by no means an easy task but somehow I know you are up for the challenge. There are so many ways to grow and expand skills. Professional pathways need to be forged but we also need to build bridges between cultures if research is going to truly become part of healthcare in the UK. Whatever your talent or interest, there is a place for you to contribute and make your mark.

More research than ever is happening in the NHS. We have a greater number of open studies and a greater number of patients taking part in studies than ever before. You are the largest body of professionals carrying out clinical research in the NHS. You are the engine that is making it all possible. You are changing the culture in the NHS. You are creating opportunities to improve services and develop new career pathways.

Whatever brought you here, I am glad you stayed. It is fantastic to be part of this network of individuals dedicated to improving healthcare through research. It is energising to be with, and to share with like-minded people who have also desired to break out, explore new territory, learn new skills and discover hidden talents. If you are new to clinical research, hang in there...the good times do come, be patient and give yourself time to transition into this new world of clinical research. It is worth it, I promise.

<https://clinfield.com/why-did-you-become-a-research-nurse/>

See <http://www.futuremorph.org/11-13/case-studies/john-clinical-trial-coordinator/> for the experiences of a Trial Co-ordinator