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Essential Healthcare Research Governance Processes

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THE 1ST STUDENT EXPERIENCE SURVEY 2014-15

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Aims

- Overview of governance processes including recent changes to remit
- Reminder of HoD and PI responsibilities
- Remit of the Health and Human-Interventional Studies Research Governance Sub-Committee

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Agenda

- Research Governance Procedure incl:
  - Appointing a sponsor
  - University vs. NHS ethics approval
  - Is it a human-interventional study?
- Is my study a CTIMP (Clinical Trial of an Investigational Medicinal Product)?
- Time to discuss individual questions and studies

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Health and Human-Interventional Studies Research Governance Sub-Committee

- Advise RIC on-
  - response to new policy & regulations
  - effectiveness of governance procedures
- Receive research governance reports
- Identify risks to the university and participants

Chair	Cindy Cooper
Secretary	Anita Kenny
School / Department Representatives	
Medicine	Liz Williams
ScHARR	Judith Cohen
Psychology	Andrew Thompson
Nursing and Midwifery & Human Communication Sciences & Clinical Dentistry	Nicolas Martin
University Research Ethics Committee	Peter Bath
RIS	Lindsay Unwin

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Research governance

- Standards to improve quality
- Planning and resourcing
- Securing of authorisations
- Ethical and scientific quality
- Safety of staff and participants
- Exploitation and dissemination of results

Research Governance Framework for Health and Social Care

- Protect human participants in research
- Strengthen scientific quality
- Clarify accountabilities & responsibilities of individuals and organisations

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Why Research Governance

- Catalyst was Aldey Hey
- Removal, retention, and disposal of human tissue
- Now the buck stops with the Research Governance Sponsor

Healthcare Research Governance Procedures

www.sheffield.ac.uk/ris/other/gov-ethics/governance
www.shef.ac.uk/ethics

Lindsay Unwin, Research & Innovation Services

Overview

1. **The Initial Decisions stage**
   - Does the Research Governance Procedure apply?
   - Who should be the sponsor?
   - Is it a human-interventional study?
   - Do I need a Research Passport?

2. **The Registration stage**
   - URMS

3. **The Approvals stage**
   - Scientific approval
   - Ethics approval
   - HRA approval
   - Insurance

4. **Sponsor authorisation & post award responsibilities**

1. INITIAL DECISIONS STAGE

- Does the Research Governance Procedure apply to your project?

(consult: http://www.sheffield.ac.uk/ris/other/gov-ethics/governance/definition)

Only if the research requires NHS REC review (part of HRA approval):

http://www.hra-decisiontools.org.uk/ethics/

(...or needs other aspects of HRA approval – as a sponsor will be needed to sign off IRAS form even if NHS REC approval not needed)

To clarify…

IF YOUR STUDY DOES NOT:

- NEED NHS ETHICS APPROVAL; or
- INVOLVE THE NHS IN ANY OTHER WAY

You don't need governance!

(but you will still need ethics approval if involves human participants/tissue/personal data)

What are the research governance requirements for your study?

Is it a human interventional study?
[The University definition of human-interventional studies can be found here: https://www.sheffield.ac.uk/polopoly_fs/1.393607!/file/TypesOfStudy.pdf]

NO → **Is NHS ethics approval required?**
[Use the Health Research Authority's decision tool to help: http://www.hra-decisiontools.org.uk/ethics/]

NO → **Does the study involve the staff/premises of NHS/Department of Health services?**

NO → **You may need ethics approval via the University/another approved body**

For guidance see: www.sheffield.ac.uk/ris/other/gov-ethics/ethicspolicy/approval-procedure

YES (from Is it a human interventional study?)

YES (from Is NHS ethics approval required?)

YES (from Does the study involve the staff/premises of NHS/Department of Health services?)

Follow the University's Research Governance Procedure:
- register the project on URMS
- identify a research governance sponsor
- provide evidence of scientific and ethical approval

*Specific requirements may vary by sponsor

NB. Clinical trials of investigational medicinal products (CTIMPs) and medical devices have additional specific legislative and regulatory requirements. CTIMPs can include administration of nicotine and dietary supplements such as probiotics that are available over the counter. For further guidance refer to the MHRA's website: https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency/services-information Practice-%28GCP%29

Is NHS ethics approval required?
[Use the Health Research Authority's decision tool to help: http://www.hra-decisiontools.org.uk/ethics/]

NO → **You may need ethics approval via the University/another approved body**

For guidance see: www.sheffield.ac.uk/ris/other/gov-ethics/ethicspolicy/approval-procedure

YES

Follow the University's Research Governance Procedure:
- register the project on URMS
- identify a research governance sponsor
- provide evidence of scientific and ethical approval

*Specific requirements may vary by sponsor

And ONLY IF THE UNIVERISTY OF SHEFFIELD IS THE RESEARCH GOVERNANCE SPONSOR,
Follow the Quality Assurance Procedure for Human Interventional Studies
- complete a risk assessment checklist to indicate the appropriate level of scrutiny for your study (see www.sheffield.ac.uk/ris/other/gov-ethics/clinicaltrials for more details).

NB. Clinical trials of investigational medicinal products (CTIMPs) and medical devices have additional specific legislative and regulatory requirements. CTIMPs can include administration of nicotine and dietary supplements such as probiotics that are available over the counter. For further guidance refer to the MHRA's website: https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency/services-information Practice-%28GCP%29

1. INITIAL DECISIONS STAGE

- Which organisation will be the research governance sponsor?

(consult: http://www.sheffield.ac.uk/polopoly_fs/1.121332!/file/sponsor.pdf)

- Pharmaceutical company?
- Sheffield Teaching Hospitals NHS Trust?
- Another NHS Trust?
- University of Sheffield?

*TUOS will not sponsor IMP trials!

NB, For work within the NHS it may be that an honorary research contract or letter of access is needed. If so, the **Research Passport** application form needs completing
(consult the guidance: http://www.sheffield.ac.uk/ris/other/gov-ethics/governance/passport]

1. INITIAL DECISIONS STAGE

- If University-sponsored, is it a human interventional study?

(consult: https://www.sheffield.ac.uk/ris/other/gov-ethics/clinicaltrials)

University definition (only if University-sponsored):

- 'research studies designed to answer specific questions about interventions in human participants, whose purpose is to investigate the effectiveness of the intervention(s) & to assess clinical or physiological outcomes'

- Previously referred to as clinical trials

Some examples:

- Surgery and other interventional procedures;
- Diagnostic tests;
- Screening;
- Behavioural and/or educational interventions designed to affect health;
- Devices;
- Administration of a food product;
- Physiotherapy and/or psychotherapy;
- Administration of a cosmetic product;
- Complementary therapies;
- Administration of human whole blood products.

2. REGISTRATION STAGE (nb. In terms of Research Governance Procedure)

- Register the project on the University Research Management System (URMS) (consult: http://www.sheffield.ac.uk/ris/application/pricing- URMS helpline: 222 1450)

*This includes **Student Projects** even if they are not funded. The supervisor, who is formally the Principal Investigator, enters the details on URMS as a 'student governance project'. (See guidance tutorial: http://www.researchoffice.dept.shef.ac.uk/shef-only%20/Tutorials/Student%20Governance.swf)

.....Registering on URMS (and stating that the DoH Research Governance Framework applies) will alert your department's Healthcare Research Governance Contact, who will contact you to request the necessary documentation.....

3. APPROVALS STAGE

For projects sponsored by another body (not TUOS)

– need to liaise with relevant research support office but will include need for scientific and ethics approval

+

- University of Sheffield needs to see confirmation that this body takes on sponsor responsibility

3. APPROVALS STAGE

For University-sponsored studies:

Confirmation of scientific approval:

- **For funded staff research:** peer review will have taken place as part of the decision-making process = funding confirmation letter sufficient

- **For un-funded staff research:** departmental peer review required

- **For student research:** confirmation from supervisor that they have scientifically approved the project

3. APPROVALS STAGE

Confirmation of ethics approval:

Possible routes for approval:

- **NHS REC (IRAS)** - (Now part of HRA approval!) Needed if participants are identified from, or because of, their past or present use of NHS services (or relatives/carers) + other specific cases e.g. human tissue, CTIMPs etc: http://www.hra-decisiontools.org.uk/ethics/index.html

- **University** - needed for ALL research involving human participants/personal data UNLESS obtained from other approved body e.g. NHS = *May still apply even if NHS ethics not needed (different definition of research)!!*

- **Alternative** - other university/research organisations' ethics review procedure (needs to be UREC approved)

IRAS – Declaration by the Sponsor

- IRAS applications need authorisation from the sponsor
- If the University is sponsor: enter email address of departmental signatory and they will be sent an automatic email
- Other sponsors will have own arrangements – contact relevant research support office
- Also need to include certificate of insurance: consult http://www.sheffield.ac.uk/ris/other/gov-ethics/governance/insurance

Departmental healthcare governance contacts

Academic department	Designated contact
ScHARR	Miss Ellen Nicolson (E.L.Nicolson@sheffield.ac.uk - 25446)
Clinical Dentistry	Mrs Sue Spriggs (S.Spriggs@sheffield.ac.uk – 817954) Dr Lynne Bingle (L.Bingle@sheffield.ac.uk – 817953)
Nursing & Midwifery	Mrs Andrea Lowery (snm.postgrad@sheffield.ac.uk – 22053)
Psychology	For DClinPsy students: Mr Amrit Sinha (A.Sinha@sheffield.ac.uk - 26650); Others: Dr Tom Webb - 26516
Medicine	Miss Anita Kenny (a.j.kenny@sheffield.ac.uk – 21400)
Human Communication Sciences	Dr Traci Walker (Traci.Walker@sheffield.ac.uk – 22420)
Other academic departments	Miss Anita Kenny (a.j.kenny@sheffield.ac.uk – 21400)

3. APPROVALS STAGE

HRA approval incorporating NHS R&D, NHS REC and other relevant approvals:

Apply via IRAS system: https://www.myresearchproject.org.uk/

Applicant guide: http://www.hra.nhs.uk/research-community/applying-for-approvals/hra-approval/

Insurance:

CHECK INSURANCE IS IN PLACE (even if NHS ethics not required):

http://www.sheffield.ac.uk/ris/other/gov-ethics/governance/insurance

3. APPROVALS STAGE

Human interventional studies only:

- Complete and return risk assessment checklist sent by R&IS;
- This will be assessed via an algorithm to establish a risk level (high/medium/low).

4. SPONSOR AUTHORISATION STAGE

Once all approvals obtained:

- University will issue an authorisation letter confirming the research can go ahead

Monitoring responsibilities of the PI:

*Establish a site file, progress reporting (to HoD and funder), adverse event reporting, arrangements for recording, reporting and reviewing significant developments, arrangements to record, handle and, as appropriate, store all information collected

Monitoring responsibilities of the HoD:

* Review progress reports, review adverse events, ensure compliance with conditions of ethics approval, regular correspondence with PI (as appropriate for risk)

Additional quality assurance process for human interventional studies only

- Sponsorship letter sent to PI by R&IS after standard requirements of research governance procedure are met (Head of Dept. cc'd);
  - Low risk projects: PI completes self-certification statement, signed by HoD;
  - Medium/high risk projects: After the project goes live, Committee meets with PI to discuss management of project.

Monitoring and audit

- Departmental healthcare research governance contacts keep relevant records
- Annual report of healthcare research projects & audit of some
- Reviewed by Health and Human Interventional Studies Research Governance Sub-Committee

Thanks to all involved!!

Help and Support

- Research & Innovation Services' Quality & Research Integrity Team:

- Anita Kenny a.j.kenny@sheffield.ac.uk x21400
- Lindsay Unwin (l.v.unwin@sheffield.ac.uk

X 21443

- Departmental healthcare research governance contacts

The University Of Sheffield.

Healthcare Governance Information Sessions

Clinical Trials of Investigational Medicinal Products - CTIMPs

Judith Cohen

Research Fellow, ScHARR

Assistant Director, Sheffield CTRU

When is a CTA required?

- **Regulations only apply to trials of medicinal products in human subjects**
- **Medicinal products are substances which:**
  - Prevent/treat disease
  - Are administered for diagnostic purposes
  - Restore, correct or modify physiological function
- **A clinical trial is an investigation intended to:**
  - Discover or verify the clinical, pharmacological, and/or pharmacodynamic effects of one or more medicinal products
  - Identify adverse reactions
  - Study the absorption, distribution, metabolism or excretion
- **Clinical studies involving only medical devices, food supplements or other non-medicinal therapies are not covered by the directive**

Is your trial within the scope of the UK regulations?

IS IT A CLINICAL TRIAL OF A MEDICINAL PRODUCT?

This algorithm and its endnotes will help you answer that question. Please start in column A and follow the instructions. Additional information is provided in the notes at the end of the table. If you have doubts about the answer to any of the questions contact the clinical trials unit of your competent authority.

A	B	C	D	E
A CLINICAL TRIAL OF A MEDICINAL PRODUCT?				A NON-INTERVENTIONAL CLINICAL TRIAL?
Is it a medicinal product (MP)?[I]	**Is it not a medicinal product?**	**What effects of the medicine are you looking for?**	**Why are you looking for those effects?**	**How are you looking for those effects?**
If you answer no to <u>all</u> the questions in column A, the activity is not a clinical trial on a MP. If you answer yes to <u>any</u> of the questions below go to column B.	If you answer yes to the question below in column B the activity is not a clinical trial on a MP. If you answer no to this question below go to column C.	If you answer no to <u>all</u> the questions in column C the activity is not a clinical trial under the scope of Directive 2001/20/EC. If you answer yes to <u>any</u> of the questions below go to column D.	If you answer no to <u>all</u> the questions in column D the activity is not a clinical trial under the scope of Directive 2001/20/EC. If you answer yes to <u>any</u> of the questions below go to column E.	If you answer yes to <u>all</u> these questions the activity is a non-interventional trial which is outside the scope of Directive 2001/20/EC. If your answers in columns A,B,C & D brought you to column E and you answer no to <u>any</u> of these questions the activity is a clinical trial within the scope of the Directive.
A.1 Is it a substance[II] or combination of substances presented as having properties for treating or preventing disease in human beings ? A.2 Does the substance function as a medicine? i.e. can it be administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action or to making a medical diagnosis or is otherwise administered for a medicinal purpose? A.3 Is it an active substance in a pharmaceutical form?	B.1 Are you <u>only</u> administering any of the following substances? • Human whole blood[III]; • Human blood cells; • Human plasma; • Tissues except a somatic cell therapy medicinal product[IV]; • A food product[V] (including dietary supplements) not presented as a medicine; • A cosmetic product[VI] • A medical device	C.1 To discover or verify/compare its clinical effects? C.2 To discover or verify/compare its pharmacological effects, e.g. pharmacodynamics? C.3 To identify or verify/compare its adverse reactions? C.4 To study or verify/compare its absorption, distribution, metabolism or excretion?	D.1 To ascertain or verify/compare the efficacy[VII] of the medicine? D.2 To ascertain or verify/compare the safety of the medicine?	E.1 Is this a study of one or more medicinal products, which have a marketing authorisation in the Member State concerned? E.2 Are the products prescribed in the usual manner in accordance with the terms of that authorisation? E.3 Does the assignment of any patient involved in the study to a particular therapeutic strategy fall within current practice and is not decided in advance by a clinical trial protocol[VIII]? E.4 Is the decision to prescribe a particular medicinal product clearly separated from the decision to include the patient in the study? E.5 Will no diagnostic or monitoring procedures be applied to the patients included in the study, other than those which are applied in the course of current practice? E.6 Will epidemiological methods be used for the analysis of the data arising from the study?

Examples of projects planned in UoS

Probiotic supplement to relieve symptoms of Irritable Bowel Syndrome.

- Clinical trial to investigate the putative beneficial effect of a probiotic supplement to relieve symptoms of Irritable Bowel Syndrome.
- Commercially available product, LAB4, presented as a food supplement.
- Patients recruited from outpatient gastroenterology clinics and asked to consume the supplement for 8 weeks.
- Patients complete a questionnaire about their bowel health at intervals during the intervention.

Examples of projects planned in UoS

Probiotic supplement to relieve symptoms of Irritable Bowel Syndrome.

Would this be a CTIMP?

Email sent to MHRA advice line, response:

After reviewing the Advice Request form, I can confirm that the Agency would consider LAB4 “Proven Probiotics” medicinal under the first limb of the medicines definition (“any substance or combination of substances presented as having properties of preventing or treating disease in human beings”). This is due to the product’s use in relieving symptoms of Irritable Bowel Syndrome.

Implications for set-up and conduct if study is a CTIMP:

- Trials must be registered on a European database (EudraCT)
- Must apply for a Clinical Trial Authorisation (CTA) from the competent authority
- Must apply for NHS ethics (even if healthy volunteers)
- Manufacture and labelling of drugs must be completed to Good Manufacturing Practice (GMP)
- Active management and monitoring
- Adverse Event Reporting
- Mandatory GCP inspections
- Notification of trial status and reporting of results

Medical Devices Trials

- Although medical device trials are not covered by the clinical trials directive, other regulations apply
- Medical Devices Regulations 2002 (and 2008 Amendment) require manufacturers of medical devices to submit details of planned clinical investigations to the MHRA and to report SAEs
- Notification is not required if the device used is CE-marked for the purpose under investigation
- Note that Apps and software can be classed as devices
- Fees of £2 - £5k for MHRA approval

Medical Devices Trials

Medical Devices Directive, Article 1:

‘medical device’ means any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of: ◄ — diagnosis, prevention, monitoring, treatment or alleviation of disease, — diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap, — investigation, replacement or modification of the anatomy or of a physiological process, — control of conception, and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means; (b) ‘accessory’ means an article which whilst not being a device is intended specifically by its manufacturer to be used together with a device to enable it to be used in accordance with the use of the device intended by the manufacturer of the device;

Medical Devices Trials

Software apps

- Mobile devices can store personal information, are always switched on, have a light source and a camera that can take high quality images. They can also provide information such as orientation through built-in sensors. The use of this type of software for medical purposes has increased.
- If these software applications meet the definition of a medical device, it will be regulated by MHRA as a medical device
- There are a number of words likely to contribute to MHRA determining if an app is a medical device. These include:

  Amplify, analysis, interpret, alarms, calculates, controls, converts, detects, diagnose, measures, monitors

Medical Devices Trials

Software apps that could be classed as medical devices:

- apps acting as accessories to medical devices such as in the measurement of temperature, heart rate, blood pressure and blood sugars could be a medical device as are programmers for prosthetics could be classed as medical devices
- apps with software that monitors a patient and collects information entered by the user, measured automatically by the app or collected by a point of care device may qualify as a medical device if the output affects the treatment of an individual

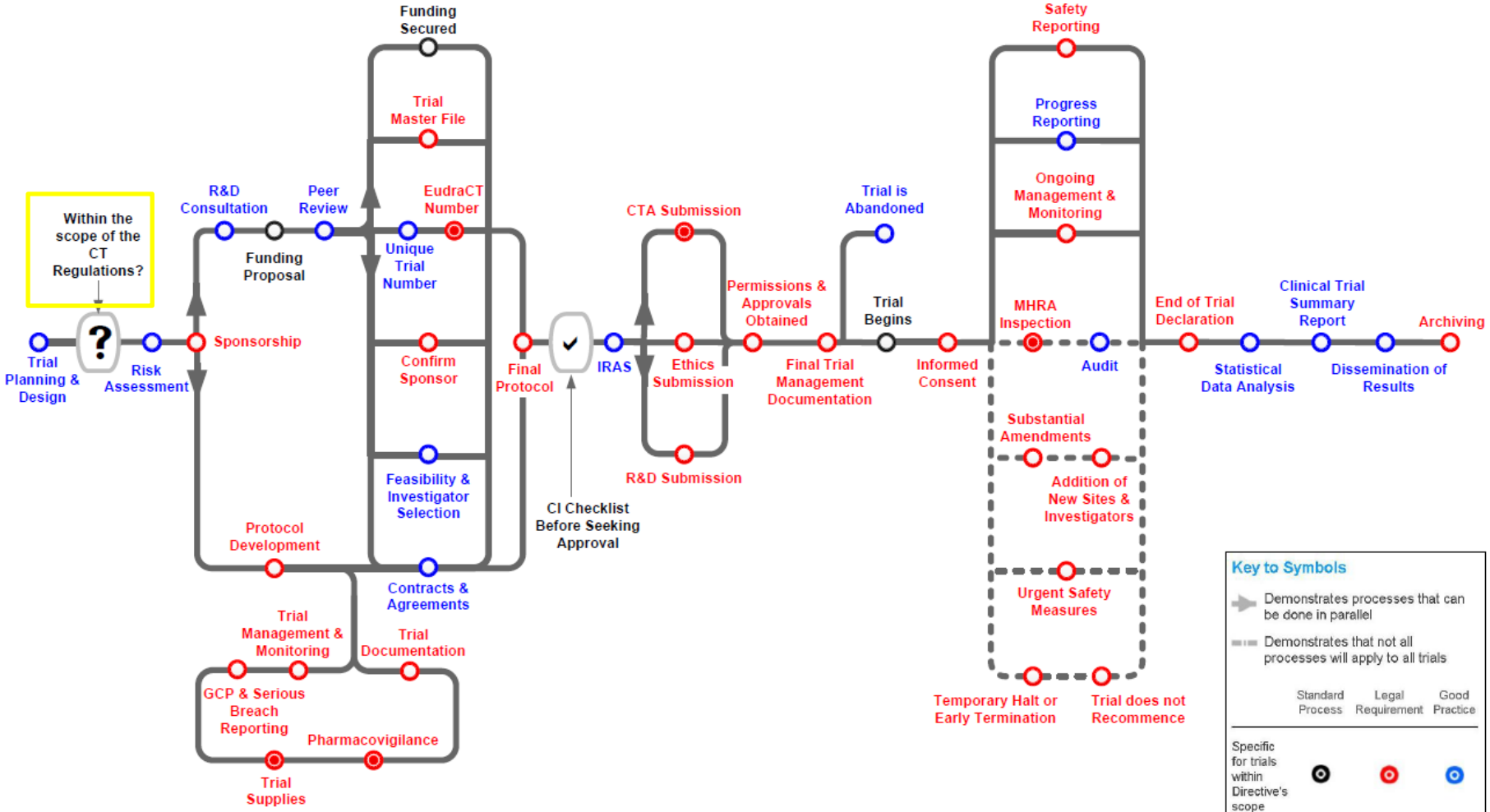
Medical Devices Trials

Software apps that are unlikely to be classed as medical devices:

- apps with software that provides general information but does not provide personalised advice, although it may be targeted to a particular user group, is unlikely to be considered a medical device
- apps with software that is used to book an appointment, request a prescription or have a virtual consultation is also unlikely to be considered a medical device if it only has an administrative function

The Clinical Trials Toolkit - Routemap

NHS
National Institute for Health Research



Key to Symbols

- Demonstrates processes that can be done in parallel
- Demonstrates that not all processes will apply to all trials

	Standard Process	Legal Requirement	Good Practice
Specific for trials within Directive's scope	○	○	○
Relevant to all trials	○	○	○

*Version 1.1 – August 2013. Please visit www.ct-toolkit.ac.uk to ensure you have the latest version of the routemap.

CTIMPs at UoS

- UoS cannot be the research governance sponsor for CTIMPs
- Another sponsor would need to be agreed if projects are deemed CTIMPs
- Students should not be the CI on CTIMPs
- Always check with the MHRA if uncertain if the study would be a CTIMP
- You may need to alter the project design if it is a student project

Any questions for the committee?