# NORWICH CLINICAL TRIALS UNIT OVERVIEW

This document provides an overview of the Norwich Clinical Trials Unit.

**Sections 1 to 3** describe the Norwich Clinical Trials Unit remit and structure. **Section 4** gives a broad overview of our current research and the types of trials that we can support. **Section 5** onwards provides information aimed at researchers who are interested in working with us.

## 1. BACKGROUND

The Norwich CTU (NCTU) has been established by the University of East Anglia (UEA) and Norfolk and Norwich University Hospital (NNUH) to provide an effective platform for the conduct of high quality clinical trials. This includes developing funding applications, trial design, management, quality assurance, analysis and reporting. The NCTU also provides a forum for training and methodological advancement in trial design, conduct and analysis.

The vision is to establish an internationally recognised clinical trials unit to conduct important trials across a broad range of clinical disciplines which influence clinical and research practice and are published in high impact journals, thus enhancing the international research reputation of Norwich Research Park (NRP).

The NCTU is fully registered as a UK Clinical Research Collaboration trials unit and receives National Institute for Health Research (NIHR) CTU support funding to help the NCTU in developing and supporting NIHR trials.

## 2. WHAT WE DO

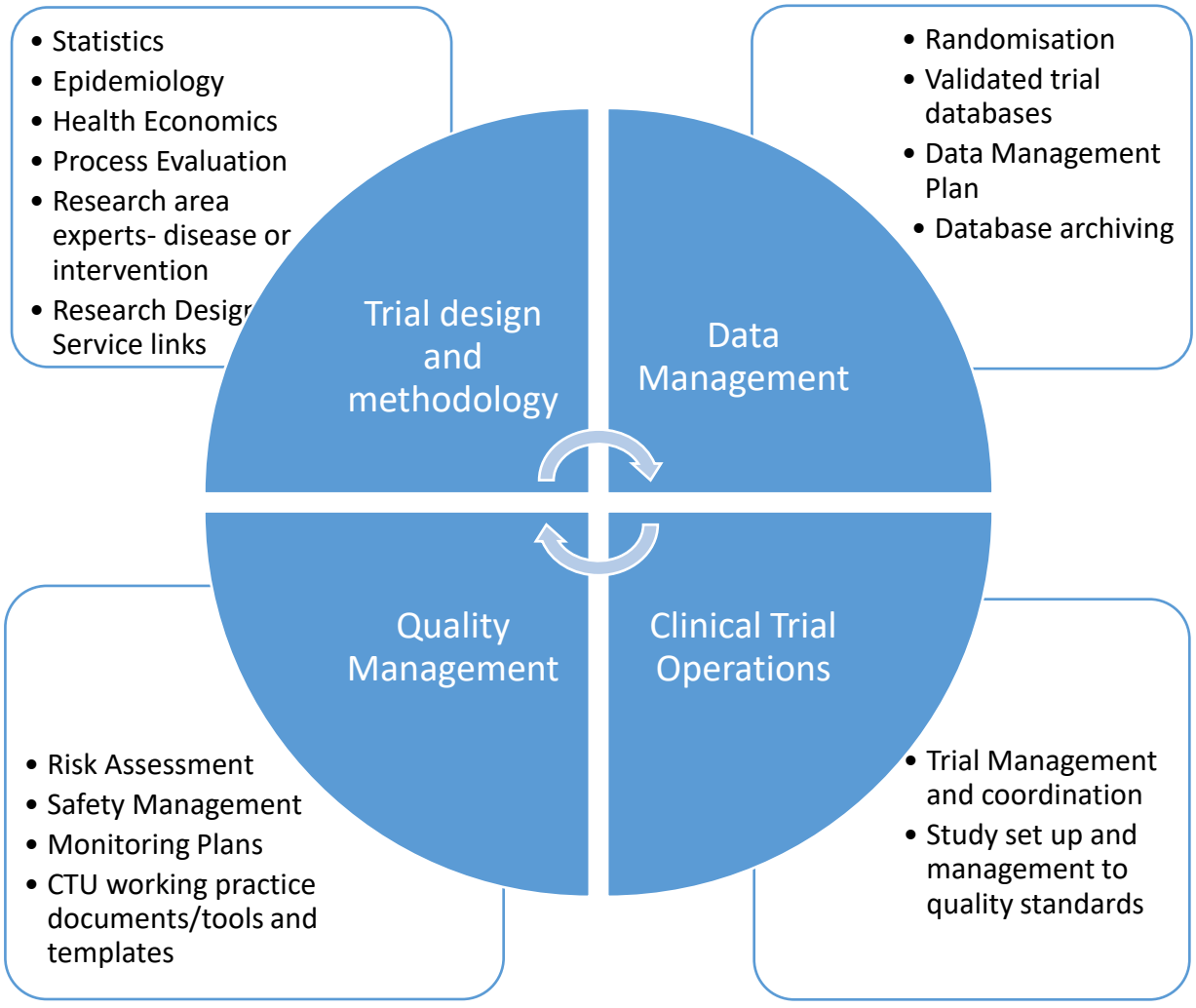
The Norwich CTU works with research teams to design, conduct, analyse and report high quality clinical trials and other well designed studies that fit with the research strategies of NRP partners including NNUH and UEA.

We do this by

- Maintaining core competencies in statistics, health economics, data management, randomisation, trial project management and quality systems.
- Developing collaborative partnerships with clinical and academic investigators at all relevant institutions.
- Working collaboratively with the Research Design Service.
- Promoting a trial governance structure that supports a compliant, risk-based, proportionate approach to the application of regulations.

- Provide clinical trials leadership and expertise across the range of activities required to deliver trials from concept to dissemination and implementation of research findings.
- Employing highly experienced staff with diverse research interests and expertise in clinical trial methodology to enhance the effectiveness of the research pathway.
- NCTU staff and collaborators supporting adoption of its policies and procedures.

**Norwich CTU: Registered CTU Overview**




## 3. WHO WE ARE AND HOW WE WORK

The Norwich CTU is led by Professor Ann Marie Swart (Director), Professor Lee Shepstone and Professor Garry Barton (Associate Directors).

Professor Lee Shepstone leads the statistics group, supported by Dr Allan Clark and Sue Stirling.

Martin Pond is the Head of Data Management and leads the Data Management team comprising of programmers and data assistants.

Dr Erika Sims is the Senior Clinical Trial Operations Manager and leads the Clinical Trial Operations Group.

Debbie Graver is the Project Manager for Trial Development.

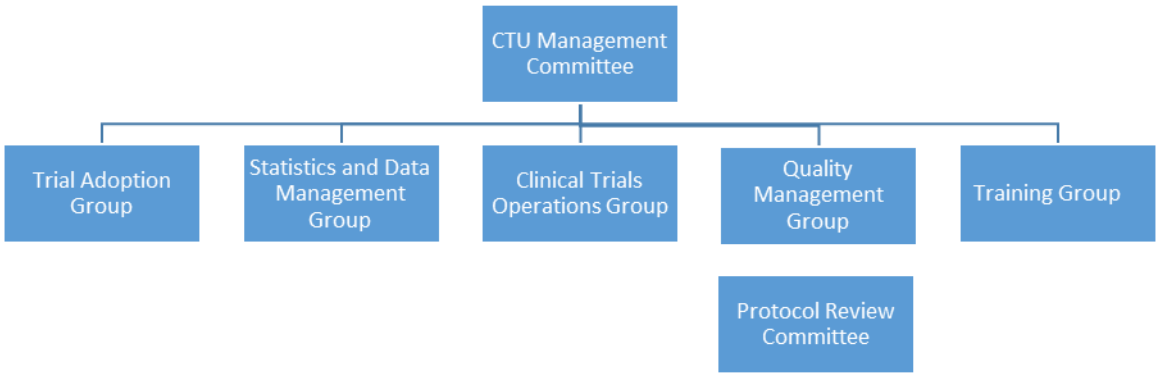
Professor Garry Barton and Dr David Turner are the NCTU Health Economics leads. Professor Barton is also Deputy Director of the East of England Research Design Service (RDS). Together with Dr Jean Craig (Research Advisor RDS), they provide an important link between the NCTU and the RDS.

Dr Jamie Murdoch is the NCTU Process Evaluation lead, he is also a Research Advisor for the RDS, providing another important link between the NCTU and RDS.

Professor Marcus Flather and Professor Kristy Sanderson provide clinical input to the NCTU and represents schools within the Faculty of Medicine and Health Sciences.

The NCTU receives executive support from the Head of the Norwich Medical School, Executive Dean Faculty of Medicine and Health Sciences and the NNUH Medical Director.

The NCTU ensures integrated working in trial design and methodology, information systems and data management, clinical trial operations and quality through linked committees and functional groups.




- The **NCTU Management Committee** supports the NCTU Director, oversees the integrated functioning of the NCTU and the conduct and delivery of NCTU trials. Members include senior staff from scientific, clinical trial operations, data management, statistics, health economics and epidemiology staff with methodological and trial operations experience. The **NCTU Management Committee** is responsible to:
    - The CTU Executive Committee
    - the **UEA/NNUH Research Governance Committee for** research governance

- The **Statistics and Data Management Group** includes all statisticians who work on NCTU trials and those responsible for database design, development, programming and maintenance. This group ensures that NCTU specific procedures and working practices are implemented and kept up to date for the specialist functions below

    - Sample size calculation and documentation
    - Randomisation - selecting methods and testing implementation
    - Statistical aspects of trial monitoring and conduct
    - Analysis and reporting
    - Database Programming
    - Meta Data Construction
    - Data imports from laboratory and routinely collected data
    - Dataset production for analysis
    - Database Reporting

- The **Clinical Trial Operations Group** includes the Senior Clinical Trial Operations Manager, Trial and Data management staff from all NCTU supported and adopted trials. This group supports development of staff and systems in the following areas**:**

    - Project Management
    - Quality Management
        - Central Monitoring
        - On Site Monitoring
    - Conduct and Trial Delivery
    - Safety and Pharmacovigilance
    - Trial Documentation
    - Risk Assessment
    - Data Management

- The **Quality Management Group**

    - Provides advice on trial specific issues, potential urgent safety measures and serious breaches of the protocol or regulations prior to escalation to the NCTU Management Committee, UEA/NNUH Joint Research Governance Committee or other relevant Sponsor organisation.
    - Ensures compliance with Clinical Trial Regulations, GCP and Sponsors SOPs and Policies and the CTU Quality Management System.
    - Oversees development of NCTU working practices, WI and TaTs

- The **Protocol Review Committee** reviews all trial protocols produced by the NCTU and maintains the NCTU protocol template

- The **Trial Adoption Group (TAG)** includes senior staff from stats, data management, clinical trial operations, and UEA Research and Innovation Services (RIN); clinicians, statisticians, health economist, operations staff, methodologists and senior programmer. The role of the group is to review new trials seeking adoption (see below) to ensure that NCTU has the expertise and capacity to deliver the proposed trial; that both the trial and collaboration fits with NCTU strategic objectives; that the NCTU is able to take on delegated activities from sponsors under the proposed trial management and governance structure and that the required funds are being requested. This will usually be done prior to, and does not replace UEA internal peer review.

- The **NCTU Training Group** ensures that training is provided to enable NCTU staff to be qualified by experience and training to carry out their role in the Unit and to maintain comprehensive, auditable training records. All staff have standard GCP training as well as customised specific training for their NCTU and specialist roles e.g. statistics, clinical trial operations, pharmacovigilance, data management.

- **Health Economics:** A Health Economics component in clinical trials is increasingly demanded by funding bodies who want to know if the intervention under evaluation constitutes value for money. The NCTU maintains a close working relationship with academic health economists at UEA, with a senior health economics lead on the NCTU management Committee.

- **Process Evaluation:** Process evaluation is an important approach used to understand how complex health interventions are perceived, understood and delivered within the context of randomised controlled trials. The approach may utilise both quantitative and qualitative methods, has the potential to provide important explanations for observed effects between different study arms, and for specifying the circumstances under which interventions may succeed or fail beyond trial findings.

The **NCTU Executive Committee** includes staff of the University of East Anglia (UEA), Norfolk and Norwich University Hospital (NNUH), Norwich Research Park (NRP) and the NCTU Director. The NCTU Executive Committee is responsible for guiding the research and business strategy of NCTU, including high level interactions with organisations that typically sponsor NCTU trials (UEA and NNUH) and others stakeholders, and advising on the long term scientific strategy of the NCTU.
The roles and responsibilities of members of NCTU committees and groups are described in Terms of Reference. These are available on request

## 4. Our Research

We have over 30 trials in our portfolio predominantly funded by NIHR. Our main research areas are in the following themes: cardiovascular, diabetes, dementia, musculo-skeletal, nutrition, psychology, respiratory and stroke. Within these themes we are investigating medical and nutritional interventions, screening, rehabilitation, lifestyle modifications and health service delivery. We have experience in designing and running a wide variety of trials including trials of complex interventions.

Our focus is on randomised multi-centre controlled trials with external funding from NIHR or major charities.

We are unable to support studies without funding. Funded single centre, and small feasibility trials may be considered for trial adoption by the CTU as long as there is a clear strategy of trial development to deliver a definitive phase III trial. CTU involvement is also possible if local Sponsors including NNUH FT or UEA require it as a condition of sponsorship and CTU costs can be met. We have the capability to help with large observational studies that require primary data collection or extraction of routinely collected data. We particularly add value where data collection systems have to be quality assured to similar standards required of clinical trials.

We can support a limited number of **fellowships** and actively encourage those considering fellowships with a clinical trials component to come and talk to us. We can provide trial support and training opportunities for trainees and exposure to all aspects/stages of our trials.

## 5. Working with us

There are many advantages to working with a **UKCRC** registered Clinical Trials Unit (CTU) and in some cases, involvement in a trial is a requirement for funding or sponsorship.

Trials with a Clinical Trials Unit involvement are more likely to deliver on time/budget and be published in high impact journals. This may be because

- Funders are more likely to support applications where CTU involvement has been agreed.
- Trial activities such as staff recruitment, training and mentoring, applying for sponsorship, developing and maintaining the risk assessment documents, etc. (Section 8 gives a detailed list) can be delegated to experienced CTU staff who work collaboratively with the CI, as part of the trial team.
- The CI can concentrate their time and expertise on the clinical details of the trial protocol and on providing overall leadership and engagement with sites and peers throughout the course of the trial, including providing clinical support and advice on patient management and an overview of safety across sites.

## 6. Seeking Norwich CTU Collaboration

We welcome requests for collaboration, particularly from local investigators. Please contact us for any new trials you are planning, **at least 3 months** before the application deadline by completing the **Collaboration Request Proforma** that can be accessed from the Norwich CTU website.

Most CTUs use a very similar form. It aims to collect information that will allow us to make an initial assessment of whether or not we can support your trial and provide the services that you require. The East of England Research Design Service (RDS) (http://www.rds-eoe.nihr.ac.uk/) with whom we have

close links, provides support to investigators who are developing funding applications, and are well placed to advise on the information needed for the collaboration request proforma.

A brief description of the headings that we use and the reasons that we ask these questions is given in Appendix 1.

Email the completed form to NorwichCTU@uea.ac.uk.

A member of the will contact you to discuss your proposal and the next steps that you will need to take. This might be to refer you to a local RDS advisor if you are not already working with them, or to have an initial meeting with NCTU staff so that preliminary discussions on feasibility can take place. We will aim to give an early decision if we are not the right Clinical Trials Unit for you or your trial.

## 7. DATA PROTECTION

During the conduct of clinical trials, Norwich Clinical Trials Unit (NCTU) may collect, store and process personal data, either directly or indirectly (for example, from pre-existing datasets or other systems).

Domestic and European law requires that NCTU has a lawful basis for the collection and processing of personal data. This lawful basis will vary depending on the nature of the underlying study. In many cases, the lawful basis might be that the study is a task in the public interest. Alternatively, where explicit consent is given for data to be captured, stored or processed, consent may be the lawful basis.

UEA is a Data Controller for NCTU. This means that we determine why and how personal data will be collected and used, typically jointly with other agencies (for example, study sponsors or chief investigators).

UEA may also be a Data Processor for NCTU. This means that we are responsible for processing personal data on behalf of a controller.

One of the responsibilities as a data controller is to be transparent in our processing of personal data and to tell the subject about the different ways in which we collect and use personal data. NCTU will process personal data in accordance with the General Data Protection Regulation (GDPR) and the Data Protection Act. In addition to these legal requirements, NCTU adheres to ethical and good clinical practice in respect of how personal information is collected, stored and processed.

In addition, study-specific documentation will explicitly address the collection and use of participants' personal data. Similarly, contracts will explicitly address the issue with third-party and partner organisations.

Our handling of personal data is regulated by the Information Commissioner's Office (ICO). NCTU is registered with the ICO as part of the University of East Anglia (UEA). UEA's registration number is Z8964916. See UEA's ICO register entry. See UEA's Data Protection Officer.

NCTU also has Level 2 compliance with NHS Digital's Information Governance (IG) Toolkit. See NCTU's IG Toolkit entry.

## 8. Trial Adoption Process

We have a process of Trial Adoption and review all new trial applications to external funders for trials that we are asked to support.

The aim of the review and adoption process is to ensure that the NCTU has the expertise and capacity to deliver the trial; that the trial and proposed collaboration fits with NCTU strategic objectives; that the NCTU will be able to take on delegated responsibilities from sponsors under the proposed trial management and governance structure and that the required funds are being requested. This will usually be done prior to, and does not replace UEA internal peer review.

At a typical Trial Adoption Group meeting, you will be asked to give a 10 minute summary of the clinical research question and the proposed intervention, your thoughts on the trial design (including primary and secondary outcome measures), potential number of sites and sample size. If the trial is at an early stage of development, your thoughts on what resources will be needed to run the trial will be helpful, but formal costing is not needed as we will apply a risk based costing to the trial if it is adopted. Following your presentation, Trial Adoption Group members will run through any outstanding considerations with you, before a decision is reached on whether the NCTU can, in principle support the trial and can allocate core NCTU resources to support further development of your application.

This support includes assignment of a NCTU lead, a senior member of the NCTU who will work closely with you to develop the application and access NCTU resource to develop

- a high level risk assessment and project plan in order to develop risk based trial costings
- sponsorship arrangements
- any other input from NCTU staff to help complete the grant application

There may be several iterations of the trial adoption process during the development of a trial. This will depend on the complexity of the trial and any changes to the design, organisation or funding requested or awarded, and the outcome of funders' peer review.

## 9. Working with the Norwich CTU - post successful funding

Working with a registered Clinical Trials Unit has many advantages for Sponsors and Chief Investigators. Trial activities can be delegated to an experienced, established group of staff, who work collaboratively with the Chief Investigator and Principal Investigators as part of a multi-disciplinary team. Clinicians are then free to concentrate their activities on where they add the most value, for example the clinical details of the trial protocol and CRFs, answering clinical questions from sites on patient eligibility and management within the trial. CIs can therefore more effectively lead the trial to successful completion.

These are some of the ways that the NCTU can help:

a. Recruit specialist data management and operations staff to support your trial as detailed in the grant application; provide training and mentoring for these staff for their trial work and

cover staff absences (sickness, maternity leave and annual leave) by cross-cover arrangements.

b. Apply for sponsorship on your behalf potential sponsors and/or formally agree delegated activities with sponsors.

c. Ensure that the study is registered on the NIHR Portfolio of Studies(if eligible) and any other databases as appropriate

d. With Chief and/or Principal Investigators and other trial team members (e.g. stats, health economics, process evaluation), write a trial protocol, Participant Information Sheet (PIS) and Informed Consent (ICF) form that is compliant with the regulations, NCTU policies, NNUH/UEA Joint Research Office SOPs and NNUH/UEA policies and submit this to the NCTU Protocol Review Committee.

e. Write the Risk Assessment and maintain this document through the lifecycle of the trial.

f. Write a Quality Management and Monitoring Plan to mitigate identified risks using QA and QC procedures.

g. Write a trial project plan.

h. Document safety management processes in a NCTU Safety Checklist and write a Safety Management Plan which includes setting up and managing a system for recording and reporting any safety events.

i. Construct and maintain a Trial Master File (TMF).

j. Write the Case Report Forms (CRFs), with your input.

k. QA all final documents (protocol, CRFs, PIS, ICF) then submit an IRAS (Integrated Research Application System) application for Ethics, Clinical Trial Authorisations (for CTIMPS) and HRA Approval.

l. Write a Data Management Plan to describe how data will be stored and accessed, then program and fully test the database.

m. Write any trial specific documentation (e.g. Working Practice Documents).

n. Support drug and device sourcing for the trial including tendering if necessary, and work with suppliers and site pharmacy to manage trial materials.

o. Engage and organise meetings for trial specific governance committees using the NCTU Terms of Reference template including:
   - Trial Management Group
   - Trial Steering Committee
   - Independent Data Monitoring Committee

p. Support Patient and Public Involvement in trial design and conduct, providing training and support for PPI reps on trial governance and oversight committees.

q. Provide information packs to sites to enable them to confirm capacity and capability
r. Develop training materials and train site(s) on trial protocol, conduct, data capture and GCP.
s. Ensure that sites receive documentation to allow them to assess capacity and capability to conduct the study after HRA approval and Initiate the trial at sites once approvals are received.
t. Write the TMG, TSC, DMC reports
u. Complete any update reports for the funding body and REC
v. Coordinate monitoring and auditing activities with reports and corrective action plans as agreed, reporting these back to Trial Management Groups and Sponsors.
w. Help to manage patient recruitment, applying remedial actions as necessary.
x. Manage trial close out.
y. Analyse and report the trial and work on the resulting publications.
z. Manage the archiving of trial materials.

**Appendix 1**

**Guidance for completing the NCTU Collaboration Request Proforma**

Please provide as much information as you can, even if your project is not completely developed.

The critical things that we need to know to assess your project are:

- What do you want to do?
- Why?
- How do you think that the trial can be delivered?
- What collaboration you need from NCTU?
- What are the planned timelines (submission, full application, first patient in/last patient out)

**Description of clinical problem and importance** The Trial Adoption Group is a mixed group of specialists, similar to those who will be sitting on funding panels who will require a strong case for the importance of the clinical problem. You therefore need to explain the nature of the problem to non-experts in your clinical field.

**How does this fit with NHS, UEA, NNUH, NRP priorities** Funders will be looking for justification of fit with NHS priorities. We would like to see if you have thought about how the trial fits with NNUH, UEA or NRP priorities. We may be able to support smaller projects that will attract less funding if we can show that they are important strategically for UEA or the NNUH, or alternatively if this is a major project of strategic importance we may be able to re-allocate staff working on less important projects to meet an important deadline.

**Level of patient and public involvement** Have you already started engaging with patient groups? We may be able to suggest ways of doing this.

**Literature review (and clinical trials.gov)** Have you done a literature review and checked on clinical trials.gov that no one has already answered/is trying to answer the same research question? If they are, that may still be fine but we need to be aware of this and be able to explain any planned duplication to trial funders.

**Can you outline PICOS for us?**

- *Patient group* - a description of the patient group you are hoping to recruit (gender, age range, type and severity of clinical problem)
- *Intervention* - what is the new treatment that you want to test? Have you considered the 'Better reporting of interventions: template for intervention description and replication (**TIDieR**) checklist and guide' (BMJ 2014; 348 doi: http://dx.doi.org/10.1136/bmj.g1687 (Published 07 March 2014)
- *Control* - what will patients randomised to the control arm receive? This would normally be 'standard care' for the condition under investigation.

- *Outcome measures* - what are you trying to influence with your new treatment? Have you considered the COMET (Core Outcome Measures in Effectiveness Trials) initiative (http://www.comet-initiative.org/)? These data sets represent the minimum that should be measured and reported in all clinical trials of a specific condition, and are also suitable for use in clinical audit or research other than randomised trials.
- *Study design* - this should usually be an RCT but we don't expect to see any more detail here. If there is any reason why it can't be an RCT (impossible to randomise in this condition, very small numbers) let us know here.

**Sample size:** If you have not done this, it is not a problem. We can do initial sample size calculations after we have had preliminary discussions with you.

**Number of sites envisaged** - **UK and international:** This is so we know the planned scope of the trial and whether you have started discussions with colleagues in other sites.

**Engagement with sites, research groups, national speciality groups** -It is helpful to know the provenance of the research question. If it has emerged as a priority from a number of sites, research groups or national specialty groups then it is an indication to us that it has a higher probability of being funded. Trials that are supported by national groups for example NCRI Clinical Studies Groups (http://csg.ncri.org.uk) in particular will be prioritised.

**Trials experience:** What is your trials experience? Have you already led trials as a CI, participated in multi-centre academic or commercial studies as a PI? Is this your first trial? We need to know this to know what level of support you are likely to require.

**Translational research planned:** Are you planning complex specimen collection and storage e.g. biomarkers alongside clinical markers?

**Marketing status of intervention:** If this is a drug trial, is the drug already licensed for this indication? If not, is it licensed for another indication in the UK, or in Europe. If you don't know that is fine, we can help you find out, but we will need to know this early to work out the regulatory aspects of the trial.

**What you think that you need from us:** We have listed many of the activities that we contribute to, from the check list pick all that you think you require. We can advise on resourcing models that enable us to provide the level of input expected by funders from a registered CTU and aim to refine resourcing as the trial application develops.