Guidance for Chief Investigators of Clinical Trials Conducted by ECTU

This document is intended to provide information for Chief Investigators seeking to collaborate with ECTU to conduct a clinical trial. This document outlines the expertise that ECTU can offer you and how to seek support.

It is never too early to contact us to discuss your proposal!

Getting in touch with ECTU

Telephone: 0131 651 9901

Email: ECTU-new.proposals@ed.ac.uk

Web: www.ed.ac.uk/usher/edinburgh-clinical-trials

Project Support Request Form: www.ed.ac.uk/usher/edinburgh-clinical-trials/supporting-trials

Twitter: @edinUniECTU

Address: Usher Institute, University of Edinburgh, Edinburgh BioQuarter – gate3, 5-7 Little France Road, Edinburgh, EH16 4UX

We welcome expressions of interest to develop new collaborations. To apply for ECTU support, please submit an 'ECTU Outline Proposal Form' at the earliest opportunity.

By completing the 'ECTU Outline Proposal Form', you confirm that you have read and understood this document.

Contents

Abbreviations

ACCORD	Academic and Clinical Central Office for Research and Development
ASTOX	Annual Statement of Expenditure (NIHR)
CRF	Case Report Form
CI	Chief Investigator
CMVM	College of Medicine and Veterinary Medicine
CTU	Clinical Trials Unit
DMC	Data Monitoring Committee
DM&P	Data Management and Programming Team (ECTU)
ECRF	Edinburgh Clinical Research Facility
ECTU	Edinburgh Clinical Trials Unit
EI	Edinburgh Innovations
ERO	Edinburgh Research Office
FPFV	First patient first visit
FTE	Full time equivalent
GCP	Good Clinical Practice
HE	Health Economics
HTAF	Healthcare Technology Accelerator Facility
HR	Human Resources
ITS	Intent to Submit (ERO)
MHRA	Medicines and Healthcare products Regulatory Agency
NHS	National Health Service
PCPIE	Patient, Carer and Public Involvement and Engagement
RA	Risk Assessment (ACCORD)
RDT	Research Development Team (ECTU)
RDTP	Research Development and Trial Planning Team (ECTU)
REC	Research Ethics Committee (NHS)
RFS	Research Funding Specialist (ERO)
R&D	Research and Development (NHS)
SATO	Sponsor Authorisation To Open (ACCORD)
SIV	Site Initiation Visit
SoECAT	Schedule of Events Cost Attribution Template
SOP	Standard Operating Procedure
SWAT	Study within a trial
TM	Trial Management
TMG	Trial Management Group
TMF	Trial Master File
TSC	Trial Steering Committee
UKCRC	UK Clinical Research Collaboration
UoE	University of Edinburgh
QA	Quality Assurance
QC	Quality Check

Introduction

The Edinburgh Clinical Trials Unit (ECTU) is committed to supporting the robust design and delivery of randomised clinical trials that have the potential to improve the health of the population, in line with The University of Edinburgh's Strategy 2030, Clinical Trials Strategy, and Behaviours Charter. ECTU follows the ECTU Portfolio Prioritisation Strategy for adoption of projects into its portfolio, and the ***develop, design and deliver*** approach of the clinical trial strategy.

ECTU works with colleagues to develop methodologically excellent randomised clinical trials and deliver them from initial concept to completion, either providing 'full collaboration' from all teams (trial management, data management and programming, methodology and statistics, and health economics) or support from selected teams within ECTU (i.e., 'partial collaboration', e.g., methodology and statistics plus data management and programming only).

About ECTU and its registration

ECTU holds UK Clinical Research Collaboration (UKCRC) clinical trials unit (CTU) registration for the University of Edinburgh, which is renewed bi-annually (subject to satisfactory review). To maintain UKCRC registration, ECTU must be able to continuously demonstrate compliance with UKCRC competency criteria as outlined below:

- A **track record and experience** of coordinating multi-centre randomised controlled trials (phase II-IV) or other well-designed clinical trials
- Presence of **a core team of expert staff** to develop clinical trials
- Presence of **robust quality assurance systems and processes to meet appropriate regulations and legislation** (e.g., the principles of Good Clinical Practice [GCP], the NHS Research Governance Framework, the Data Protection Act 2018, and any other legislation relating to Clinical Trials)
- Evidence of longer-term viability of **capacity for trials coordination and the development/ maintenance of a trials portfolio**, including core funding or evidence of a rolling programme of grants, with evidence of commitment from the host institution

Which clinical trials does ECTU adopt?

- Projects that meet the ECTU Portfolio Prioritisation Strategy (summary in Table 1 overleaf) can be adopted into the ECTU portfolio. The Portfolio Management Meeting is held weekly and attended by the ECTU Operations Team and Clinical Director who will assess if a proposal can be accommodated, (e.g., can comply with all ECTU SOPs unless alternatives are available and are acceptable to ECTU QA). Further details are in the Grant Application process section below.

Note that adopted clinical trials will be listed against our registration number and included within our annual UKCRC report and may be subject to additional inspection / review.

Table 1: ECTU Portfolio Prioritisation for adopting new studies

Priority	Criteria*
1	Full collaboration randomised controlled trial led by an Edinburgh CI
2	Full collaboration non-randomised clinical trial led by an Edinburgh CI
3	Partial collaboration randomised controlled trial led by an Edinburgh CI
4	Partial collaboration non-randomised clinical trial led by an Edinburgh CI
5	Randomised controlled trial led by an External CI (not UoE or NHS Lothian)
6	Observational or methodological research led by an Edinburgh CI
7	Other study types/requests led by an Edinburgh CI (considered on a case-by-case basis)
8	Other study types/requests led by an External CI (considered on a case-by-case basis)

* Studies that are funded by eligible funders according to NHS Research Scotland will be considered as priority

What can ECTU provide?

Firstly, we will work together and in collaboration with you. This means being responsive to communication and respectful of your expertise, as well as complying with University HR policies (in particular the University's Dignity and Respect Policy and Behaviours Charter).

ECTU also provides a comprehensive structure reflecting the knowledge and expertise to design, develop and deliver clinical trials. The key teams are:

- Research Development to support grant applications
- Project Planning to support trial planning activities ahead of the grant start date for funded studies
- Methodology and Statistics
- Trial Management
- Data Management and Programming
- Health Economics
- Research management and business planning of awarded trials
- Quality Assurance
- Clinical Advisory Group, including coaching for new Chief Investigators (CIs)

Examples of the support provided by each of these groups along with an organisational chart are provided in this document.

What ECTU can and cannot do

✓ We can support full or partial collaboration projects where ACCORD or the University of Edinburgh act as the Study Sponsor.

✓ We can provide statistics/methodological, data management/programming and health economics support for projects where other institutions and/or organisations act as the Study Sponsor. In order to do so, they will need to provide a full suite of SOPs and required documents.

X We cannot provide trial management support for projects where other institutions and/or organisations act as the Study Sponsor.

X We do not support monitoring or pharmacovigilance activities.

X We cannot take responsibility for completing the SoECAT form, but we do expect to review this with you before submission.

X We cannot provide you with access to the trial email account or TMF as these host regulatory and controlled documents, etc.

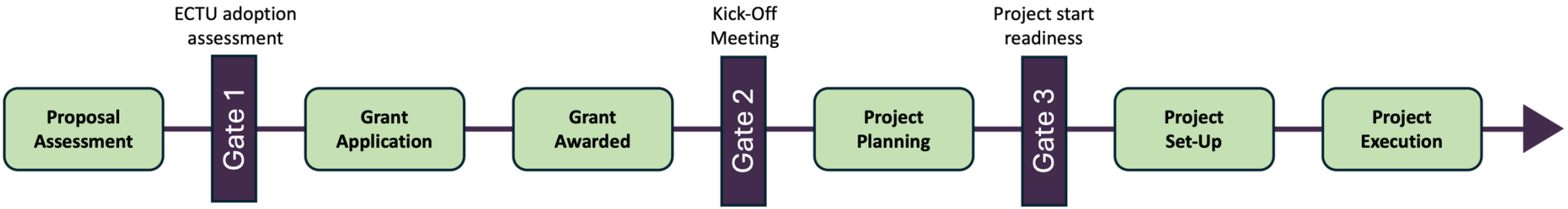
Who ECTU collaborates with

We have built close working relationships with many collaborators across Edinburgh and the Lothians, as well as the organisations listed below, and ECTU can act as the link between multiple partners. There are, of course, other infrastructure resources to support your study within the University of Edinburgh and NHS Lothian. ACCORD (Academic and Clinical Central Office for Research and Development) may act as Sponsor and provide pharmacovigilance and monitoring for clinical trials.

- Patient, Carer and Public Involvement and Engagement (PCPIE) – delivered via https://www.ed.ac.uk/clinical-research-facility/patient-and-public-involvement
- Funding agencies (government, charity, etc), including experience of sitting on multiple funding committees
- Specialist drug suppliers
- Colleagues across the University, including Funding, Contracts, Legal, and Edinburgh Innovations
- NHS Lothian – support NHS costing requests for applications, local approvals and data sharing framework
- Edinburgh Imaging – research imaging and image management
- Edinburgh Clinical Research Facility – on site clinical management of patient/volunteers, as well as core laboratories, and phase 1 clinical trial facilities
- Investigational Supplies Group and the Healthcare Technology Accelerator Facility (HTAF) - drug packaging, labelling and shipment
- Edinburgh Research Office (ERO) – pre-award costings and approvals, post-award financial management (e.g., invoicing, ASTOX reporting)
- R&D offices across the UK
- MHRA, Health Research Authority and associated regulatory bodies

The use of Stage Gate Methodology

ECTU uses a Stage Gate Methodology approach for successful clinical trial execution. The graphic below illustrates the position of the stage gates which represent a review of risks and study progress to ensure the clinical trial can successfully transition to the next stage.



What to expect at each stage of a clinical trial

	Grant Application	Project Planning	Project Set-Up	Project Execution	Project Execution
	Grant Application	**Project Planning (before start of grant)**	**Project Set-Up (after start of grant)**	**Recruitment & Data Collection**	**Close-Out & Reporting**
Chief Investigator	• Research question • Stakeholder engagement • PCPIE • Proposal development • Resource assessment • Funding application	• Protocol drafting • Document set drafting • Identification of required contracts & supply agreements • Scoping of data management & programming requirements • Identification of oversight committee members	• Protocol completion • Documents (CRFs) • Contracts & approvals • Stakeholder engagement • Oversight (TSC, DMC) • Attendance at frequent Trial management group (TMG) meetings • PCPIE • Table of Responsibilities • Regulatory approvals • Delivery of SIV training	• Support to sites • Protocol and document amendments • Leadership for TMG, TSC, DMC meetings	• Review and interpretation of analyses • Reporting • Dissemination • Adhere to ECTU publication policy

	Grant Application	Project Planning	Project Set-Up	Project Execution	Project Execution
	Grant Application	**Project Planning (before start of grant)**	**Project Set-Up (after start of grant)**	**Recruitment & Data Collection**	**Close-Out & Reporting**
Research Development & Trial Planning	• Coordination of proposal development • Project Gantt chart • Editorial support • Justification of resources • ECTU resource assessment • Letter of Support	• Support drafting protocol & key documents for Sponsor Risk Assessment • Support identification of required approvals, contracts and supply agreements • Scope data management and programming requirements • Support identification and mitigation of risks for project delivery • Liaise with internal and external stakeholders to prepare study for scheduled start • Prepare hand-over to ECTU project execution teams	• Support handover to project execution teams	• Finance support for substantive project changes (requesting reconciliations, coordinating extension costings)	
Methodology & Statistics	• Robust methodology • Sample size • Proposal development • Resource assessment • Funding application	• Protocol drafting • Identification of oversight committee members	• Protocol completion • Documents (CRFs) • Advice on randomisation system • Draft TSC/DMC report • Table of Responsibilities	• Statistics master file • Statistical analysis plan • DMC report • Protocol amendments • Advice to TSC and TMG	• Analyses • Reporting • Dissemination • Data sharing
Health Economics	• Robust methodology • Proposal development • Resource assessment • Funding application	• Protocol drafting	• Protocol completion • Documents (CRFs) • Table of Responsibilities	• Health economic analysis plan • Health economic modelling/ design/ parameter resourcing	• Analyses • Reporting • Dissemination

	Grant Application	Project Planning	Project Set-Up	Project Execution	Project Execution
	Grant Application	**Project Planning (before start of grant)**	**Project Set-Up (after start of grant)**	**Recruitment & Data Collection**	**Close-Out & Reporting**
Trial Management	• Proposal development • Resource assessment		• Finalise protocol and documents • Sponsor Risk Assessment • Regulatory approvals • Table of Responsibilities • Support CRF development • Vendor assessments/audits • Caldicott/IT security appls • R&D submissions/approvals • Site feasibility Qs • Organisation and conduct of SIVs	• Maintain TMF • Support to sites • Progress reporting • Protocol and document amendments • Finances • TMG, TSC, DMC mtgs	• Supporting Analyses • Reporting • Dissemination • Archiving of TMF
Data Management & Programming	• Proposal development • Resource assessment		• Support CRF development • Table of Responsibilities • Build study database • Build randomisation system • Data Management Plan	• Reports • QC checking & audit • Protocol amendments • Implementation of data management plan	• Database lock • Archiving of electronic data • Data sharing
Quality Assurance	• Gap analysis	• Gap analysis	• Identify relevant SOPs • Table of Responsibilities	• Monitor SOP compliance • Support audit / inspections as required	• Monitor SOP compliance • Support audit / inspections as required

Grant application process

The grant development journey begins months, sometimes years, before a grant application is submitted. CIs generally begin to develop their idea for a clinical trial in collaboration with their clinical and research colleagues, and they may engage at an early stage with a triallist/methodologist to begin developing the trial methods. ECTU has expert triallists/methodologist who are happy to have informal chats with you about your trial and provide advice on trial methodology at the earliest stages of development.

When your idea for the trial is sufficiently developed that you are thinking of writing a grant, please get in touch with ECTU formally, by completing the 'ECTU Outline Proposal Form' found on the ECTU website. It is okay if the form is not fully completed before you submit it to us. One of the main purposes of this form is so that ECTU has early awareness of your planned grant application.

For colleagues based in CMVM, ERO's 'Intent to Submit' (ITS) form should also be completed. For clinical trials, the ITS form must be submitted at least 8 weeks before the grant submission deadline (correct as of Oct 2024). For colleagues in other colleges, please familiarise yourself with your College/School grant submission processes.

After the 'ECTU Outline Proposal Form' is submitted, the Research Development Team (RDT) will send you an email to acknowledge receipt of the form and confirm next steps. Upon receipt of the form, the project support request is added to the weekly Portfolio Management meeting agenda (held on Tuesdays). ECTU endeavours to discuss new project requests at the next Portfolio Management meeting, but occasionally there may be a delay due to other urgent projects requiring discussion. There may be instances when ECTU needs more information before assessing your request. In these instances, the RDT will email you to ask for further information or clarification, or ask to meet with you to discuss your project more fully.

Once the Operations team and Clinical Director have received sufficient information on the proposed project, then they will proceed with an assessment of the request, including a ranking using the Portfolio Prioritisation Strategy and an assessment of ECTU capacity to provide support. The outcome of this meeting (adopt, decline or recommend to defer submission) will be communicated to you by the RDT team within one week of the meeting date.

If ECTU is unable to adopt your project, then we will let you know why in the email response. In cases when ECTU cannot provide support, ERO will be able to help you with finding an alternate CTU, if this is needed. If you would like to challenge ECTU's decision to not provide support, then the RDT will escalate your concerns to our Chief Operating Officer for further review and discussion.

When ECTU formally adopts your project into the portfolio, the RDT will set up a TEAMS channel for your project, and work with your Research Funding Specialist (RFS) based in ERO to arrange recurring meetings with you and relevant colleagues to help develop the grant application. The assigned RFS will lead on coordinating your grant application, including developing the budget (your costs, ECTU costs, partner costs, NHS costs from SoECAT, etc). ECTU will support you with developing the trial methodology, and can help write the justification of resources, develop a project Gantt chart, and provide editorial support for your proposal. Once the draft proposal is at an advanced stage, we will undertake a costing review and provide the ECTU costs to you and the RFS. The ECTU costing review can take 1-2 weeks, and it's a good idea to factor in another week to review the collated budget and

make any required adjustments, so it is important to allow enough time for these activities when planning your submission timeline. ECTU will also provide you with a Letter of Support, if required by the funder.

CIs working with ECTU for the first time may find a summary of the CTU costing model useful. ECTU uses a team and role-based approach to deliver its large portfolio of clinical trials. The project delivery teams are supported by infrastructure support staff, such as our Chief Operating Officer, administrators and senior managers, to enable them to undertake work on trials. ECTU is largely funded by external research grants, with some support for core posts received from NHS Lothian R&D and the University of Edinburgh. This means that research grants have to cover some infrastructure support costs associated with running the trials unit, as well as cover the staff salaries that are directly contributing to the project. We are cognisant of the budget pressures placed on research grants, and we carefully and continuously re-assess the level of infrastructure support costs we must include in grants to meet our cost-recovery obligations. ECTU staff costs also include the requirements for University of Edinburgh employees, such as consideration of annual leave entitlements, time required to attend university-required training, etc, as well as requirements specific to ECTU staff, for example, additional training and SOP reading to ensure regulatory compliance, and unit-specific meetings.

The way ECTU costs staff salaries may also seem unusual for first time CIs; there are often “many posts with low FTEs”. We’ve found that using a team and role-based approach is the most efficient and cost-effective way of costing and running a clinical trial. Each post within a team undertakes specific, complementary tasks over defined periods in the lifecycle of a study. Using the Trial Management (TM) team as an example, there is often a “core team” comprised of:

- Team Lead (zero costed in grants, provides line management and oversight for ECTU’s whole portfolio of trials)
- Senior Trial Manager (Grade 8, small FTE, provides line management and oversight for the project team)
- Trial Manager (grade 7, substantive FTE)
- Assistant TM (grade 6, substantive FTE, supports project team), and/or
- TM Support Officer (grade 5, substantive FTE, supports project team)

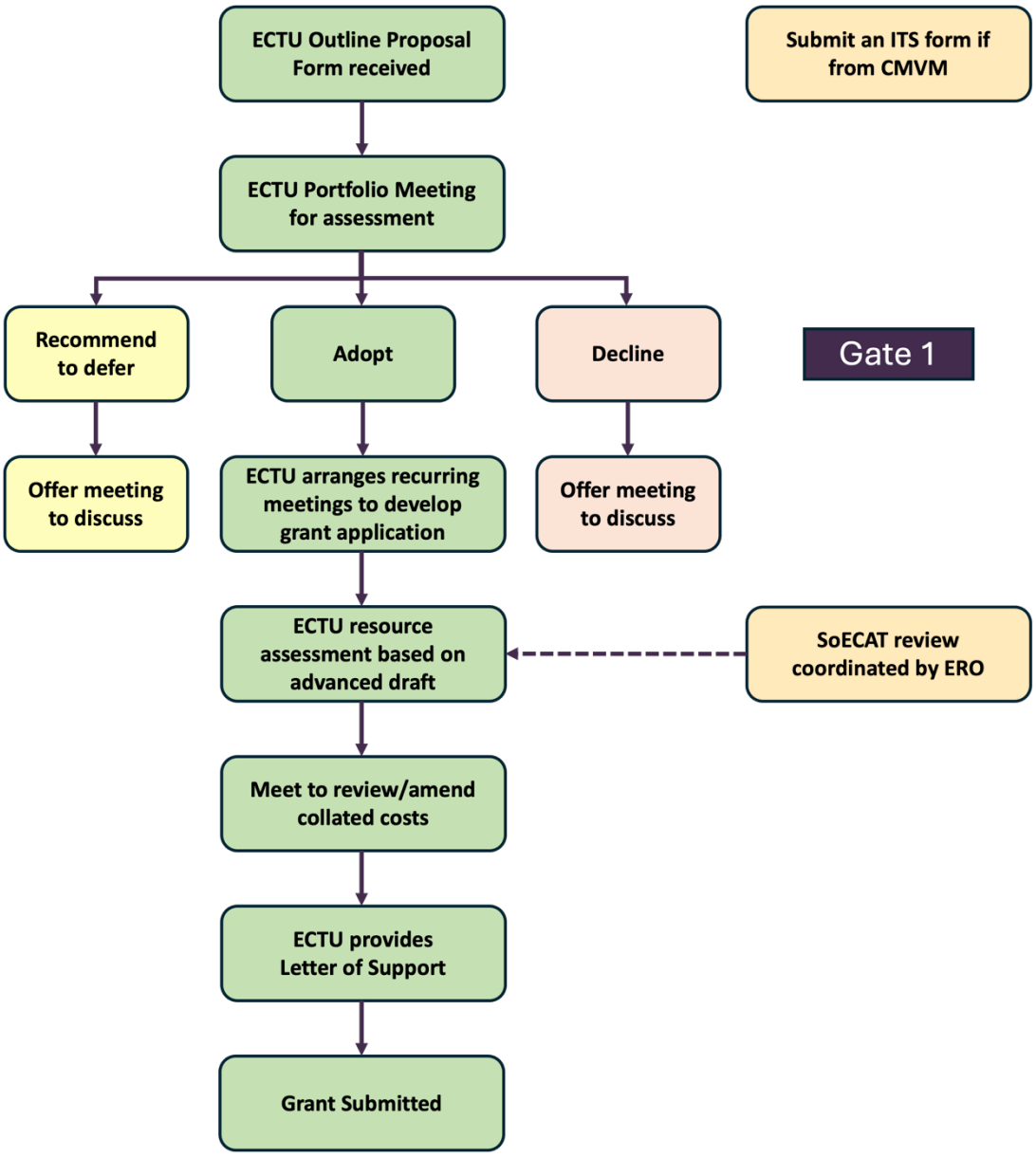
Collectively they are responsible for the day-to-day management of the trial for the full duration. This includes working closely with the CI to obtain all required regulatory approvals, supporting database build & site set up, contractual requirements and meeting the standards/regulatory requirements within sponsor SOPs. Trial set-up, coordination and management of study sites is a substantive component of activity for this team. Additional TM staff may be required for specific activities to provide additional support, for example, for rapid site activation to enable recruitment.

Study Within a Trial (SWAT)

We are keen to embed studies of clinical trial conduct / methodology within our trials. These are best designed and costed as part of the initial grant application, and there are various options for funding them. Possible ideas for such studies are listed at:

http://www.qub.ac.uk/sites/TheNorthernIrelandNetworkforTrialsMethodologyResearch/SWATSWARInformation/Repositories/SWATStore/

ECTU Grant Application Process



Project (trial) planning (awarded projects before start date)

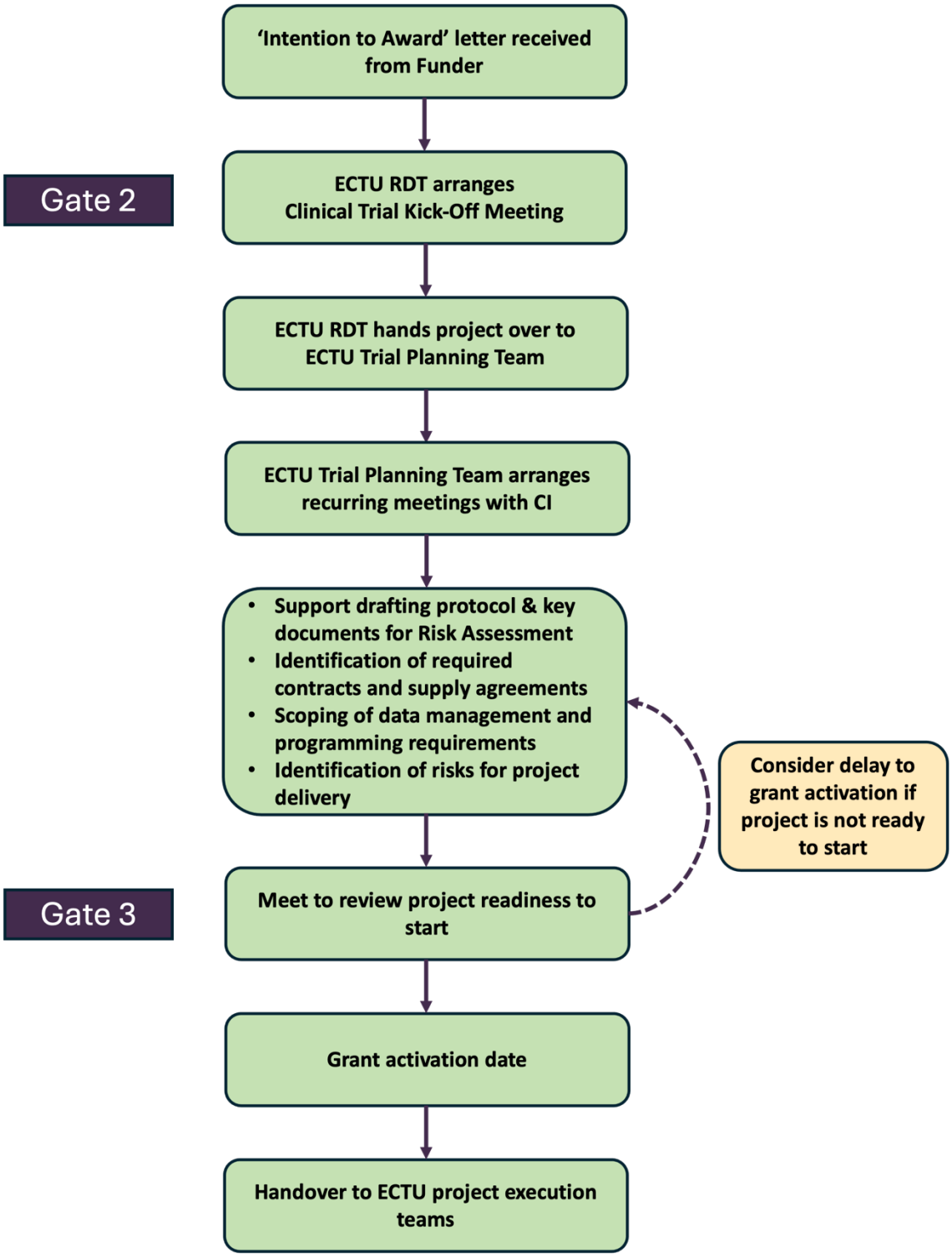
When you are notified by funder of the outcome of your grant application, in addition to notifying your co-applicants, please also let your RFS (ERO) and the RDT (ECTU) know as soon as practicable.

Once ECTU is made aware that the grant application for a clinical trial has been successful (this may not yet be the award letter), we will begin to work towards arranging a Clinical Trial Kick-Off Meeting, attended by the CI and key Edinburgh stakeholders (Sponsor, Contracts, ERO, ECTU, Edinburgh Innovations (EI), Research Nurses, ECRF, etc). In this meeting, each stakeholder discusses the key considerations and priorities from their perspective, and agrees upon a set of action items with timelines for completion. This meeting also serves as the official hand-over within ECTU between the Research Development Team and the Trial Planning Team.

The Trial Planning Team is involved in the period from the Kick-Off meeting to when the study is handed over to the ECTU trial execution teams (usually 4-6 months). The team works with the CI and other stakeholders during this period to prepare the project for successful execution and to identify and mitigate risks. It is essential that the CI engages fully with this process to ensure the best possible study progression. It is unacceptable for a CI to not engage nor maximise the use of this time and still expect the trial to run to timelines. The Trial Planning Team is comprised of two complementary roles:

1. The first role is the Senior Trial Manager Start-Up Specialist, who supports CIs with early trial management set-up activities during the period from notification of the grant award until the grant starts (if Trial Management has been included in the budget). These activities include facilitating the initial development of key study documents (e.g., study protocol, patient facing materials) with the CI, which are required for combined review submission (ethics, MHRA (if required) and R&D), and liaising with Sponsor/Contracts/EI as required, to maximise study activity during this period to help ensure that the study meets start-up timelines. The idea is to commence production of these documents – they **will not** be finalised until the grant starts and the whole trial team is deployed.
2. The second role is the Data Management & Programming Architect (if the DM&P team is included in the budget), which supports Chief Investigators with the data management and programming set-up activities, including ensuring that the processes involving data are well defined, so that when the grant starts, the DM&P team have all the information they require to efficiently develop the eCRF, the database specification and build the study database. Again, the idea here is to begin the process – it will not be finalised until the grant starts and all key staff are employed (in particular, statistics and methodology colleagues will need to carefully input to the process).

ECTU Trial Planning Process

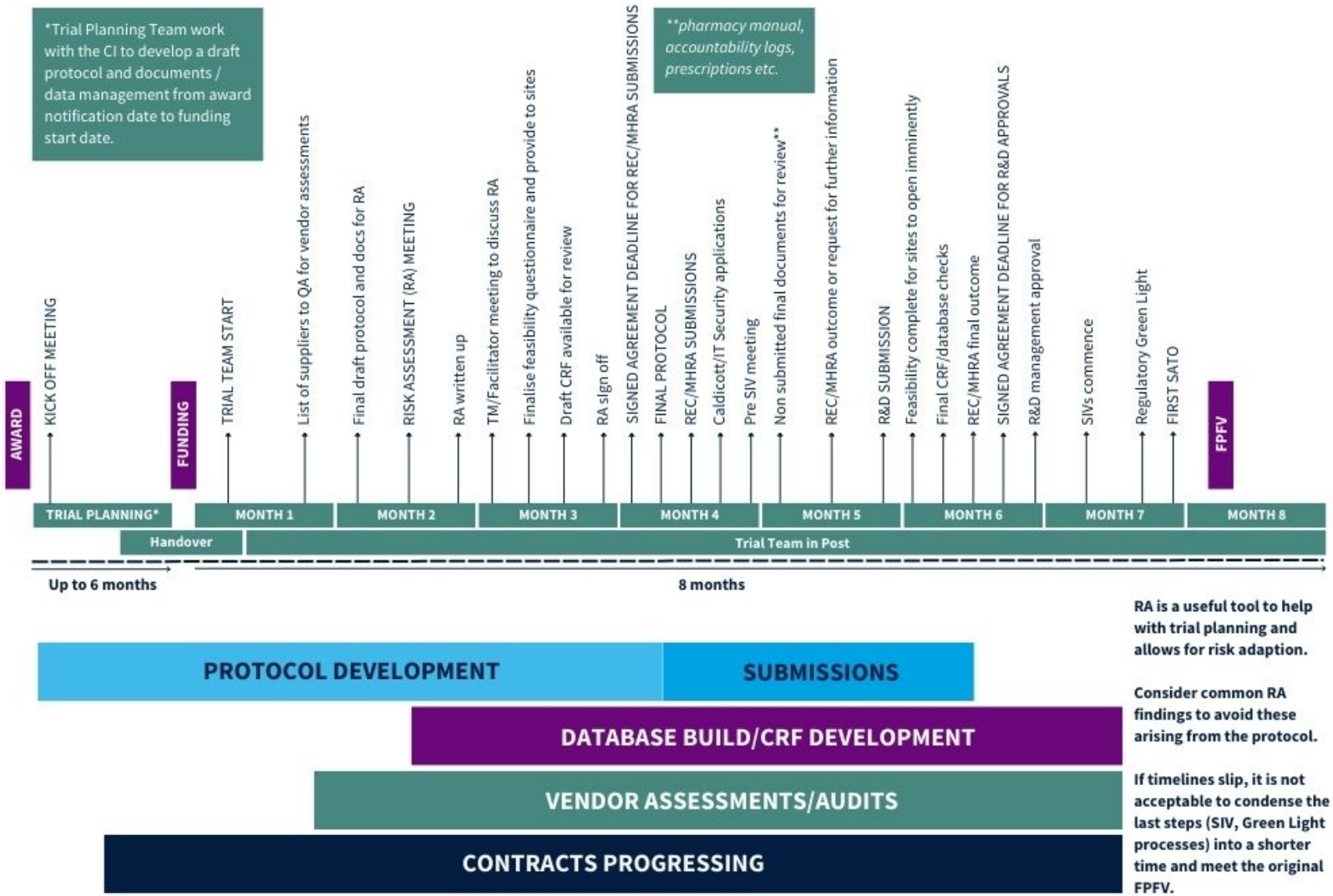


Project set-up (after grant activation)

Typically, during the first 8 months of a grant start date, time sensitive set-up activities are undertaken (see table below for a typical timeline for a risk assessed trial) in order to enable the first participant to be recruited/randomised. This is a very intense period and requires engagement with many stakeholders to ensure that timelines are met. During this time, the study Sponsor will undertake a formal risk assessment (typically if regulated or considered complex, which usually accounts for 1-2 months of the timeline for regulatory approvals), the necessary regulatory approvals will be submitted, and sites will be approached to complete feasibility in readiness for site initiation visits. Additionally, the table of responsibilities previously drafted will be finalised as per the sponsor SOP.

TARGET CLINICAL TRIAL TIMELINE FOR ECTU FULL SERVICE RISK ASSESSED TRIALS

Based on a funded 8 month lead to FPFV



This timeline was developed in collaboration with our colleagues in ACCORD.

Role of the Chief Investigator

The named Chief Investigator (CI) takes overall responsibility for the conduct of the clinical trial. The CI should normally be professionally based in the UK so that they are able to oversee the research activity effectively. The CI MUST be able to keep in close communication with ECTU, the Research Ethics Committee (REC) and other regulatory bodies during the application process and during the conduct of the research. The CI is responsible to the funder for delivery of the project in accordance with the terms and conditions of the award, and also for delivering the primary publication of the work with the collaborating investigators.

The employing organisation of the CI is usually the Sponsor of the study. The Sponsor carries the legal risk and insurance for the study, and as such has legal responsibility for the conduct of the study, or oversight of conduct where it delegates responsibilities. If you are a University of Edinburgh or NHS Lothian employee, then the Sponsor is represented by the ACCORD office.

Our expectations of Chief Investigators

- Work together and in collaboration with us. This means being responsive to communication and respectful of our expertise, as well as complying with University HR policies (in particular the University's Dignity and Respect Policy and Behaviours Charter).
- Understand that ECTU may interact differently with first-time vs. established chief investigators.
- First time CIs may benefit from engagement with CI coaching provided through the ECTU Clinical Advisory Group
- Include members of ECTU staff as co-applicants on funding applications as appropriate (typically a senior methodologist/statistician, senior health economist and/or a senior trial manager).
- Comply with our SOPs (where relevant). Our current SOPs are available on our website.
- Be available for inspection and audit as required (via ECTU / MHRA or other body).
- Comply with our Publication and Acknowledgement Policy.
- Notify us of any requests to change the agreed table of responsibilities – these may have resource implications, so these must be agreed in advance.
- Advise at the earliest opportunity of any issues which will have a significant impact on trial progress / resources or funding.
- Disseminate results to ECTU, for example, by presenting on the trial at an ECTU meeting.
- Understand that staff changes throughout the lifecycle of a trial may be required and this will be done with care and prior notification when possible.
- Be available to support all stages of the trial including being available for regular and ad hoc (as required) meetings with the trial team.

What Chief Investigators can expect from ECTU

- Work together and in collaboration with you. This means being responsive to communication and respectful of your expertise, as well as complying with University HR policies (in particular the University's Dignity and Respect Policy and Behaviours Charter).
- Provide responses to your questions/queries in a timely manner; including for new project support requests, which are discussed and assessed against the ECTU Portfolio Prioritisation Strategy at our weekly Portfolio Management meetings.
- Once ECTU adopts your project into the portfolio, we will help design your clinical trial before funding application and support you through the application process.
- Provide you with a Letter of Support to the funder, if required.
- Work to Sponsor and ECTU SOPs.
- Develop study-specific working practice documents where required.
- Host the Trial Master File (TMF), or relevant sections of it, ensuring availability and readiness for inspection if delegated.
- In line with our use of stage gate methodology for successful project execution, we will advise you at the earliest opportunity of any issues which we consider will have a significant impact on trial progress.
- Review ECTU budgets to ensure quality and value for money.

ECTU Organogram (October 2024)