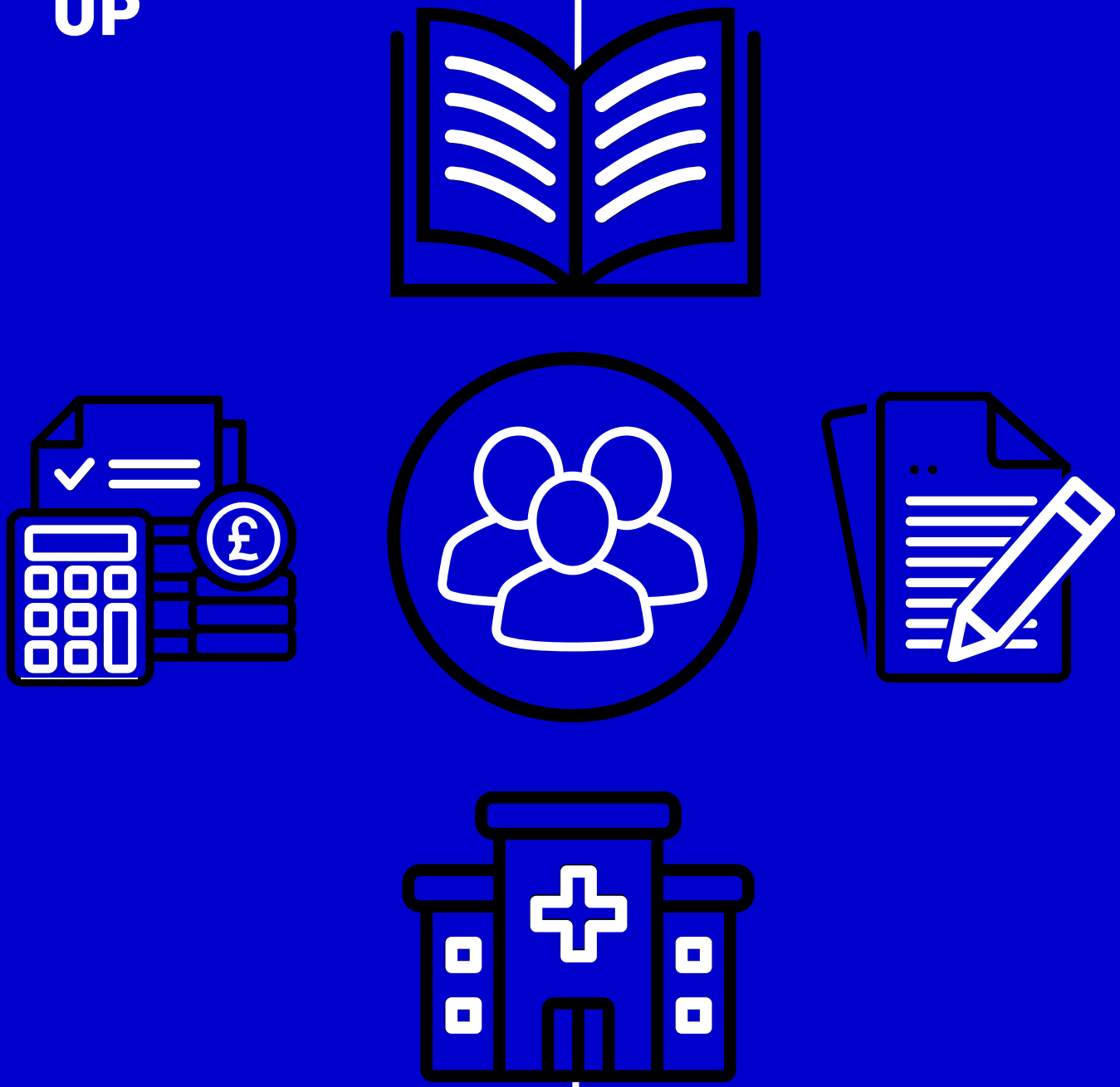
IMPERIAL

MedTechONE

CLINICAL TRIAL START UP



MT1

COLLABORATIVE

www.imperial.ac.uk/medtechone/

CLINICAL TRIAL START UP

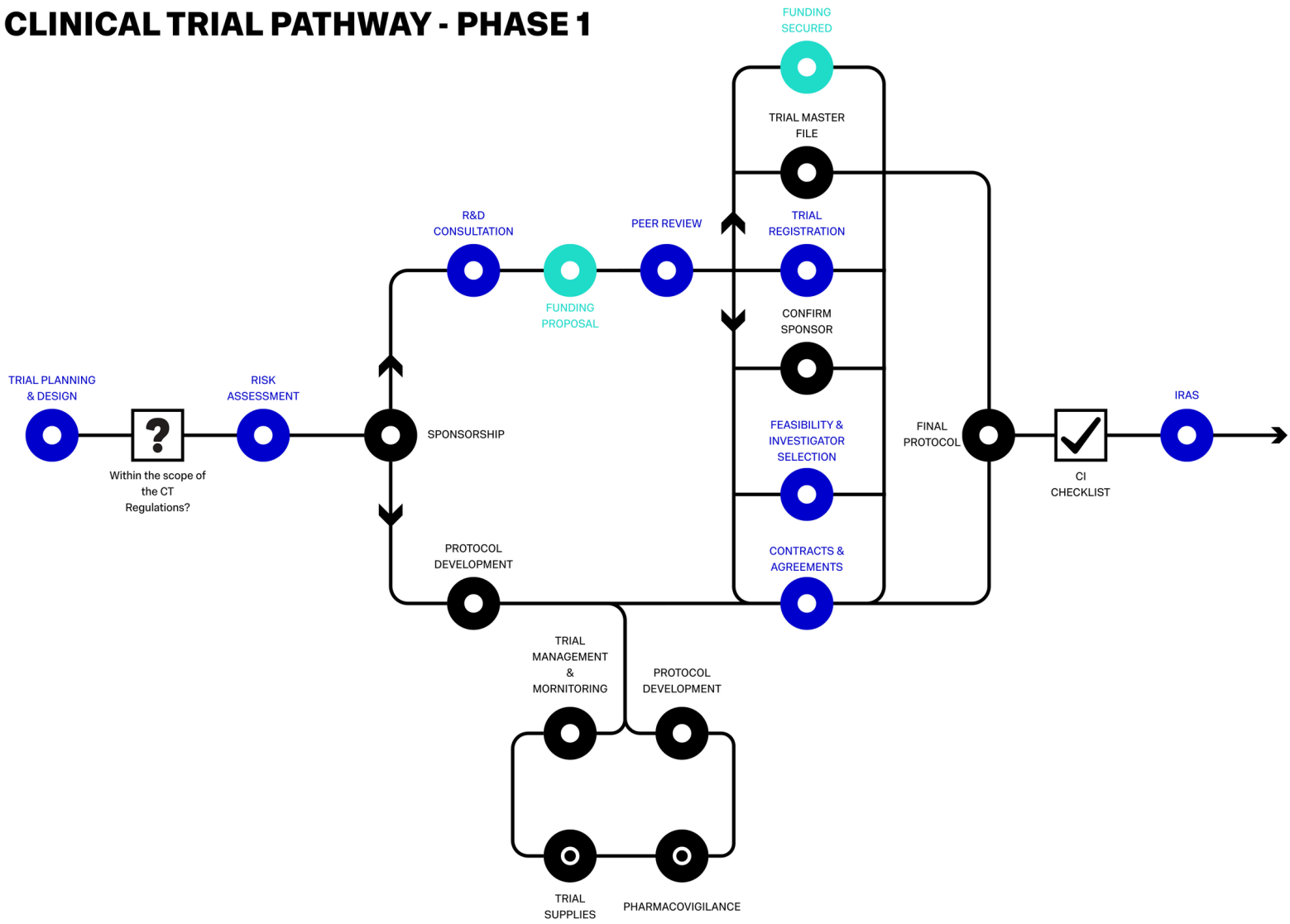
Trial set up processes can vary between CTIMPs and non-CTIMPs. The following advice is general, you should speak to your relevant departmental expert for more tailored guidance.

You should consider:

- **The Research Question** - The nature of the question will determine which regulations the trial must adhere to.
- **Where are you in the trial process?** - The key stages are shown in the pathway on the next page.
- **Organisation and trial team expertise** - Use the following pathway to identify any skills gaps in your team, and see the information on sourcing expertise at Imperial in the following pages.
- **The importance of Patient & Public Involvement** - Consider how best to involve members of the public in your work including using Imperial's PPIE Team.

CONTENTS

THE CLINICAL TRIAL PATHWAY

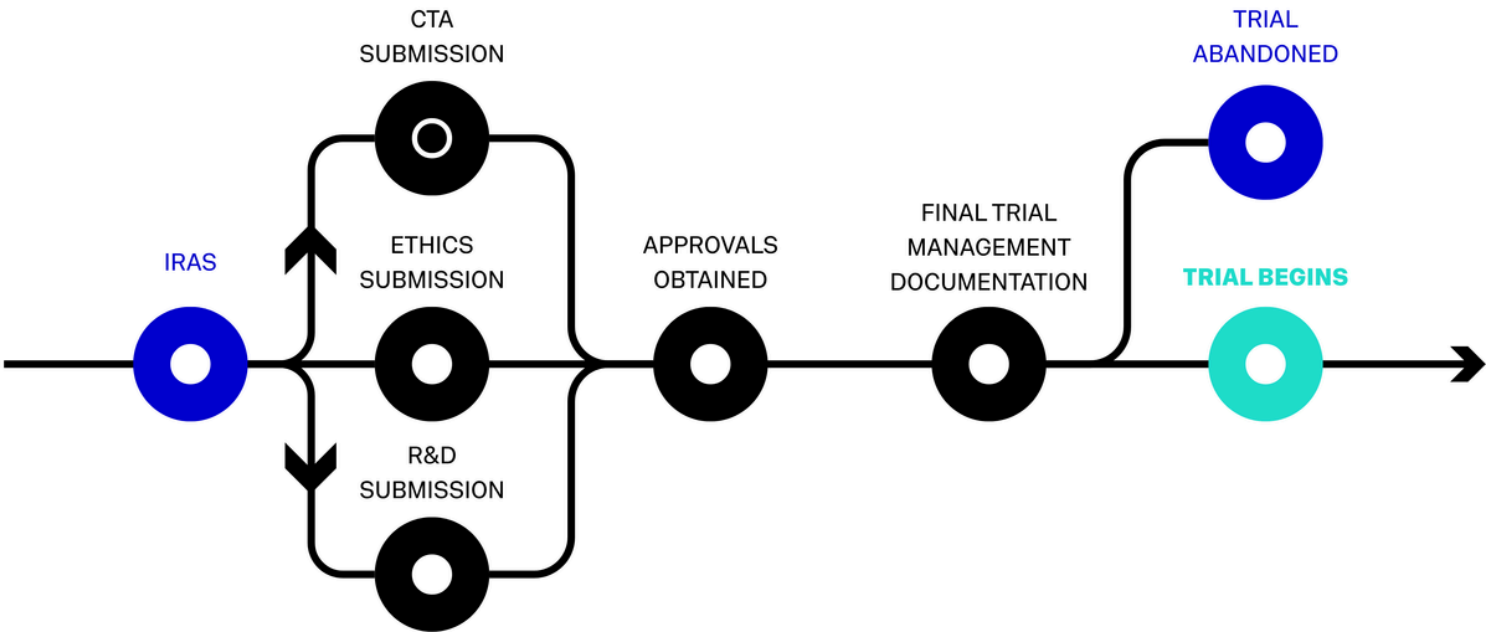


The first section of the clinical trial pathway describes the pre-trial **processes that must be undertaken prior to ethics.** These include:

- Planning and risk assessments
- Sponsorship agreements
- Funding acquisition
- Documentation and protocol development
- Related peer review processes

THE CLINICAL TRIAL PATHWAY

CLINICAL TRIAL PATHWAY - PHASE 2

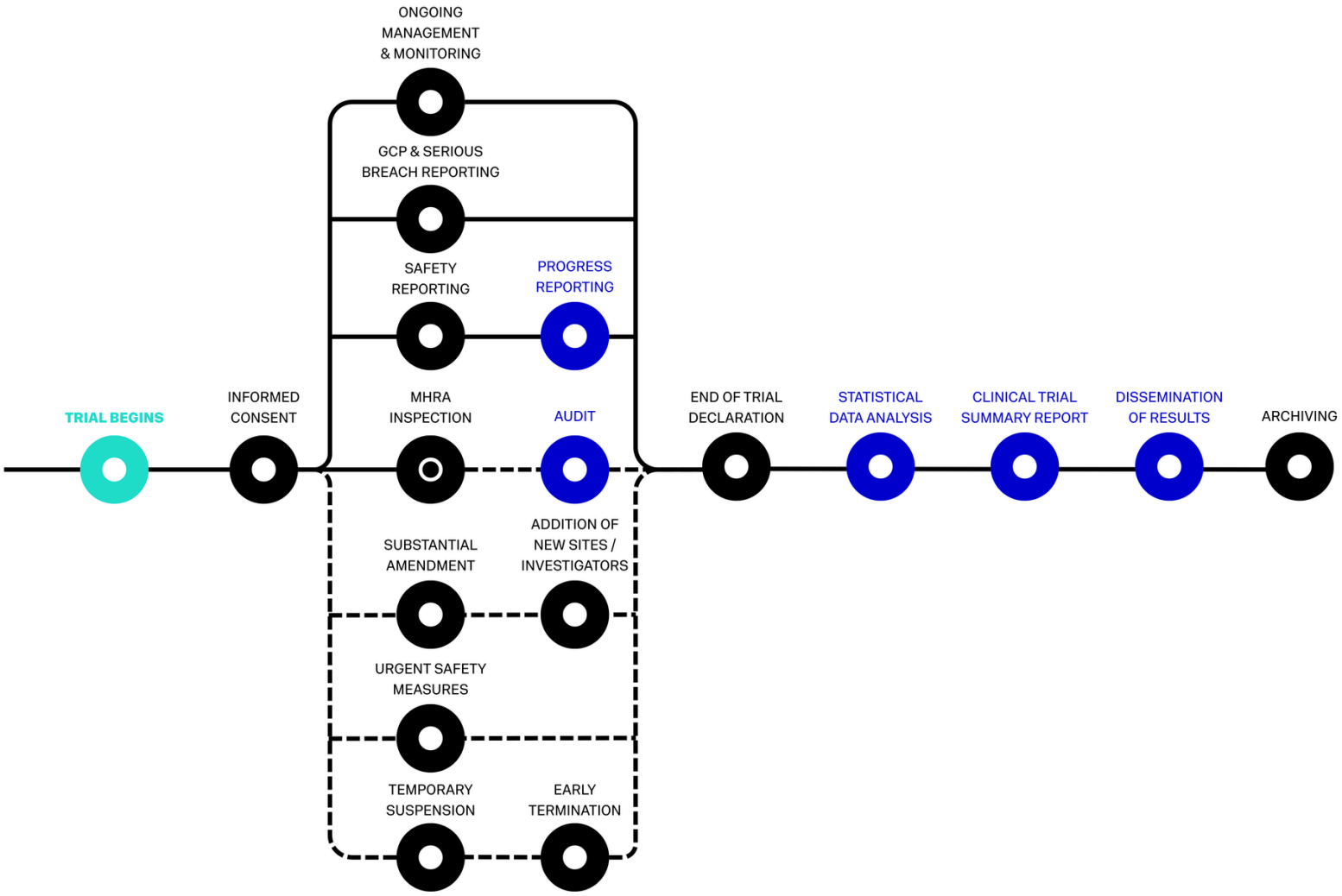


The second section of the clinical trial pathway describes **the ethics process.** This includes:

- IRAS submission
- Any other ethics or approvals such as MHRA submissions
- Time allowed for approvals
- The final decision on whether the trial can commence or needs to be abandoned.

THE CLINICAL TRIAL PATHWAY

CLINICAL TRIAL PATHWAY - PHASE 3

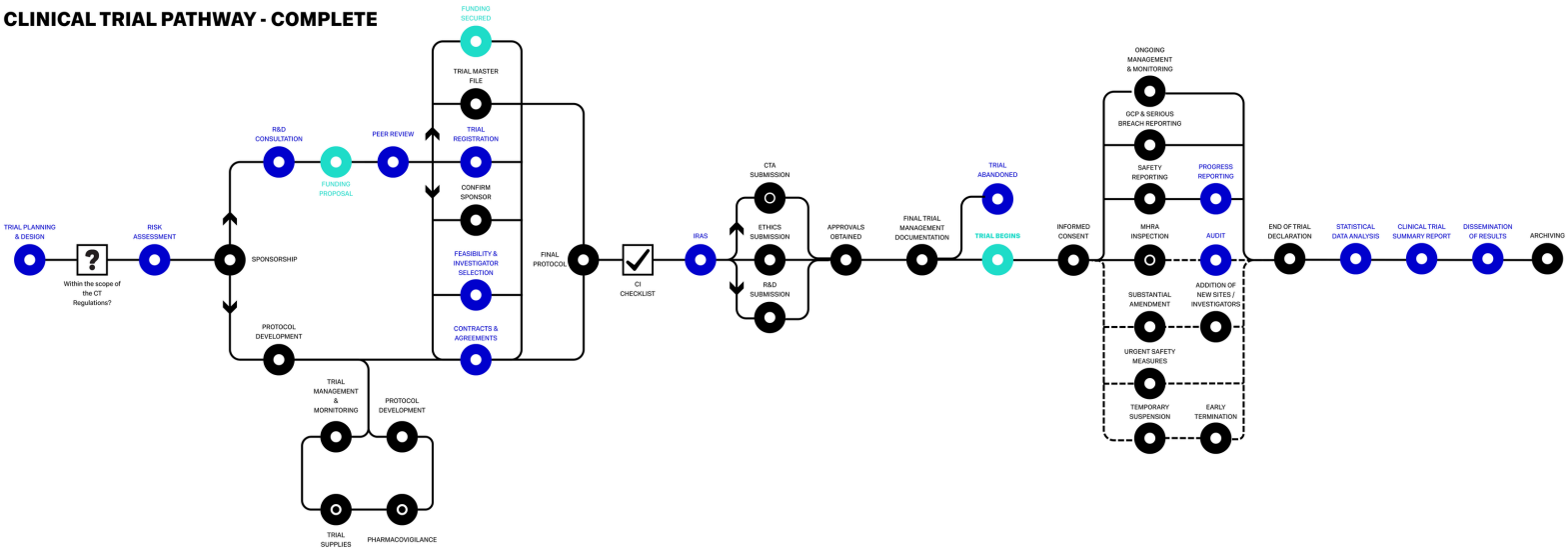


The third section of the clinical trial pathway describes the **post-commencement trial management processes.** These include:

- Inspections and monitoring, including audits
- Participant recruitment and progression, including informed consent
- Safety and progress reports
- Analysis, dissemination and archiving

Dotted lines indicate processes that may not apply to all clinical trials.

THE CLINICAL TRIAL PATHWAY



You can find the original version of this pathway diagram at:
https://www.ct-toolkit.ac.uk/routemap

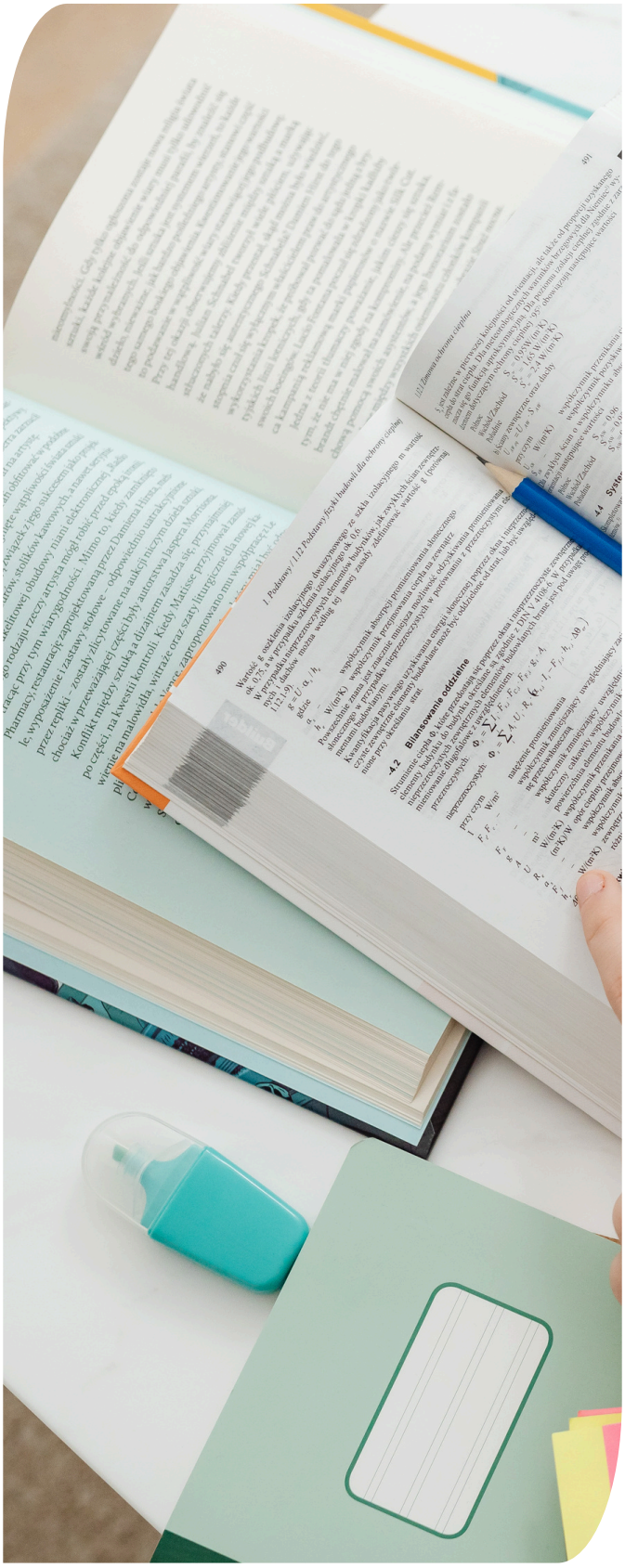
TRIAL DESIGN & PLANNING

Good study design is important.

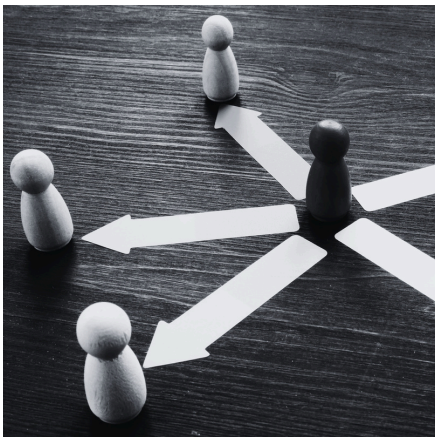
The **trial design should be considered before the protocol is developed** to ensure that all requirements are identified and met, particularly with regard to appropriate funding sources and amounts.

A good study plan will help with the development of funding applications, ethics committee and R&D approvals, NHS approvals, and any other regulatory permissions required.

Imperial offers a research design service that can support the development of your study design



IMPORTANT DOCUMENTS



DELEGATION LOG

The Delegation Log is a vital record of the project or study team and designates the responsibilities and permissions of the team for the execution of the project.
The Delegation Log is a good example of a living document. It should be checked regularly for accuracy and should be updated promptly when there are any changes to the project team or their responsibilities.

INVESTIGATOR SITE FILE (ISF)

The ISF includes all of the important documentation that demonstrates the project is being undertaken in line with regulatory requirements.
This includes items like the SOP, participant consent forms and information sheets, delegation logs, safety reports, IMP manuals etc.
ISFs should be kept at all sites.

TRIAL MASTER FILE (TMF)

Similar to the ISF, the TMF forms a record of the important project documents, but is usually kept solely at the coordinating project site, under the supervision of the CI or study leads.
The TMF should contain all major documents related to the project, from funding agreements and contracts, to copies of the SOP and participant-facing documents, to the statistical analysis plan.

IMPORTANT DOCUMENTS

RESEARCH AGREEMENTS / CONTRACTS

Written records of agreements with your Sponsor, the research facility or facilities where your project will take place, and any other similar agreements. Some projects will have dissemination agreements which lay out how the results of the project will be made public after the end of the study.

FUNDING AGREEMENTS

The specific documents recording any funding you are being awarded, the financial amounts, from whom the funding is being provided, and the duration for which the funding is valid. These documents will also cover any stipulations or conditions relating to the funding, such as the items or project needs the funding may be used for.

RECORD OF REC APPROVAL (FAVOURABLE DECISION)

The official letter of the Research Ethics Committee's approval of your project, also known as a "Favourable Opinion".

You must have this in place before starting your project.

IMPORTANT DOCUMENTS

TRIAL TEAM CVs

You must obtain and store the CVs of all team members who will be working on the project so that you have a written record demonstrating the competencies and qualifications of your team.

TRIAL TEAM INSURANCE

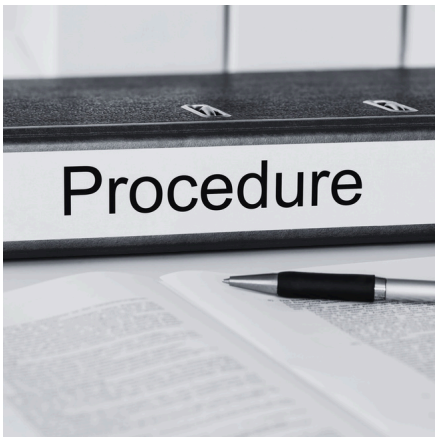
Some team members, usually senior team such as the CI / PI, or clinical staff like doctors and nurse, may require liability insurance to be in place when they work on your study. For clinical staff, this may be taken care of by the NHS or their normal employer.

You may also need more general liability or indemnity insurance for your project - Check with your Sponsor.

TRIAL TEAM TRAINING & CERTIFICATES

You should store copies of any training certificates obtained by, or required by, your team. This can include Good Clinical Practice training, First Aid, ANTT training, and data security trainings, amongst others.

STUDY DOCUMENTS

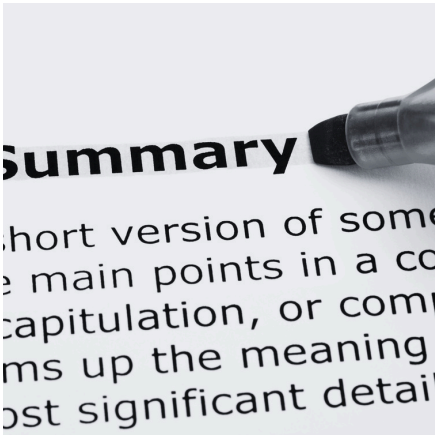


STANDARD OPERATING PROCEDURES (SOP) / MANUAL OF PROCEDURES (MOP)

This document includes the full information about the project. It should include a brief summary of the supporting literature, but should primarily focus on the subject of the project, how you plan to carry out the project, and specific items such as participant recruitment criteria, appointment structures, and outputs.

PARTICIPANT INFORMATION SHEET (PIS)

This is the document that will form the basis of the information prospective participants receive about the project. It should be detailed enough for participants to make an informed choice about joining the project, but should be in clear and easy-to-understand language.



PARTICIPANT INFORMATION SHEET SUMMARY (PIS-S)

Provided to participants, this document should succinctly summarise the PIS, which may be quite lengthy depending on the project, into a single side of A4. You should try to include all the key information, and should make an effort not to omit any major points.

STUDY DOCUMENTS

CONSENT FORM

This form will be read, understood, and signed by participants after they have read the PIS and have had time to ask questions about the project. The consent form should thoroughly record consent for all aspects of participation in the project.

CASE REPORT FORM (CRF / eCRF)

The CRF or eCRF record all data related to the project. They may be completed at participant appointments, and will be the primary data source for the project. The CRF should be thorough, and should be designed to record all relevant data.

FILE NOTE

Used by the study team to record any additional notes about a participant, a specific visit, an incident relating to a participant, or regarding corrections / errors in other paperwork.

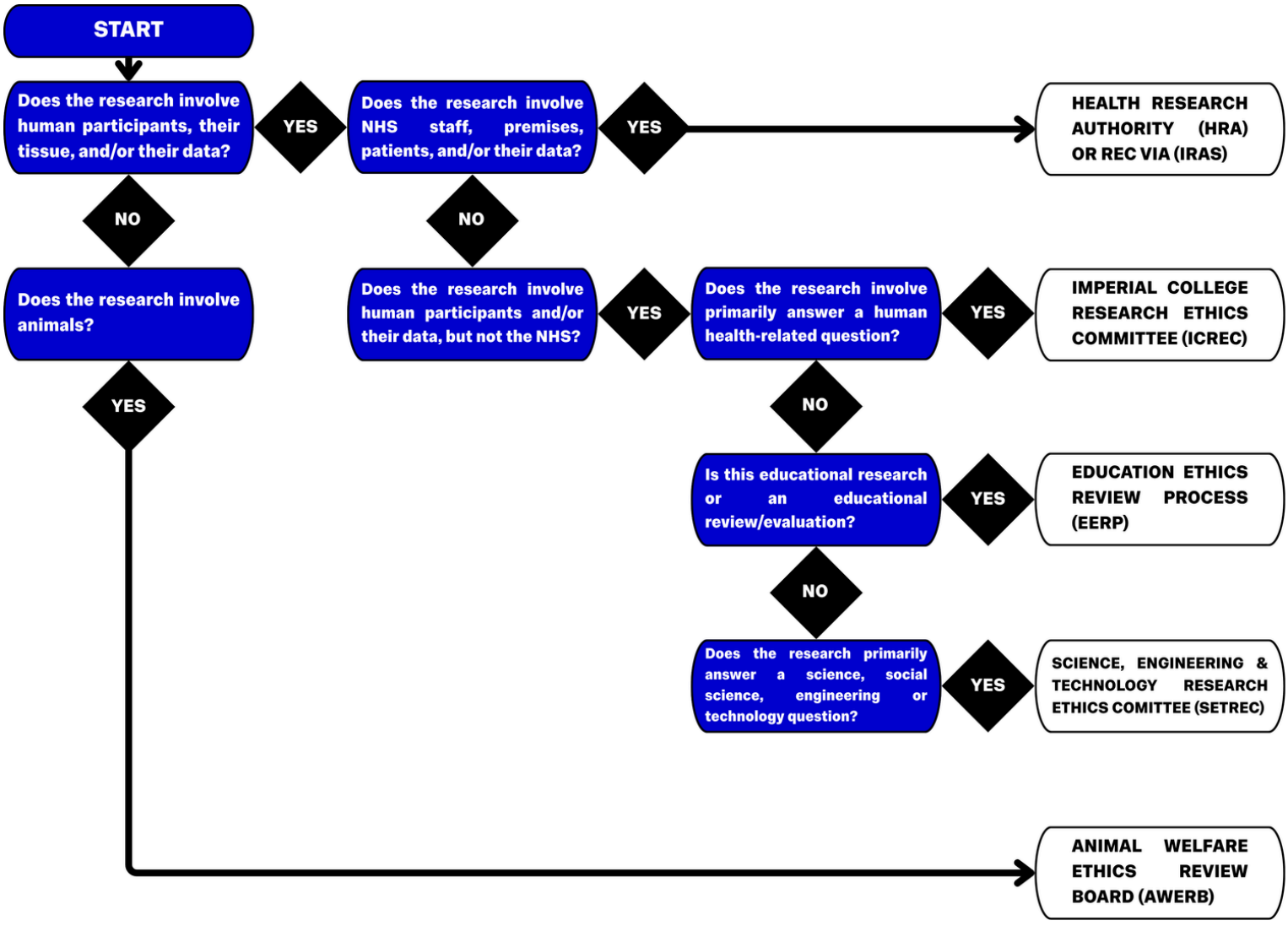
SPONSOR

The Sponsor is responsible for ensuring appropriate arrangements are in place for:

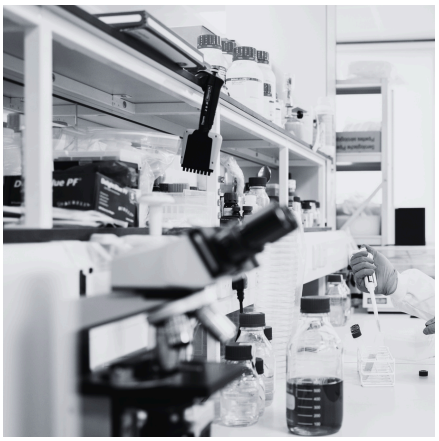
- The Site Initiation Visit (SIV)
- The management and oversight of the project.
- The overall management of financing the project.
- Safety reporting.

For projects conducted at Imperial, Imperial will usually be the Sponsor. You do still need to secure a sponsorship agreement, however.

DO I NEED TO APPLY FOR ETHICS?



RESEARCH ETHICS COMMITTEES



Health Research Authority RECs via IRAS

HRA RECs mainly assess project proposals for research that uses human participants, and is planned to take place within the NHS.

You can find out more at:
https://www.hra.nhs.uk/approvals-amendments/what-approvals-do-i-need/research-ethics-committee-review/

Imperial College Research Ethics Committee (ICREC)

Imperial College Research Ethics Committee (ICREC) is the College Ethics Committee which reviews health-related research involving human participants and/or their data that is undertaken by Imperial staff or students.

You can find out more at:
https://www.imperial.ac.uk/research-ethics-committee/committees/icrec/

Education Ethics Review Process (EERP)

This process is designed for educational projects, i.e. projects completed as part of education, only.

You can find out more at:
https://www.imperial.ac.uk/research-and-innovation/support-for-staff/education-ethics/the-eerp-process/

RESEARCH ETHICS COMMITTEES

Science, Engineering and Technology Research Ethics Committee (SETREC)

This committee reviews non-health related research that involves human participants and/or their data. They also review high-risk educational research projects.

You can find out more at:
https://www.imperial.ac.uk/research-ethics-committee/committees/setrec/

Animal Welfare Ethics Review Board (AWERB)

AWERBs review projects that intend to use animal subjects.

You can find out more at:
https://www.imperial.ac.uk/research-and-innovation/about-imperial-research/research-integrity/ethics/animal/

THE INTEGRATED RESEARCH APPLICATION SYSTEM (IRAS)

You will need to prepare:

- **Study documents** including the Study Protocol, Research Agreements, Confirmation of Sponsor, Funding Agreements, Case Report Forms (CRFs) etc.

- For clinical trials using human participants, you will need any and all **participant facing documents** such as the Participant Information Sheet and Consent Forms.

- All details of, and **documents relating to the study team**, including CVs, insurance details (where applicable), and the Delegation Log.

- **Documentation or manuals for any medical devices or medicines** related to the trial.

- **A comprehensive background to the project** including relevant literature, scientific background, and any existing data.

IRAS
INTEGRATED RESEARCH APPLICATION SYSTEM

SITE INITIATION VISIT (SIV)

Once all of the relevant approvals are in place, all documentation has been finalised, and all sites have the information they need, the trial can go ahead.

Typically, **a site initiation meeting, or "visit", is held at each site** (in person or virtual). The Chief Investigator is then able to confirm all technical aspects of a trial and that protocol requirements are fully understood by all site staff, and necessary documents are in place.

The visit also provides the site team with an opportunity to ask questions.

Trial or facility specific training normally happens at this stage.

N.B. The core research team must attend in person where possible

AT IMPERIAL

FACILITIES AT IMPERIAL

If you are an Imperial researcher or staff member, or if your project is Sponsored by Imperial, you may be eligible to access the Imperial NHS Trust Clinical Research Facility (ICRF). The ICRF is a clinical facility at Hammersmith Hospital, London, specifically designed to accommodate research projects.

SPINOUTS AT IMPERIAL

Imperial is committed to supporting spinouts for Imperial-developed innovations. The point at which you spinout will depend on the specific innovation, and any specific project needs.

FURTHER READING & RESOURCES

IMPERIAL RESEARCH DESIGN SERVICE
https://www.imperial.ac.uk/medicine/fom-staff/support-and-services/research-support/research-design-service/

IMPERIAL - STUDY DOCUMENT TEMPLATES
https://www.imperial.ac.uk/research-and-innovation/research-office/research-governance-and-integrity/sop-associated-documents--templates-/

STUDY SPONSORSHIP GUIDANCE
https://www.imperial.ac.uk/research-and-innovation/research-office/research-governance-and-integrity/project-planning/obtaining-sponsorship/responsibilities-for-imperial-or-icht-as-a-sponsor/

RESEARCH ETHICS - ADDITIONAL EXPLANATION
https://imperial.cloud.panopto.eu/Panopto/Pages/Embed.aspx?id=8ff22531-0c2d-4f05-8498-acb1010e34d2&v=1&autoplay=true

IRAS GUIDANCE
https://www.myresearchproject.org.uk/help/hlpcollatedqsg-nhsrec.aspx or
https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/clinical-trials-investigational-medicinal-products-ctimps/combined-ways-working-pilot/step-step-guide-using-iras-combined-ways-working-cwow/

THE ICRF
https://www.imperial.ac.uk/nihr-crf/research/who-can-use-crf/

GUIDANCE FOR SPINOUTS
https://www.imperial.ac.uk/enterprise/staff/creating-a-spinout-company/imperials-vision-for-spinout-companies/

FURTHER READING & RESOURCES

RESOURCE	TOPICS	LOCATION
MEDICAL RESEARCH COUNCIL	Information published by the MRC giving guidelines on conducting research with human participants and their tissues and data.	https://www.ukri.org/councils/mrc/
NIHR: PLANNING AN RCT	A paper summarising some of the trial activities that would need to be considered.	https://www.ct-toolkit.ac.uk/documents/planning-a-randomised-controlled-trial-rtc-points-to-consider/27168
NHS RESEARCH & DEVELOPMENT FORUM	The NHS R&D Forum is a network for those involved in managing and supporting R&D in health and social care. Information on key activities and developments is regularly updated.	https://rdforum.nhs.uk/
NIHR CLINICAL TRIALS GUIDE	Designed to support NIHR trainees interested in getting involved in clinical trials.	https://www.nihr.ac.uk/documents/clinical-trials-guide/20595
DIRUM	An open-access Database of Instruments for Resource Use Measurement.	https://www.dirum.org/
MULTI-ARM MULTI-STAGE TRIALS	Some recommendations on the design of MaMs	https://journals.sagepub.com/doi/10.1177/0962280212465498
INFORMING RCTs	Outlines the key issues to consider in the optimal development and review of operational progression criteria for RCTs with an internal pilot phase.	https://bmjopen.bmj.com/content/bmjopen/7/2/e013537.full.pdf
PILOT STUDIES	Tips for developing and using progression criteria for internal pilot studies.	https://www.methodologyhubs.mrc.ac.uk/files/1114/8768/7541/Infographic_pilot_studies.pdf

FURTHER READING & RESOURCES

RESOURCE	TOPICS	LOCATION
STATISTICAL ANALYSIS PLANS	Recommendations for a minimum set of items that should be addressed and included in Statistical Analysis Plans for clinical trials.	https://jamanetwork.com/journals/jama/fullarticle/2666509
AVOIDABLE WASTE IN RESEARCH	Recommendations and guidelines.	https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2809%2960329-9/fulltext https://pubmed.ncbi.nlm.nih.gov/24411645/
THE EXPERIMENTAL MEDICINE TOOLKIT (MRC)	Resources supporting research using health data and human tissue samples, designed by the MRC.	
NIHR CENTRE FOR ENGAGEMENT & DISSEMINATION	leads NIHR's work to make health and care research representative, relevant and ready for use. The centre brings together its activities in patient and public involvement (PPI), engagement and participation with its strengths in research dissemination.	https://www.sscr.nihr.ac.uk/nihrs-new-centre-for-engagement-and-dissemination/
PATIENT & PUBLIC INVOLVEMENT (PPI)	Resources relating to Patient & Public Involvement	https://www.nihr.ac.uk/documents/ppi-patient-and-public-involvement-resources-for-applicants-to-nihr-research-programmes/23437 https://pubmed.ncbi.nlm.nih.gov/25475243/ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4459695/

FURTHER READING & RESOURCES

RESOURCE	TOPICS	LOCATION
PATIENT & PUBLIC INVOLVEMENT (PPI) CONTINUED	Information on how to find PPI volunteers.	https://www.peopleinresearch.org/
	Showcases a range of different experiences in healthcare including participation and involvement in health research.	https://healthtalk.org/
HEALTH RESEARCH AUTHORITY (HRA)	The HRA Framework for research provides the basis of legislative regulation for research in the UK.	https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/uk-policy-framework-health-and-social-care-research/

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