
Industry pack

Guidance for the set-up of hosted clinical trials



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Section 1

Introduction to The Royal Marsden and General Information

The Royal Marsden NHS Foundation Trust along with its academic partner, The Institute of Cancer Research, London (ICR), are ranked in the top four centres for cancer research and treatment worldwide, with over 40,000 patients from the UK and abroad seen each year. Research is an integral part of The Royal Marsden's activities with an extensive portfolio of studies open at any time.

The National Institute for Health Research (NIHR) Biomedical Research Centre (BRC) at The Royal Marsden and the ICR is the only BRC to specifically focus on cancer.

Please note the following:

- The Royal Marsden is located across two *locations*: Sutton in Surrey and Fulham Road in Chelsea. In addition there is a Royal Marsden Medical Day Unit (Sir William Rous Unit) based at Kingston Hospital.
- Research activities are undertaken at all three locations. A clinical trial may be open at one or more location subject to local agreement with one R&D Capacity and Capability covering all.
- In addition, the following documents apply to all Royal Marsden research locations:
 - Royal Marsden Trust policies
 - Royal Marsden Standard Operating Procedures (SOPs)
 - Approved research agreements and contracts
- All Royal Marsden research staff receive face-to-face Good Clinical Practice (GCP) training from a TransCelerate accredited trainer on behalf of the Trust. If a course is not immediately available, as an interim measure, the NIHR provide accredited GCP training in the form of an e-learning exercise. All Royal Marsden research staff update their GCP training every 2-3 years.
- **It is considered that training provision for GCP has been industry accredited and it is therefore not necessary for further training to be undertaken.**
- Data Privacy Training for Investigator Site Staff (Information Governance) – All NHS and therefore all Clinical Research staff undertake training for managing Information Governance annually. The training is mandated by the Health and Social Care Information Centre and is in line with requirement 112 of the Information Governance Toolkit. Therefore all staff receive a high standard of training and it is not deemed necessary for staff to complete any additional training. Further details are available upon request.
- Any additional training required for the conduct of the study should be identified during the feasibility stage of the set-up process. This can then be discussed in advance and a decision made as to whether or not the requested training is a duplication of what we already provide. If it is agreed that the training is necessary then this will be accommodated within the contract.
- A comprehensive set of SOPs have been developed at The Royal Marsden, to which all clinical trial staff are required to adhere.
- **During the set-up, delivery and close out of a clinical trial, the Trial Coordinator should always be primary point of contact for the Sponsor.**

- The Royal Marsden and ICR laboratories are fully accredited and will usually process samples where required and local reference ranges will be provided upon request.
- Information requested by the Sponsor will be provided in the standard Trust format. Any re-formatting of such information to meet Sponsor requirements is the sole responsibility of the Sponsor. The Trust holds a 'Site Profile Form' which can be forwarded if needed.
- Clinical trials will be run as per Trust SOPs. As a Trust, generally we cannot accommodate differing practices for different trials. However, valid requests will be considered.



Section 2

Royal Marsden Clinical Trial Support Services

Local Support Service review aims to be completed within 10 working days from the date all required documentation (Checklist 1)

is provided from the Sponsor via the Trial Coordinator.

2.1 Radiology review

Clinical trials involving exposures to radiation require Radiology, Nuclear Medicine and Radiotherapy departments to complete, if involved, two reviews:

- A capacity review within specific areas (i.e. MRI / CT / ultrasound etc.) to establish whether protocol specific requirements can be met.

- A local IRMER review to assess The Royal Marsden's legal compliance against the requirements of the Ionising Radiation (Medical Exposure) Regulations 2000 (IRMER) whilst taking part in the trial (see below for further details).

The Trial Coordinator will liaise with the Radiology Review Coordinator.

Radiology/ Nuclear Medicine / Radiotherapy capacity review

The Royal Marsden Radiology, Nuclear Medicine and Radiotherapy Departments will carry out a feasibility / capacity review if involved to ensure adequate resources are available to meet the requirements of the clinical trial protocol. In order to assess capacity the departments require the clinical trial

protocol and any associated imaging manuals / documents / radiotherapy protocols. These documents allow the departments to understand the technical requirement of a protocol. If these documents are not provided the review cannot take place, which may lead to delays.

IRMER review

IRMER governs the exposure to ionising radiation of patients or volunteers participating in clinical and therapeutic research studies in the UK. Compliance with IRMER is a legal requirement for each site participating in a trial and can only be checked by the site itself.

According to current NRES guidance, IRMER applies to ALL trial procedures involving ionising radiation, not just to exposures that are additional to routine clinical care. The following procedures will expose participants to ionising radiation:

- Any type of X-ray

- DEXA or bone densitometry scans
- Radionuclide imaging such as bone scans, MUGA scans, PET scans
- Radiotherapy (including brachytherapy and therapy using unsealed sources)

In order to streamline the IRMER review, lead Medical Physics Experts (MPE) and Clinical Radiation Experts (CRE) inform the REC about the generic radiation issues associated with the trial so that the participating sites need to deal only with local issues. For further information about IRMER, please refer to appendix 2 (useful web addresses).

Participating site (i.e lead IRMER review has been conducted elsewhere)

The local IRMER review (a legal requirement) is carried out by local MPEs and CREs. The following documents are required from the Sponsor to enable the Trial Coordinator to initiate local review:

- Trial protocol
- Signed IRAS application form
- REC approval letter (if the REC have already given approval)
- Patient Information Sheet (PIS) / Consent Form and GP letter

- Imaging guidelines / radiotherapy protocol
- If these documents are not provided the review cannot take place, this may lead to delays.

Outcome of the local IRMER review will generally be favourable, but from time to time the experts will identify problems with the lead IRMER assessment meaning that The Royal Marsden is unable to participate in the trial and meet its legal obligations. In these instances the Trial Coordinator will work with the sponsor to rectify the problems raised.

Lead Site with input to REC application

When The Royal Marsden is the lead site and required to have input into the NHS IRAS form, the Trial Coordinator will liaise with the Radiology Review Coordinator to obtain the lead MPE and CRE statements. In this instance the following documents are required from the sponsor to enable the Trial Co-ordinator to initiate local review:

- Trial protocol
- Imaging guidelines

- Draft copy of the NHS IRAS application form
- The PIS (in draft form to allow comment by the lead CRE and lead MPE and must be approved by them as appropriate.)

Full Support Service review can take place in parallel with IRMER review / input to NHS IRAS form if all required documents, as set out in Checklist 1, are provided.

The Trial Coordinator will liaise with the Radiology Coordinator.

2.2 Nuclear medicine

Where nuclear medicine examinations are required as part of a clinical trial that are classed as above standard of care, feasibility / capacity review will take place and an ARSAC licence may be required. This will be determined

by a Royal Marsden nuclear medicine CRE. For further information on ARSAC, please refer to appendix 2.

The Trial Coordinator will liaise with the Nuclear Medicine Coordinator.

2.3 Pharmacy review

The Royal Marsden Pharmacy will review every IMP trial to assess capacity and capability of Pharmacy running the trial and identify any issues. The Royal Marsden Pharmacy is able to support all phases of studies and has an on-site aseptic unit that can prepare chemotherapy, injectable anticancer agents and gene therapy products.

The Clinical Trials Pharmacist will require specific pharmacy documents (as set out in (checklist 1) in order to carry out the pharmacy review. If these documents are not provided to the Trial Coordinator the review cannot take place, leading to delays in granting R+D Capacity and Capability. For any injectable IMP, Pharmacy must be supplied with written information on the preparation, stability and storage conditions of the final product.

Pharmacy review consists of:

- Review of Investigational Medicinal Product (IMP) requirements such as: Dosing, safety data, storage requirements, reconstitution and stability data, handling and safety requirements, label review and labelling requirements
- Sourcing of IMP and related Good Manufacturing Practice (GMP) requirements, including QP certificates if applicable.
- Handling of non-Investigational Medicinal Products (non IMPs)
- Supportive care required
- Sponsor requirements as dictated by the protocol including drug ordering, accountability, temperature monitoring etc.
- Resource and cost review
- Capacity review

Drug accountability forms

Royal Marsden in-house drug accountability forms, registration logs and destruction forms will be used for all studies. These templates will

be adapted as per Pharmacy SOPs for each trial and will be available for review by sponsor prior to trial opening if requested.

Pharmacy at both Chelsea and Sutton locations

There is a Pharmacy Department at both Sutton and Chelsea with each Pharmacy managing prescriptions and medicine supplies for patients at that location, including clinical trials. Where trials are conducted across both locations the Pharmacy department need to be able to order IMP independently of each other. It is not possible to store IMP at one location and ship to the other as required. Management of the clinical trials at both locations is overseen by

the Pharmacy Clinical Trials Team which works across Chelsea and Sutton.

It is a UK legal requirement that HRA Approval, R&D Capacity and Capability and a signed clinical trial agreement must be in place before drugs can be received on site. If stock is inadvertently delivered to site prior to both HRA Approval and R&D Capacity and Capability it should be immediately collected and returned to the distributor at cost to the Sponsor.

Pharmacy monitoring visits

The Pharmacy Clinical Trials Team request adequate notice is given when booking monitoring visits to ensure provision of space and staff time. **A minimum of two weeks** is recommended but please be aware that at busy times the Pharmacy can be booked up to four

weeks in advance. Two hours per visit is usually allocated for an appointment but should the visit be longer, please make this known at the time of booking. If there will be more than one person in attendance at the monitoring visit please let the Pharmacy Clinical Trials Team know.

Pharmacy Standard Operating Procedures (SOPs)

The Pharmacy Department have developed a comprehensive list of SOPs including temperature monitoring and the quarantine of stock in the event of a temperature deviation. The SOPs apply to both locations to ensure the same working practices are applied at the

Sutton and Chelsea sites. Should the Sponsor wish to use an SOP other than those of The Royal Marsden, they should discuss and agree during trial set up.

Pharmacy fees

Any queries relating to Pharmacy costs must be directed through the Finance Team via the Trial Coordinator.



2.4 Finance review

Where available, The Royal Marsden is adhering to the fees and prices as per the NIHR UKCRN template. If there is not a suitable price included in the template The Royal Marsden will add in the local price. It is the responsibility of the Sponsor to provide a completed copy of the NIHR UKCRN costing template as soon as possible to the Trial Coordinator. The Royal Marsden Finance Department work in

conjunction with the Trial Coordinator to review the feasibility of the trial by ensuring all protocol activities are accurately and fairly reflected in the costing template. All finances, including set up fees and pharmacy costs will be reviewed and confirmed by The Royal Marsden Finance Department.

2.5 Contract review

The Clinical Trial Agreement (CTA) must be in the format of the Standard NHS model ABPI Clinical Trial Agreement (mCTA). Please be aware that if the agreement is not provided in this format then the negotiation process may be subject to delays as there may be points that require further negotiation. The mCTA template can be found on the NIHRs website (see appendix 2)

In the first instance the Sponsor should send a draft mCTA to the Trial Coordinator. If Sponsors have additional specific clauses they should be highlighted and, where appropriate, rationale for the modifications should be provided. This

will allow the Contracts team to carry out an initial review of the wording. The Contracts team encourage Sponsors to provide a draft CTA for initial review. It is the Sponsor's responsibility to insert the appropriate trial information into the agreement before sending to the Trial Coordinator. The Sponsor is also responsible for transcribing the agreed budget into a Royal Marsden template to form the financial appendix to the mCTA. Please note that the final approval of the contract cannot be given until The Royal Marsden Finance and Pharmacy departments have completed their feasibility / capacity review.

Checklist 1

Essential documents to be provided by Sponsor for The Royal Marsden Support Service Feasibility Review (HRA Local Information Pack)

Full Support Service review cannot commence until the following documents have been provided by the Sponsor:

- Final protocol (not password protected)
- Investigator's brochure / SmPC (if applicable)
- (IRAS form) (complete or draft)
- Patient information sheet(s) / consent form(s) / assent form(s)
- NIHR UKCRN costing template
- Draft ABPI model Clinical Trial Agreement (mCTA) (pending completion of Finance/ Pharmacy appendices)

- Delegation log
- Laboratory, Imaging and Pharmacy manuals
- Material Safety Data Sheet

Please also provide the HRA Initial Assessment Letter when issued from the HRA

The only exception to the above is when The Royal Marsden is the lead site with input to the NHS IRAS application form (as set out in section 2.1).

Please be aware that requested documents are essential for full Support Service review of the trial and failure to provide these may cause significant delays to trial set up.

Section 3

The Royal Marsden Genetic Modification Safety Committee and Clinical Product Review Committee

Clinical trials involving medical devices or genetically modified products need approval from the relevant Royal Marsden committee.

3.1 Genetic Modification Safety Committee

The Royal Marsden must ensure it meets its statutory obligations under the Genetically Modified Organisms (Contained Use) Regulations. As such any clinical trial involving the use of a genetically modified organism (GMO) or genetically modified microorganisms (GMMs) must be formally approved by the Royal Marsden Genetic Modification

Safety Committee (GMSC). The Committee consists of both management and employee representatives from all areas involved with GMO work.

Further information regarding the GMSC is available upon request from the Trial Coordinator.

3.2 Medical Device Committee (MDC)

Clinical trials involving any medical devices not currently in use in The Royal Marsden must be approved through the MDC. This includes equipment being studied as well as equipment that may be required by the protocol for use within The Royal Marsden, but is not currently a device used e.g. a different ECG machine or a new type of surgical equipment.

The PI and Trial Coordinator will complete and submit the relevant documentation to the Chair of the MDC for consideration at the next meeting. The Royal Marsden MDC is held on a two monthly basis.

Section 4

Trial Set up Meeting (TSM) and set up timelines

All new hosted interventional clinical trials (i.e. clinical trials that are sponsored by either a pharmaceutical company or another NHS Trust/ University) are set up via the TSM with the use of the Capacity Planning Form (CPF).

This process has been developed to streamline the set-up / communication between Clinical Units, Support Services, R&D and Sponsors / CROs, and to reduce set-up times so The Royal Marsden can offer new treatments to patients sooner.

4.1 Capacity Planning Form (CPF)

The Royal Marsden has devised and implemented the CPF to enable internal Support Services to carry out assessments on feasibility and capacity and demands on resources at an early stage and to reduce unnecessary delays. The Trial Coordinator / Research Nurse / Clinician completes the CPF within 7 days of documents in Checklist 1 being received.

The CPF and associated documents (as per Checklist 1) are submitted to Support Services involved in the trial who perform their own review of the trial and liaise direct with the Trial Coordinator. The Trial Coordinator liaises direct with the Sponsor / CRO to resolve issues where necessary.

4.2 Trial Set up Meeting (TSM)

Support Services will complete their reviews within 10 working days from receipt of the CPF and required documents (Checklist 1). The trial is then scheduled to attend TSM. The TSM is chaired by the Associate Director of Clinical Research and convenes fortnightly. Representatives from each Support Service are present at the TSM where progress of the new trial is discussed and unresolved or foreseen issues are highlighted. Summary letters are circulated to the PI, Trial Coordinator and Support Services. The Trial Coordinator will

liaise with the Sponsor / CRO to progress with trial set-up.

**Please note – the TSM is a facilitatory meeting and does not have the ability to grant any approvals. Its purpose is to escalate outstanding issues with aim to assist in resolution of issues and progress towards R&D Capacity and Capability. The TSM does not have to convene prior to progressing towards R&D Capacity and Capability providing all Support Services have confirmed feasibility and capacity.*

Section 5

NIHR CRN Portfolio Adoption

We encourage Sponsors to apply to the NIHR local CRN for portfolio adoption. To do this, you must submit the portfolio Application Form (PAF) before submitting for HRA Approval. The PAF is created in IRAS by ticking Yes to 5b in the filter questions. The HRA will share information about your application with the CRN to allow them to make a decision on NIHR CRN

Portfolio eligibility. With effect from 1st April 2016 the PAF should be submitted via email to portfolio.applications@nihr.ac.uk who can assist with queries and advice.



Section 6

R+D Confirmation of Capacity and Capability, Site Initiation Visits (SIV) and site activation

6.1 R+D Confirmation of Capacity and Capability

R+D Confirmation of Capacity and Capability will be issued that allows trial activity to be conducted at Chelsea, Sutton, and the Sir William Rous Unit (at Kingston) where applicable. The Trial Coordinator will collate all required documentation (checklist 2) and forward to R&D once Support Services and Sponsor / CRO have confirmed all outstanding issues are resolved.

The Sponsor should provide a non-password protected electronic version of the current clinical trial protocol prior to R+D Confirmation of Capacity and Capability. R&D will upload the protocol onto The Royal Marsden intranet so that all medical and out-of-hours staff has ready

access to the trial information in order to be able to safely clinically assess and treat the patient at any time, day or night. Password protected protocols are inaccessible to out-of-hours staff and could lead to compromised patient care.

R+D confirmation of capacity and capability cannot be issued prior to receipt of all essential documents as per checklist 2, including a fully executed CTA. The fully executed CTA will be released by the Trust in parallel to R+D Confirmation of Capacity and Capability will be issued within five working days from the date all required documentation (checklist 2) is submitted to the R&D office via the Trial Coordinator.

Checklist 2

In addition to the documents outlined in Checklist 1, the following documents should be provided by Sponsor for submission to R&D.

- Fully executed CTA
- Any protocol amendments

If all relevant documents are not provided this may result in delays with processing local R+D Capacity and Capability.

6.2 Site Initiation Visits (SIV)

In order to reduce recruitment delays, SIVs may be scheduled prior to R+D Capacity and Capability being issued. The Sponsor / CRO should schedule a suitable SIV date with

the Trial Coordinator to ensure the relevant members of the research team, including the PI, are available.

6.3 Site activation (Sponsor 'green light')

Once full R+D Capacity and Capability has been issued the Sponsor can arrange for shipment of IMP and complete site activation.

Once the Sponsor has given the 'green light' The Royal Marsden can open to recruitment.



Section 7 Data Entry

Clinical trials will be allocated a Research Nurse/Trial Coordinator/Clinical Trial Administrator or Data Manager, dependant on resource/number of patients etc., who will be responsible for entering trial data into trial specific eCRFs. Data will be entered in a timely manner as agreed in the signed CTA and in line with Trust reporting systems.

It is the Sponsor's responsibility to ensure

adequate training is provided to the allocated members of the clinical unit in a timely manner. This may include training on eCRF systems, IVRS, central imaging labs. All relevant login details and access codes must be provided in good time.

Trial specific workbooks to capture source data in conjunction with the electronic patient records may be also be used.

Section 8 Monitoring arrangements

Sponsors and / or CRAs are asked to provide as much notice as possible (ideally a minimum of three weeks) when booking monitoring visits. Please also note that only one monitor should attend per visit. However, it is recognised that there will be times where more monitors are required to attend i.e. data locks, audits, and training of new CRAs. Such special circumstances must be agreed with the Trial Coordinator in advance.

When Sponsors and / or CRAs are on site they should agree with research staff a suitable time to meet to discuss the trial. Research staff including Trial Coordinators are not able to dedicate whole days as they have a number of clinical trials to manage.

Sponsors and / or CROs should not arrive on site before 9am and must leave by 5pm unless agreed in advance with Trial Coordinator.

8.1 Electronic Patient Records (EPR)

Patient information is stored centrally on The Royal Marsden EPR system which is accessible via the Trust's networked computers. The Trial Coordinator will provide login credentials giving the Sponsor / CRA access to patient data for those enrolled onto a particular clinical trial so that trial data verification (SDV) can be conducted.

The following functions are NOT available to Sponsors / CRAs within the EPR system:

- Copy
- Paste
- Print

The Sponsor / CRA will be requested to change their login credentials every 30 days in line with Trust policy and are therefore responsible for keeping track of their details.

EPR user guidelines are available from the Trial Coordinator upon request.

Section 9 Invoicing

The Royal Marsden follows The Department of Health Attributing the costs of health and social care research and development (AcoRD) guidance which states "The NHS is required to recover, from industry, all costs over and above the standard NHS Treatment Cost." All entered data shall be monitored in a timely manner, and all data entered up to the end of the quarter shall be invoiced in the first month following the end of the quarter. If there is a delay in monitoring invoices will continue to be raised quarterly (or at the interval agreed in the CTA) in line with the contract and in relation to work undertaken.

Any queries relating to invoicing should be directed to the Trial Coordinator (other than specific trial activities outlined below) who will liaise with Trust Finance where appropriate.

Not all trial activity is invoiced by the Trial Coordinator. Please see the list below for the departments and contacts within The Royal Marsden who are responsible:

- 1) R+D invoice for set-up fee is raised by the R+D department.
- 2) Pharmacy costs are invoiced by the Pharmacy department.
- 3) All other activity is invoiced by the Trial Coordinator.

Appendix 1 and 2 - glossary and useful websites

ABPI - Association of the British Pharmaceutical Industry

ARSAC - Administration of Radioactive Substances Advisory Committee

CPF – Capacity Planning Form

CRA – Clinical Research Associate

CRE – Clinical Radiation Expert

CRN – Clinical Research Network

CRO – Clinical Research Organisation

CT – Computerised Tomography scan

CTA – Clinical Trial Agreement

DEXA – Dual Energy X-ray Absorptiometry

ECG – Electrocardiogram

eCRF – electronic Case Report Form

EPR – Electronic Patient Records

GCP – Good Clinical Practice

GM – Genetic Modification

GMM – Genetically Modified Microorganisms

GMO – Genetically Modified Organism

GMP – Good Manufacturing Practice

GMSC – Genetic Modification Safety Committee

GP – General Practitioner

GTAC – Gene Therapy Advisory Committee

HRA – Health Research Authority

ICF – Informed Consent Form

ICR – Institute of Cancer Research

IMP – Investigational Medicinal Product

IRAS – Integrated Research Application System

IRMER – Ionising Radiation (Medical Exposure) Regulations

IVRS – Interactive Voice Response System

mCTA – model Clinical Trial Agreement

MDC – Medical Device Committee

MHRA – Medicines and Healthcare Products Regulatory Agency

MHRA CTA – Medicines and Healthcare Products Regulatory Agency Clinical Trial Authorisation

MPE – Medical Physics Expert

MRI – Magnetic Resonance Imaging scan

MUGA – Multigated Acquisition scan

NIHR – National Institute for Health Research

NRES – National Research Ethics Service

PET – Positron Emission Tomography Scan

PI – Principal Investigator

PIS – Patient Information Sheet

QP – Qualified Person

REC – Research Ethics Committee

SDV – Source Data Verification

SIV – Site Initiation Visit

SmPC – Summary of Product Characteristics

SOP – Standard Operating Procedure

SSI – Site Specific Information

STC – Senior Trial Coordinator

TC – Trial Coordinator

TSM – Trial Set up Meeting

UKCRN – UK Clinical Research Network

Useful websites

Further information on the NIHR GCP training can be found here: www.crn.nihr.ac.uk/learning-development/good-clinical-practice/

Further information about IRMER compliance can be found at: www.nres.nhs.uk/applications/approval-requirements/ethical-review-requirements/requirements-for-ethical-review-under-legislation/exposure-to-ionising-radiation/

Further guidance regarding ARSAC can be found here: www.gov.uk/government/organisations/administration-of-radioactive-substances-advisory-committee

The latest version of the NIHR UKCRN costing template can be found here at: www.crn.nihr.ac.uk/can-help/life-sciences-industry/setup-service/

The mCTA template is available at: www.nihr.ac.uk/industry/industry-tools.htm

Further information about CSP is available here: www.crn.nihr.ac.uk/can-help/funders-academics/gaining-nhs-permissions/

Further information about the London South CRN and contact details can be found here: www.crn.nihr.ac.uk/south-london/

