**Items that a CI should consider when taking on the role**

# Items that a CI should consider when taking on the role in addition to the legal responsibilities of a CI as defined in the UK.

# The list below states some tasks/responsibilities that might be required from a CI by the trials group co-ordinating a trial – note this list is not exhaustive and will be dependent upon both the trial, trials group and CI.

# *Note: It is meant to provide food for thought for all parties – this is not a mandated list of actions/tasks required*.

**At all times, the CI should:**

* Communicate key decisions with OCTRU senior staff.
* Ensure that the Trial Manager is copied into all key communications throughout the trial.
* Defend the trial and represents the Trial Group and OCTRU positively at all required reviews (peer review, grant submission, Research Ethics Committee (REC), collaborators meetings, trial set-up meeting, audit, inspections etc.) and to the research community.
* Provide clinical and scientific leadership and will sign-off the protocol and trial related materials as required and in a timely fashion.
* Oversee the Trial Management Group (TMG) ensuring it is properly constituted, meets regularly and is responsive to all regulatory, clinical and performance issues arising in the running of the trial.
* Oversee recruitment and delivery of the trial not only within their own centre (if applicable) but at all participating sites by acting as a positive role model and assisting site Principal Investigators (PIs) with problem solving at their local site if requested by the trial team.
* Support trial staff in complying with SOPs and processes.
* Ensure safety monitoring and data quality are being reviewed throughout the trial at TMG meetings, and that any trends acted upon appropriately.
* Engage with trial group staff and the Sponsor to respond to queries promptly in order to drive a timely progression of the trial from concept to completion and, in doing so, treats the trial group staff with respect.
* Be available to the trial team for meetings, questions and for document writing, review and sign off. CI sign-off is often required to evidence the CI’s agreement with the documentation or instruction put in place for his/her trial.
* Provide or arrange more detailed training and information for trial specific staff particularly if the trial involves a new disease area/type or novel treatment or intervention.

**During trial development and set-up**

* Originate the research idea and concept for trial design.
* Present the trial at internal peer review meetings and at external meetings as required. Work with Trial Development Teams to finalise all aspects of trial design, in light of input from internal and external review.
* Generate (with collaborators as necessary) ideas for translational research studies within the trial (as applicable and as appropriate).

**Funding**

* Identify areas of cost with the Trials Group and supporting finance staff to develop the budget for the trial if requested.
* For trials requiring external funding, work with the Trials Group to develop grant submissions, being primarily responsible for scientific rationale, clinical relevance, clinical feasibility, schedule of tests/events and recruitment strategy.

**External collaborations**

* Work with the Trials Group and contracts staff to negotiate and agree drug supplies that fall outside the normal drug requirements (if applicable).
* Work with the Trials Group to negotiate and agree supplies/services that fall outside the normal requirements e.g. pharmacy services, radiotherapy technique, provision of biomarker tests or imaging studies etc. (if applicable).
* Work with the Trials Group and Sponsor office to agree contracts required, providing input and review as requested.

**Setting up a trial (through to recruitment start)**

**Protocol**

* Ensure the protocol is written according to the current Trials Group protocol template and reviewed in compliance with OCTRU SOP: GEN-005 (Protocol Development).
* Take instruction and advice from experienced editors as necessary to produce a final draft protocol to agreed deadlines. The aim is to prioritise specified operational sections and identify/resolve any feasibility/resource problems early.
* Support the Trials Group as it co-ordinates and documents the protocol development process.

**Risk Assessment and Monitoring Plans**

The risk assessment is a process that identifies risks to research participants, data quality and successful delivery and agrees mitigating actions. Some assessment of risk may be done prior to a funding submission so that appropriate resources/funding can be requested.

* Support and provide clinical guidance in developing the risk assessment and monitoring plans.

**Ethics (all trials/studies) & MHRA (CTIMPs and Device trials that fall under the MHRA)**

This includes the preparation of the IRAS forms and supporting documents. The process is co-ordinated and documented by the Trials Group. However, the CI should:

* Input into and approve the submission bundle – this is essential.

**Pharmacovigilance/Safety**

The development of appropriate pharmacovigilance/safety systems prior to patient recruitment is essential. The CI must ensure arrangements for safety processing review and reporting are in place before the trial starts and the procedures specified in OCTRU SOP: GEN-013 (Safety oversight: Pre-trial activities) are adhered to. However, the CI:

* Provides clinical guidance to the content of reporting documentation.
* Supports the Trials Group in designing appropriate codebreak procedures (if required by the trial).

**Site set up**

* Contribute to identification of trial sites by confirming facilities and experience required.
* Answer questions raised during the selection and set-up of trial sites.

**Trial contracts/agreements**

The Trials Group will arrange for appropriate Sponsor delegation documents to be prepared for signature by the CI and the Trials Group will co-ordinate this process. However, the CI should:

* Give clinical guidance and input into contracts as requested.
* Input into the review and agreement of contracts with third parties (e.g. labs, drug providers) (as requested) as these often affect the way in which the trial will run and place particular responsibilities on the CI.

**CVs & GCP training**

* Provide a valid GCP CV to the Trials Group.
* Provide written evidence of recent GCP training – essential for a CTIMP, good practice for any other research.

**Data management**

* Input into the design of Case Report Forms (CRFs) is essential to agree what data are to be collected at what time points and in what format.
* This will be a multi-stage process and will involve review by the CI, TM team and Trial Statistician to ensure accuracy and appropriateness of the final version. CI approval of CRFs must be documented before the trial opens to recruitment and there should be no ambiguity in the protocol about which CRFs are required at what time points throughout the trial.

**Trial committees (where applicable)**

* Identify and invite co-applicants.
* Help identify and invite members for each committee (e.g. Data and Safety Monitoring Committee (DSMC), Trial Steering Committee (TSC)). Trials Group will document membership and arrangements in the TMF.

**Samples (where applicable)**

There is a need for clear processes for the collection, processing and storage of samples and these must be in place whether collected for assessment of eligibility, trial endpoints or exploratory sub-studies. To aid this, sample collection kits need to be available (where applicable). In addition, the CI should:

* Ensure that there is an appropriate lab/sample handling manual.
* Ensure that appropriate systems are in place for tracking of samples.

Although it should be noted that the responsibilities for these tasks may be delegated to a collaborator or other party.

**Radiotherapy and Imaging (where applicable)**

* Prepare detailed radiotherapy (RT) protocol.
* Agree RT protocol with Trials Group.
* Develop radiation therapy quality assurance (RT QA) plan in consultation with The National Cancer Research Institute Radiotherapy Trial Quality Assurance (NCRI RTTQA) group if multi-centre trial or with RT physics locally.
* Agree imaging protocols.
* Ensure radiation protection advice has been obtained and all necessary permissions are in place for extra trial based radiation exposures.
* Agree data and image storage requirements for both imaging and RT planning.

**During the trial:**

**Pharmacovigilance/safety procedures** (arrangements for safety reporting will vary from trial to trial but it is likely that the following tasks will require CI input)

* Review SAEs reported for trial patients on a regular basis if this model was agreed to be used prior to the start of the trial. The frequency of review will be indicated by the risk assessment of the trial and may change during the trial as new safety information emerges.
* Support the Trials Group staff in the review and interpretation of SAE reports.
* Review AEs for trends and patterns.
* Confirm the System Organ Classification (SOC) of the individual SAE reports as per Common Terminology Criteria for Adverse Events (CTCAE) where required and if applicable.
  + - On an annual basis, review sections of the Development Safety Update Report (DSUR) (for CTIMPs), in particular the section on ongoing risk:benefit ratio (TM team can prepare background and tables of events). The CI must sign the DSUR prior to submission.
    - Reviews changes to Investigator Brochures (IBs) and/or Summary of Product Characteristics (SmPCs) to determine effect on risk/benefit of the IMP(s) and must prepare communication to the sites if there is a need to do so based on new information arising for CTIMPs.
    - Supports the Trial Group in implementing appropriate actions.
  + Answer queries about patients’ eligibility and treatment as required.
  + Discuss any proposed updates to the protocol with the Trials Group and Trial Statistician. Support with the amendment, review and sign-off of associated documents.
  + Review and approve any updated CRFs as required.
  + Contact site PIs to address particular concerns (e.g. in the event of safety concerns, persistent protocol deviations or violations, poor data return) or to highlight outstanding performance as required.
  + Support the Trials Group in developing and implementing recruitment strategies.
  + Maintain regular contact with the Trials Group, ensuring that they are aware of times when the CI will not be contactable (ideally suggesting alternative clinicians to provide appropriate cover).
  + Review update reports (e.g. for trial committees, funding bodies).
  + Oversee the TMG and ensure that regular meetings are held.
  + Review and sign-off Annual Progress Reports for REC.
  + Be available to discuss the management of deviations/violations and serious breaches of the protocol and GCP.
  + Be available for audits and inspections.
  + Review the statistical analysis plan (SAP) with Trial Statistician throughout trial and prior to final analysis.
  + Ensure that requests and correspondence relating to trial funding are provided to the Trials Group in a timely manner.
  + Give as much notice as possible of reports he/she needs the Trials Group to prepare or submit on his/her behalf (e.g. annual reports to funders, updates to collaborating companies).
  + Ensure that the Trial Statistician and Co-ordinator are informed in good time to provide data for any proposed publication or presentations relating to the trial. Analysis must comply with protocol, statistical plan, trial publication policy and the terms of any trial agreement with a third party.
  + Work with the Trials Group and Sponsor to assess and resolve concerns/complaints relating to the trial.

**At trial closure and in preparation for archive:**

* Write with the Trial Statistician, the manuscript(s) arising from the data, and ensure submission for publication of at a minimum the trial’s primary outcome ideally in high impact peer reviewed journal in a timely fashion and in line with contractual agreements.
* Lead and co-ordinate all translational activity related to the trial (biomarkers, imaging etc), maximising benefit from the trial in terms of added value publications etc, unless this has been specifically delegated to another individual or is not applicable to the trial.
* Remain supportive of any queries raised by sites where the Trials Group need support or information from the CI.
* Ensure that the Trials Group are notified of any publication/presentation resulting directly or indirectly from the data and/or samples collected as part of the trial.