UKCRC Registered Clinical Trials Units

UKCRC Registered CTU Network – Tasks considered by Trial Management teams to be highly resource intensive: A review

UK Clinical Research Collaboration

igniting our potential

Tasks considered by Trial Management teams to be highly resource intensive: A review

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1. Abbreviations

CPMS – Central Portfolio Management System

CRF – Case Report Form

CRN – NIHR Clinical Research Network

CTIMP - Clinical Trial of an Investigational Medicinal Product

CTU – Clinical Trials Unit

CV – Curriculum Vitae

DMC – Data Monitoring Committee

DSA – Data Sharing Agreement

GCP – Good Clinical Practice

HEI – Higher Education Institute

HRA – Health Research Authority

IRAS – Integrated Research Application System

NIHR – National Institute for Health and Care Research

MHRA – Medicines and Healthcare products Regulatory Agency

MTA – Material Transfer Agreements

Non-CTIMP – not a Clinical Trial of an Investigational Medicinal Product

PI – Principal Investigator

PMG - Project Management Group

REC – Research Ethics Committee

SIV - Site Initiation Visit

SoECAT – Schedule of Events Cost Attribution Template

SOP – Standard Operating Procedure

TM Ops – UKCRC Registered CTU Network Trial Management Operations Group

TMC – Trial Management Committee

TMF – Trial Master File

TMRP - MRC-NIHR Trials Methodology Research Partnership

TSC – Trial Steering Committee

UKCRC - UK Clinical Research Collaboration

UKTMN – UK Trial Managers' Network

2. Introduction

The UKCRC Trial Management Operations (TM Ops) Group aimed to explore the development and sharing of best practice in trial management and enable networking and learning for trial managers working across the UKCRC CTU network.

To this aim, the group were aware through meeting members and anecdotal evidence, that there are tasks undertaken that felt like 'tick box' exercises. The TM Ops group sought to consider how risk adaptive approaches could improve trial management processes within CTUs for highly resource intensive activities by surveying the UKCRCs Registered CTUs trial manager representative.

3. Methods

3.1. Survey

Aim: To identify activities within trials that take a lot of time or resource and where they are considered by Trial Managers not to add value to the quality of the trial, safety of trial participants or the trial endpoints.

Method: A survey was conducted (see Appendix 1) using JISC Online Surveys [formerly Bristol Online Surveys] and circulated to all UKCRC Registered CTUs via the Network's Trial Managers JISCMail list in May 2022 requesting one response from each CTU.

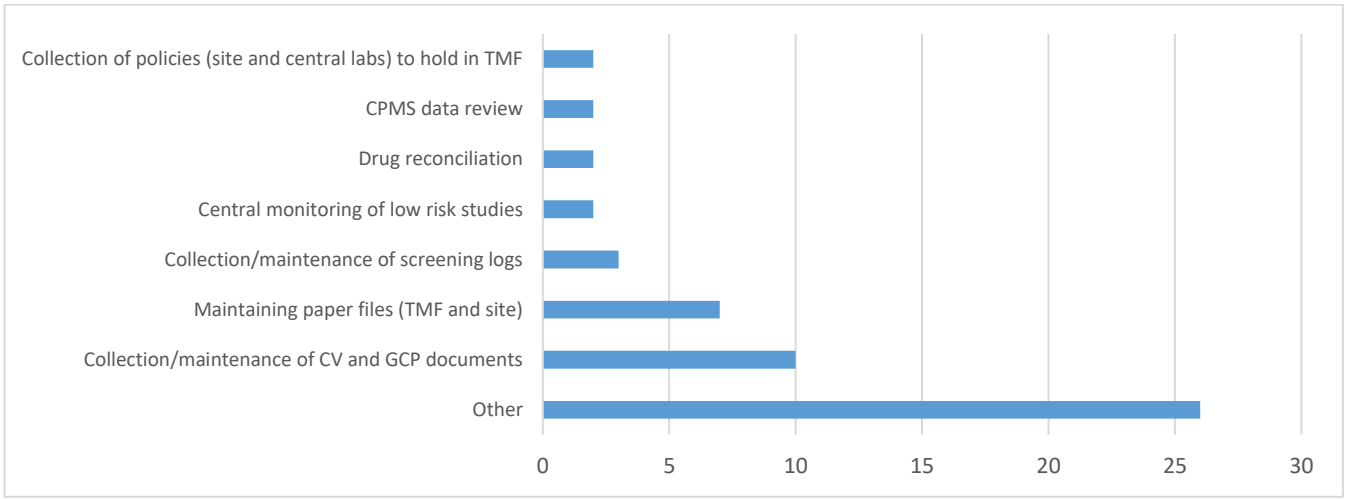
Results: The survey was open to be completed between 09 May 2022 and 27 May 2022.

34 responses were received from the 52 registered units at the time of the survey distribution, although 2 did not consent to their data being aggregated for presentation. Results will be presented from the 32 consenting responses (units).

81% of respondents were trial managers. 90% of responders were based in HEI and the CTUs varied in staff size (25% up to 25; 12.5% 26-50; 46.9% 51-100 and 15.6% 100+)

Respondents were asked to identify two trial management activities they perform that they felt were resource intensive and to which they considered have little value. 54 activities were recorded by respondents.

Figure 1: Bar chart showing activities CTU staff consider to be resource intensive and of little value and the number of units that cited the activity as part of its ability to nominate two



26 activities were recorded as 'other' as they were all different activities although many mentioned 'duplication' in terms of where things are filed and/or reported to. 'Other' activities are tabled in Appendix 2.

Collection and maintenance of CV and/or GCP certificates was the single most reported activity (10 of 32 responders). Maintaining paper files, both the TMF at the CTU and provision of paper site files to participating sites was reported by 7 responders.

75% (24 of 32) responders cited either CTU SOPs, Sponsor, GCP or regulations as the reason for performing their activity. Of those reporting collection/maintenance of CV and GCP documents all cited CTU SOPs, Sponsor, GCP or regulations as the reason for the activity.

Conclusion: On review of the data, the collection of CVs and GCP certificates was highlighted as an area to discuss further. Whilst continuation of paper filing systems is an area to look at further, this was already being taken forward by the UKCRC Registered CTU Network Policy Group and other groups looking at e-technologies.

3.2. UK CRC Trial Management Operations National Meeting 2023: Breakout sessions

To learn more about how CTUs process and collect CV and GCP evidence breakout sessions were used at the national Trial Management Operations annual meeting to discuss this topic with representatives from CTUs. 31 delegates attended the meeting representing 24 CTUs.

Method: A sheet of topic questions was given to each table (Appendix 3). Approximately 45 minutes were scheduled for table discussion with 15 minutes for feedback to the room after. After the meeting, the comments were collated and summarised.

Summary of discussions for each topic:

- ***Topic 1 CVs: Demonstrating appropriate qualifications and experience***
    - Most CTUs collected some CVs for site staff. Some CTUs focused collection to just the site PI but others collected for all staff listed on the delegation log. Variation in whether long/short CV.
    - Some CTUs simply collected and filed the CV others checked for evidence of GMC number, GCP training, date/signature. The level of checking of CVs varied and it wasn't always clear what CTU staff were expected/required to check on review.
    - 1 CTU had been inspected twice, they only collect PI CV and there were no findings.
    - The majority of attendees stated that they had the same approach to CTIMPs and non-CTIMPs.
    - Discussion considered the responsibility for demonstrating qualifications / experience is the responsibility of the employer (NHS Trust) and through the site agreement.

- ***Topic 2: Evidencing GCP Training***
    - Most CTUs collated some GCP certificates. There was a slight variation across the discussions, with some stated that in non-CTIMPs they chased for these less.

- Units varied as to whose is collected depending on their role in the trial – there was no consistency across units
- Some CTUs (either their own SOPs or the sponsors SOPs) required evidence of GCP training to be updated (at set intervals), others considered the employer of the staff member to be responsible for ensuring GCP training remains current as per their own Trust policy
- Discussion as to how formal GCP training given – online is easy to cheat but in person is variable in quality
- Some CTUs incorporate key GCP activities within SIV slides
- Time consuming for CTU staff to monitor
- Considered should push to employing institution to be responsible and/or have a central system (e.g. NHS Gateway) which could log GCP and flag when it needs updating.

4. Conclusion:

Suitability and training of site staff is well recognised as the responsibility of the Principal Investigator at site, and this is usually documented via an agreement between the participating site and the sponsor.

The collection of CVs and GCP evidence by CTUs was confirmed as an area that required high resource and is potentially not the role of CTUs. ICH E6(R3) does state in its essential records table that there should be relevant documents evidencing qualifications of investigator(s) and sub-investigator(s) involved in conducting the trial, but it does not state that these need to all be held by the CTU. Some staff from CTUs performed the activity as they considered it was required to ensure full compliance with regulations and trials guidance/SOPs, whereas others felt that all of this documentation did not need to be held centrally.

The UKCRC TM Ops group concluded that CTUs should consider a risk-adapted approach for collection and review of curriculum vitaes and GCP certificates centrally. This risk-adapted approach should continue alongside the implementation of the new Clinical Trial Regulations and Guidance with CTUs balancing the resources available to ensure the delivery of the trial and whether the collection centrally is required.

Appendix 1 – Survey on Resource Intensive Activities – April 2022

Page 1

Thank you to those who completed our previous scoping survey to identify key strategic and operational issues that present a challenge to efficient trial management. The key findings from this were:

- **Recruitment, retention and career development for CTU staff** – The Network has established a group to take this forward and potential activities are currently being scoped in light of the ongoing changes to the research landscape. More information will follow in due course. The TM Ops group will also be liaising with the UKTMN in line with their professional development strategy.

- **Identification and implementation of e-trial technologies** – Some activities in this space are being taken forward by other Network Groups and collaborations including the project on eConsent are being undertaken collaboratively with the UKTMN and the TMRP.

- **Securing sufficient resource and funding to deliver the trial** – the TM Ops Group has escalated these concerns to CTU Directors, the Executive Group, and other key stakeholders. We are pleased to note that the NIHR has released data underlining the value of CTUs. Directors will be working on ways to promote this information.

- **Updates to approval processes (frequency and changes)** – The Group has representation on the HRA Partnership Board through Lucy Culliford (Bristol Trials Centre), which allows CTU concerns to be raised in a timely manner. We have also established direct links with the HRA and NIHR regarding key projects.

The remit of the UKCRC CTU Network Trial Management Ops group is to improve trial management working practices by identifying and sharing good practice. We are aware through meeting with you and in our own work that there are tasks we all undertake that feel like 'tick box' exercises. The TM Ops group would now like to consider how risk adaptive approaches could improve trial management processes within a CTU for highly resource intensive activities.

Please tell us about 2 activities within your trials that take a lot of time or resource and where you don't consider that (or aren't sure if) they add value to the quality of the trial, safety of trial participants or the trial endpoints. You may also be unsure as to if/why they are needed, such as collecting CVs for site staff and logging their receipt.

Responses to this survey are anonymous. However, we have included some (optional) questions about your CTU and your role to help us understand more about the responses. Alternatively, if you would like to discuss your responses in more detail, please include your contact details in the field below.

The deadline for responses is Friday 27 May 2022.

I am happy for my responses to this survey to be included in aggregated data presented by Network representatives at national meetings or conferences.

- ○ Yes
- ○ No

If you would be happy to discuss your responses in more detail please put your name and email address here.

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What is your role in your unit

- ○ Trial Manager
- ○ Data Manager
- ○ Administrator
- ○ Other

If you selected Other, please specify:

How large is your CTU? (approximate)

- ○ Up to 25 staff
- ○ 26 to 50 staff
- ○ 51 - 100 staff
- ○ 100+ staff

What type of host institution is your CTU based in?

- ○ HEI
- ○ NHS
- ○ Other

If you selected Other, please specify:

Page 3: Activity 1

What trial management activity do you do that is resource intensive that you think has little value?

Please specify why you do this activity. (e.g. CTU SOPs state should be done, sponsor office requirement etc.)

Page 4: Activity 2

What trial management activity do you do that is resource intensive that you think has little value?

Please specify why you do this activity. (e.g. CTU SOPs state should be done, sponsor office requirement etc.)

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Many thanks for completing this survey.

Appendix 2 – 'Other' Activities

26 verbatim responses coded as 'other' in answer to 'What trial management activity do you do that is resource intensive that you think has little value?'

Internal trial PMG meeting minute takes a lot of resource as it is more than just go through "to do list". Sometimes internal meeting is all about politics game and as a minute taker, it takes extra time to make "official minute" more politically correct when I can spare the resource elsewhere. Wonder if there is any way of having progress chart etc to keep the meeting focused.
(1) Dealing with MTA/DSAs regarding samples attached to trials for other applicants who wish to use these for other research (2) Sorting out issues with translational samples and getting them to labs etc in time when there are public holidays (3) Arranging study specific meetings
Trial Master File: filing and tracking
Nothing specific, but there is a lot of admin associated with Trial Management which is incredibly time consuming.
Completing the SoECAT.
Creating spreadsheet trackers where there is no standard template available
Collecting delegation logs with handwritten signatures!!
In person SIVs
Risk assessments and mitigation plans for phase 3 trials using licensed products, has to be completed every time an amendment is made and/or annually - incredibly time intensive and often of little value as so little changes - feels very much like a tick box activity
Completing all the different types of reports, everyone seems to have a different format, funder reports, TSC/DMC/TMG reports, reports to the sponsor, REC, MHRA
Amendment and contract amendment for PI changes
This is probable mostly a Monitors activity, but at smaller units such as ours, we do not have separate monitors so the TMs do monitoring too. Checking / completion of site files for all documentation is very labour intensive. Most sites due to workload are not able to keep site files up to date, so it falls to the monitor to do so at monitoring visits or prior to audits / inspections etc. The checking / printing / filing of documents is the bulk of the job, and takes so much time. Removes time for any thought processes about what is actually happening within the site, and conversations about the study with the clinical teams.
Manually tracking and filing individual documents. This could be done much more rapidly using an intelligent platform. e.g. alerting staff when their GCP is close to renewal.
Multiple documents having to go to each site, it would be great to centralise this

Maintaining financial records separate to institutional records because the institutional records are often not fit for purpose (contain sufficient detail) when it comes to financial reconciliation
Completing different data protection impact assessments, data management plans, outlines of data management for IRAS, etc - information is often duplicated across documents. Having a data management plan and doing due diligence around this is important, but satisfying all the different bodies' requirements for documenting this is time-consuming and also increases the likelihood of inconsistency between documents.
Repetitive CRN meetings
10% data check from experienced data entry personnel
Ensuring PI sign off on CRFs - this doesn't seem to add any value to the study (and is therefore often treated as a "tick box" - or "sign here" activity)
Completing internal forms that duplicate information in regulatory forms e.g. internal amendment forms that duplicate information in the IRAS form or amendment tool
Obtaining signatures for forms and documents, and authorisations that I can use/insert signature images, and saving the authorisation for each person/document (surely there is an easier way, e.g. DocuSign?)
If the data on a paper CRF has been amended by the site, but the change has not been initialled and/or dated, we have to ask the site to initial/date and re-send the CRF, even if the corrected data is clear and unambiguous. This generates a lot of queries and is time consuming for us and the sites.
SOPs, reviewing SOPs so frequently is frustrating and takes up a lot of time
Manned randomisation lines
Reading all SOPs when the timing is not relevant, e.g. reading about study closedown at the start of a 5 years project
Submission of changes in PI as amendments (especially if before site activation)

Appendix 3 –Topics for discussion at breakout sessions

TOPIC 1: Demonstrating appropriate qualifications and experience

CVs are a common method for demonstrating trial staff are suitably qualified and experienced for their role. Site staff CVs may be collated centrally by the CTU or locally at site level.

a. Do you collate CVs for site staff at your CTU?

b. Do you use any other methods of demonstrating qualifications/experience instead of a CV? If so:
   - Has there been any feedback on this from regulators following an inspection?
   - Has there been any pushback from stakeholders?

c. Do you treat staff working on CTIMPs and non-CTIMPs differently?

d. Can you think of other ways of complying with GCP/legislation without the use of a CV?

TOPIC 2: Evidencing GCP Training

GCP training repeated every 2/3 years is often used to fulfil the need for trials staff to be 'suitably trained'. GCP certificates for site staff may be collated centrally by a CTU or locally at a site level.

a. Do you collate GCP certificates for site staff at your CTU?

b. Do you have a requirement that all or some site staff are GCP trained? Do you have a requirement that GCP training is repeated at regular intervals?

c. Do you use any alternatives to full GCP training? If so,
   - has there been any feedback on this from regulators following an inspection?
   - Has there been any pushback from stakeholders?

d. Do you treat staff working on CTIMPs and non-CTIMPs differently?

e. Can you think of alternatives that would comply with GCP/legislation?