GUIDANCE FOR CTUS UNDERTAKING COVID19 CONTINGENCY PLANNING

This UKCRC CTU Network guidance has been developed for CTUs in consultation with regulators, funders and the Department of Health to provide advice on assessing priorities and operating in a risk proportionate way during the Covid19 pandemic and to ensure a joined-up approach across the system.

There will be large pressure on the NHS and other healthcare systems during the Covid19 pandemic that may fluctuate over time, between regions and patient populations and may last for up to 6 months. The expectation is that business as usual can continue after pressures have been relieved.

Throughout consultation it has been agreed by all that research sites are in the best place to decide their own policies on capacity and capability to undertake research during this period and are responsible for the safe care and treatment of their own patients.

The key message from all parties is that flexibility throughout clinical trials systems and processes, is key throughout the pandemic to enable COVID19 research and the ongoing safety of participants already on trials to be prioritised and to minimise the burden on the NHS.

All parties have agreed that continuing dialogue is essential as the situation unfolds. The role of the UKCRC CTU Network is to speak with one voice, on behalf of CTUs to regulators, funders and the Department of Health and to act as a conduit for information to CTUs from these parties.

The following provides advice and considerations for academic clinical trials at this time to ensure that patient safety within clinical trials is maintained.

1. Business Planning

CTUs will already have Business Continuity Policies and Plans in place. These should be reviewed to ensure they are up to date and tested against the expected scenarios. Expected scenarios that could be faced by CTUs during the Covid19 pandemic are likely to include:

- Staff shortage due to illness or caring responsibilities.
- Clinical overload, both on the trial research team and at research sites.
- Supply chain difficulties.
- IT problems, specifically pressure on IT systems that are not designed to support the expected increased demand for remote working.
- Communication problems with suppliers, the NHS, collaborators, Chief Investigator.
- Travel restrictions.

Actions to support CTU continuity and sustainability

I. Identify a Business Continuity Team including members of staff who can represent each part of the business, including delegates.

II. Identify trial and business activities that are critical to ensure ongoing patient safety and ensure these can continue during each scenario.
III. Identify activities and actions needed to prevent irreversible disruption to critical activities.
IV. Identify non-critical activities.

Consider

Do you have any single points of failure?
Do you have additional requirements for staff back up & extra training?
Are business documents up to date and accessible to the Business Continuity Team (staff lists, trial lists)?
Are trial documents up to date and accessible to other members of staff (in case cross cover is required?)
Are there unnecessary barriers to accessing information that people will need to perform their duties?
Are your IT systems and equipment fit able to cope with additional new demands, such as remote working?
Are there risks to accessing your offices / estates and what would you do if this was limited?

2. Principles for Prioritising Trial Conduct during Covid19

❖ **Patient safety is paramount.**

Depending upon the risk of the trial (e.g. phase, intervention, complexity, setting, patient population), critical activities to ensure patient safety are likely to include:

- Ensuring continuity of trial supplies.
- Ensuring continuity of tests / results that inform ongoing treatment decisions.
- Pharmacovigilance including independent safety oversight (Safety Review Committees and DMCs).
- Maintaining clinical oversight of trial participants and changes to their treatment / care pathway.
- Onsite triggered monitoring for patient safety purposes only.

❖ **The integrity of sites, Sponsors, and trial teams is important (including compliance with national guidelines and policy).**

- Actions should be proportionate to the need and research site capacity. **Do not create additional work for trial research sites.**
- Data quality for ongoing clinical trials is important and approaches may need to be changed to reflect the fact patients may not be able to attend clinical visits. Other options should be explored which do not add additional burden to research sites.

- Delays to obtaining data are expected and unless the data is for safety purposes research sites should not be chased to return data where they have capacity issues.

❖ **Protocol and Regulatory compliance**

The following issues have been agreed with the MHRA:

Research sites may need to make decisions to protect patient safety that are not in line with the protocol. These should be documented and a proportionate approach taken when assessing whether these meet the definition of an urgent safety measure. For example: On some Type A/B trials where the treatment profile is well understood and the treatment can be transported and stored at ambient temperature, research sites may make the decision to send chemotherapy treatment to the patient to take at home, therefore pre-treatment bloods are not able to be taken prior to treatment commencing. Unless the Sponsor does not agree with this approach, this would not be classed as an urgent safety measure but should instead be recorded as a site level deviation. The MHRA have indicated they would be willing to work with CTUs to develop scenarios about risk proportionate approaches to add to their blog.

Capacity issues may prevent timely reporting of SAEs, DSURs and End of Trial Reports. Where this occurs they should be reported as soon as possible after the capacity issue is resolved. Deviation from protocol defined timelines for these does not require a trial amendment.

Emails are permitted to be used in place of wet ink signatures where it is not possible to obtain a wet ink signature in a timely manner.

Online guidance from the MHRA can be found here: Managing clinical trials during Coronavirus (COVID-19.

The following issues have been agreed with the HRA:

Due to capacity issues, research sites may temporarily halt recruitment into a trial. Even where all sites temporarily halt recruitment at the same time, unless the Sponsor officially decides to halt recruitment into the trial this does not require a trial amendment.

There may be cases where certain communications to trial participants from Sponsors / CTUs does not require a substantial amendment. The HRA have indicated they would be willing to work with CTUs to develop scenarios about risk proportionate approaches to add to their guidance.

Online guidance from the HRA can be found here: Health Research Authority - COVID-19: Guidance for sponsors, sites and researchers.

❖ **Matters of importance to the MHRA (for CTIMPs)**

MHRA have indicated that the following is important for them:

Timely reporting of SUSAR and other safety events / incidents which put participant safety at risk on a trial or have the potential to impact participants of other trials e.g. a new safety signal relating to Covid19.

Amendments or Urgent safety measures taken by Sponsors to protect participant safety such as closing a whole trial due to serious incidents resulting from insufficient capacity.

3. Operational Considerations

Contact your Sponsor, Chief Investigator (and TMG as necessary) to discuss trial continuity and specific risks

- **Does your trial needs to officially close to recruitment and if so, the reason why.** Note: consider the work involved in closing / halting and then reopening trials and whether it is only necessary to officially close those trials where there is a specific safety concern e.g. that key safety checks could not be made or where trial supplies or central laboratory testing required to inform treatment cannot be maintained.
- **Do you have sufficient clinical cover in the absence of the CI**, is this information known to all relevant people and documented in your TMF?
- **Are there any other specific risks to patient safety or serious risks to data quality and what is the plan to mitigate these?**
- **Do patients need specific communications?**

Check:

- **Are there any potential trial supplies issues?** If you have supplies planned during the next 6 months speak to your supplier / distributor to determine whether there are any risks to trial supplies and agree mitigation strategies. What if distributors become overwhelmed? Can you increase stocks at your distributors or sites to cover the period of disruption?
- **Are there any central laboratory test issues?** E.g. how will you deal with labs becoming overwhelmed?
- **Do you need to talk to contract holders to seek additional flexibility with contractual terms and conditions?**
- **Are your trial documents, Work Instructions and contacts up to date?**
- **Are the lines of communication between the trial team and trial sites clear?** Are there any unnecessary barriers which need to be resolved, if so how will this be achieved and by when?

Plan for More Remote Working

- Can you support virtual meetings?

- When supporting staff to work from home ensure that information governance is not compromised and that any changes to working practice are in line with host institution policies.
- Think about any tasks that could not be done virtually/from home, are these critical and need another solution or could be postponed or not done.
- Plan for the return to work and business as usual. This will mean factoring in dealing with any back logs that need to be tackled e.g. if paper based follow-up is conducted centrally by the CTU plan how this will be tackled on the return to the office
- Can paper based questionnaires be sent out early before working from home is mandated?
- Are there suitable answer machine messages on all office-based phones to direct enquiries?
- Speak to your institution about how to facilitate home working. (The UKCRC Network is preparing a letter for Directors to use to help raise the profile of CTU requirements within host institutions; this will be available next week)

Funding

NIHR will be issuing guidance on Monday and will be reassuring that payments will continue unless a specific contractor indicates otherwise. NIHR HTA has indicated additional flexibility with funding deadlines to support researchers in ensuring longer term business continuity. You may wish to check with other funders e.g. charity or industry.

Regulator and funder specific guidance can also be found online including:

MHRA Inspectorate - Managing clinical trials during Coronavirus (COVID-19) (https://www.gov.uk/guidance/managing-clinical-trials-during-coronavirus-covid-19)

MHRA Inspectorate - Clinical trials applications for Coronavirus (COVID-19) (https://www.gov.uk/guidance/clinical-trials-applications-for-coronavirus-covid-19)

Health Research Authority - COVID-19: Guidance for sponsors, sites and researchers (https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/covid-19-guidance-sponsors-sites-and-researchers/)

NIHR - Q&A on the impact of COVID-19 on research funded or supported by NIHR (https://www.nihr.ac.uk/documents/qanda-on-the-impact-of-covid-19-on-research-funded-orsupported-by-nihr/24467)

Health and Care Research Wales - COVID-19 Statement & Updates (https://www.healthandcareresearch.gov.wales/covid-19-updates/)

FDA - Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic - Guidance for Industry, Investigators, and Institutional Review Boards (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-pandemic)