Western Health

Western Health
Contingency Plan for COVID-19 Interruption to Research and Clinical Trials

Date: 23 March 2020

COVID-19 has and will continue to bring about considerable changes to how we conduct our daily activities, with further changes anticipated over the coming weeks. As a result, all departments that have research and clinical trials underway must ensure that they have appropriate contingencies in place to ensure that the safety and wellbeing of participants is upheld, and that staff are not unnecessarily placed in harm's way or resources unduly expended during these challenging times. The contingencies will also aim to help maintain trial activity for as long as possible during these challenging times. Keeping our sponsors informed of how our contingency directives may affect our obligations to them will be essential in ensuring that we minimise disruption to existing and planned trials and working with them in adapting for sustainable solutions.

It is critical that research teams *continue to effectively* communicate with participants on how the pandemic may affect their participation in a trial/project and what contingencies could be put in place to ensure their safety, wellbeing and as far as possible their continuance on the trial/project. Where certain research activities can be conducted remotely, this should be promoted and agreed with the sponsor as well.

Research teams *should start considering* at what point they should enter a 'maintenance' phase for their existing projects and restrict active recruitment or the commencement of new projects, unless the protocol can be accommodated under the anticipated contingency measures or sponsor has made special provisions. However, it is encouraged that research teams continue to work up new trials/projects to the point of ethics and governance submission in anticipation of being ready to initiate new trials once the pandemic contingencies are lifted.

Studies that are recruiting from the community or volunteers must cease further recruitment unless study visits can be safely conducted away from any Western Health (WH) premises.

Commitments provided to trial/project sponsors should be prefaced on the possibility that clinical research staff may need to be deployed to deliver essential clinical services if the health care system is overwhelmed.

It is important that you contact your project sponsors to inform them of our proposed COVID-19 contingencies and the conduct of research activities during the active phase of the pandemic. It is critical that you also obtain from the sponsors their proposed contingency planning around:

- Any anticipated interruption in the supply of trial drugs or devices, central kits, study supplies, central labs, specimen shipping abroad and support to any trial specific portals
- unavoidable protocol breaches
- monitoring
- Site Initiation Visits (SIVs) completion
- Possible consenting approaches that would accommodate the COVID-19 'social distancing' or organisational/State quarantine provisions under the prevailing circumstances, and that would still be in alignment with Human Research Ethics Committee (HREC) approval and Good Clinical Practice (GCP) requirements.

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Please advise the sponsor and seek their approval for the follow <u>potential</u> WH research contingencies, <u>as will be determined by the WH Executive and Department of Health and Human Services (DHHS) directives</u> at various stages of the COVID-19 pandemic period.

Visitors not permitted to enter WH premises:

- Advise sponsor that a ban is now in place and seek approval in writing that the following procedures will be enacted:
    - All non-essential visit activities will be postponed
        - SIVs will be performed via phone in combination with information provided electronically
        - Monitoring visits postponed. Remote monitoring visits may be possible on an as need basis. Remote access to sponsors to EMR/BOSSnet is not possible.
        - SIVs will be postponed or completed via teleconference
        - Audits will be postponed

Non-essential visits (i.e. non treatment visits) are banned:

- Participants will be contacted by telephone by Research Nurses (RN), Principal Investigators (PI) or Study Investigators (SI) to conduct Adverse Event (AE) and concomitant medication assessments
- Participants will have pathology samples (e.g. bloods/urine) and ECGs testing taken at local pathology collection centres close to their home if practical
- Central laboratory blood collection may need to be suspended on non-dosing days
- Enrolment of participants to dose escalating studies will need to be discussed with sponsors on a case by case basis due to long Pharmacokinetics (PK) days and the protocol requirement of multiple visits
- *Access to oral drugs for participants will be discussed with sponsors on a case by case basis including dispensing of drugs, delivery of drugs via courier or increasing the amount of drug dispensed.
- Safety investigations will be prioritised, however longer visit windows for all other activity needs to be discussed with sponsors
- Participants requiring essential imaging may need to attend a local imaging centre

Clinical trial/Research participants that may have COVID-19 infection:

- Unless requiring admission, participants will not be allowed access to WH sites and won't attend any scheduled visits
- Investigators will maintain contact with the participant by phone during the period of isolation by a RN/PI or SI, particularly with respect to safety and treatment interruption
- Participants will not be allowed to visit local pathology centres, imaging centres or GPs, therefore local and central pathology will be curtailed during this period
- Efficacy visits will be delayed until the participant has recovered

Participant refusing to attend trial/project visits:

- AE and concomitant medication assessments may take place over the telephone by a RN, PI or SI of study
- have safety pathology completed in a local pathology collection centre
- ensure participants contact the site with any safety concerns
- *Access to oral drugs for participants will be discussed with sponsors on a case by case basis including dispensing of drugs, delivery of drugs via courier or increasing the amount of drug dispensed.
- Participants requiring essential imaging may need to attend a local imaging centre

- In exceptional circumstances, and will approval of the sponsor, a visit may be arranged at another site or facility.

***Access to Drugs for the Clinical Trial:**

- Oral drugs may be able to be couriered to participants depending on the drug and temperature requirements. This must be discussed with the sponsor first and then Clinical Trials Pharmacy. “Cc” Clinical Trials Pharmacy with the sponsor confirmation. Units will need to arrange courier services.
- Investigators should contact the sponsor to check availability of drug as drug manufacture and supply may be impacted.
- Additional storage of extra stock (especially refrigerated items) for the study will need to be discussed and approved by the Clinical Trials Senior Pharmacist as storage space is limited.
- Couriers may need to be organised by the local sponsor where indicated.
- Investigators considering provision of an increased amount of dispensed drug should contact the sponsor first and the Clinical Trials Pharmacist. “Cc” Clinical Trials Pharmacy for all communications between the sponsor and the investigator.
- Clinical staff assisting trial staff in dispensing trial drugs must be on the delegation log even if it is not signed by the PI, if the PI is unavailable.
- Investigators will need to consider contingency plans for the possibility that Clinical Trials Pharmacy staff are redeployed to other pharmacy services or are unable to provide a service. Such plans will need to be discussed and endorsed by the Senior Clinical Trials Pharmacist

Research staff may have COVID-19 and/or are unable to come to work:

- Research activity during the period of absences will need to be prioritised and reduced.
- The remaining staff priority will be to ensure that enrolled participants are reviewed and treated.
- If there is no research staff for a particular clinical trial/project, where permissible staff from other research units may need to assist to execute the minimum requirements to ensure continued participant safety.
- Research teams must also prepare for the fact that clinical research staff may need to be deployed to deliver essential clinical services if the health care system is overwhelmed.

The following may also be initiated, depending upon the number of research staff affected:

- All data entry reduced – priority will be given to essential Serious Adverse Event (SAE) reporting. AE reporting subject to resources
- All protocol amendments (unless directly related to patient safety) may be suspended
- All administrative tasks will be prioritised based on staff’s ability to perform such activities
- Research Governance Office (RGO) and ethics submissions for new projects may be delayed
- Data lock timelines not able to be adhered to.

Remote Monitoring of Clinical Trials during Covid-19 crisis as of 23 March 2019 until further notice and subject to staff availability.

Trial/Research Source Data:

Trial/Research staff will agree to provide scanned de-identified Source data that is needed for source data verification of Trial/project primary endpoints or SAEs. For example, in the setting of cancer trials:

- Primary endpoint: progression free survival – Scan reports, RECIST table
- Primary endpoint: Phase 1, safety and dosing – accountability logs, AE logs, SAE reports and supporting data.

Source data will also be supplied to verify eligibility where patient enrolment is still permitted. Data would need to be requested at least 5 business days ahead of the date the sponsor requires it so that it can be located, de-identified and scanned. ***Data requests should be kept to a minimum and should only be for 'critical or essential data" as sites must prioritise clinical activities over data at this very difficult time. For example requests for all routine lab data, fridge logs, machine calibration records are not essential and should not be requested until this current crisis is over.***

In the specific examples listed above, source data will be provided to sponsors without any fee being levied. Please note that all other requests for site staff to scan through study documentation will incur a fee, since they are outside of the scope of work as is detailed in our current clinical trial agreements, including drug accountability logs and other pharmacy logs. Extensive additional time spent on phone monitoring calls will also incur the fee. We will be keeping records of time spent and expect sponsors will be understanding of our request for reimbursement outside the scope of our agreements.

Staff time would be documented and billed to the Sponsor at $100 per hour plus overhead (excluding GST). If an hourly rate for remote monitoring requests is not already defined within the Clinical Trial Research Agreements (CTRA) (or equivalent) for that study, a CTRA Amendment may be implemented to incorporate this if the sponsors regard this as necessary. Requests will only be fulfilled once the site has received an agreement in writing from the sponsor to reimburse for these additional activities. An email acceptance will be sufficient,

Departments that use Site Docs for iSF, this can already be reviewed remotely and site staff will upload logs in future to enable these to be monitored. For those Sites that do not, requests from Sponsors for iSF documents to be scanned through (in lieu of on-site review) will also be billed at an hourly rate, as defined above.

For Western Health sponsored projects:
Coordinating site staff should implement contingency plans in respect to the above information and their obligations for safety monitoring.

Reporting to the Ethics Committee and Western Health RGO:
As this situation is unprecedented, it is acknowledged that protocol and GCP breaches are inevitable. There is no suitable guidance covering reporting currently available.

As safety in clinical trials and research is the priority, all significant safety issues, urgent safety measures and serious breaches impacting on participant safety and rights should be reported.

With respect to non-serious breaches, in lieu of reporting individual events, a post COVID-19 deviation report should be submitted after the situation has resolved.
The report will require summary information on:

- number of participants impacted
- changes to medication dispensing

- dose interruptions
- changes to visit schedule and visit activities
- use of external services (e.g. pathology, imaging, visit sites)
- missing data

Ethics and Governance Review

- The WH Low Risk Ethics Panel (LREP) and the Office for Research will continue to review and process applications however, the review of studies concerning COVID-19 will be expedited as required.
- Delays will occur in the processing of Quality Assurance (QA), LREP and Site Specific Assessment (SSA) submissions as staff and reviewers affected by this may not be able to process your submission within usual processing timelines.
- All submissions will be electronically processed during this time, please ensure that our Mandatory Electronic Naming Format is followed for all submissions.
- No phone calls will be manned during this time, please send all queries and correspondence to ethics@wh.org.au
- Only hardcopy contracts and agreements should be mailed to the Office for Research or dropped off in our Dropbox to ensure we comply with social distancing guidelines.

We thank you for your support of the Western Health contingency plan.

Yours sincerely,

Bill Karanatsios
Research Program Director
Western Health

Relevant links:

- DHHS Coronavirus Information: https://www.dhhs.vic.gov.au/victorian-public-coronavirus-disease-covid-19
- Australian Governance – Department of Health. Coronavirus (COVID-19) news & media: https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-news-and-media
- Western Health Novel Corona Virus Information: https://coronavirus.wh.org.au/
- FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic March 2020: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-pandemic