19th March 2020

Guidelines for COVID19 Interruption to Clinical Trials

Austin Health has provided this guidance document to support our researchers and clinicians conducting clinical trials at Austin Health. Advice will be updated and reviewed regularly as required.

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 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.

Contact your Sponsor

It is important that you contact your trial sponsors to inform them of Austin Health's proposed COVID-19 plan and the conduct of trial activities during the active phase of the pandemic. Sponsors should be advised that clinical research staff may need to be deployed to deliver essential clinical services if required.

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 and support to any trial specific portals
- unavoidable protocol breaches
- monitoring
- SIV 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 HREC approval and GCP requirements.

Changes effective from Friday 20th March 2020

New studies will not be permitted to commence until further notice.

- Exceptions may be granted for therapeutic COVID-19 trials. This will require executive approval.

Recruitment of new study participants is on hold effective from Friday 20th March 2020.

- This action has been taken to mitigate risks to participants and staff. It is possible that there may not be sufficient resources (eg. Diagnostic services, clinical workforce, pharmacy) to support additional trial participants. Exemptions may be considered under exceptional circumstances and will be approved by the COVID Clinical Trial Governance Group. Please contact Dr Sianna Panagiotopoulos (research@austin.org.au)

The following non-essential visit activities are all on hold effective 20th March 2020

- Monitoring visits postponed. Remote monitoring visits may be possible on an as need basis. Teams should explore this capability with sponsors and participants, subject to what hardware is required (i.e phone, computer with camera for TeleHealth etc))
- Site Selection Visits will be performed via phone in combination with information provided electronically
- Site Initiation Visits (SIV's) will be postponed or completed via teleconference
- Audits will be postponed

Participant Study visits and Risk Assessments

- It is important that you perform a risk assessment **24 hours before** a participant attends for a planned visit (see Appendix A), to determine if it is safe for participants to attend for that visit.
- It is important that you repeat a risk assessment **at the start of the planned** visit (see Appendix A)
- A carer for research participants must only attend the planned visit when absolutely necessary. A risk assessment should also be performed for the carer.
- If possible, consider telehealth options instead of face to face meetings.
- Adopt social distancing policies and ensure that waiting areas allow for this.
- Provisional approval will be given for face to face visits to be conducted via phone/telehealth. Clear documentation is required in the Medical record and case report form where this has taken place.

In the event that a Clinical Trial Participant refuses to attend trial visits:

- AE and concomitant medication assessments may take place over the telephone by a PI or study coordinators
- The safety pathology may be completed in a local pathology collection centre where possible
- Ensure that participants contact the site with any safety concerns
- To continue access to oral drugs for participants, you should discuss with the sponsor, on a case by case basis, whether dispensing of drugs via a courier or increasing the amount of drug dispensed is possible.
- Participants requiring essential imaging may need to attend a local imaging centre

In the event that Clinical trial participants may have COVID19 infection:

- Unless requiring admission, participants will not be allowed access to Austin Health sites and will not be able to attend any scheduled visits
- Investigators will maintain contact with the participant by phone during the period of isolation by a PI or study coordinator, 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

In the event that non-essential visits (i.e. non treatment visits) are banned:

- Participants will be contacted by telephone by, PI's or study coordinators to conduct 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 (where feasible)
- 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 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 via courier or increasing the amount of drug dispensed.
- Safety investigations will be prioritized, 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

In the event that Visitors are not permitted to enter Austin Health premises:

- Advise sponsor that a ban is now in place.

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. A copy of the sponsor confirmation should be provided to Pharmacy.
- Investigators/study staff should contact the sponsor to check availability of drug as drug manufacture and supply may be impacted.
- Clinical Trials Pharmacy has some limited additional storage for extra stock if required.
- Investigators considering provision of an increased amount of dispensed drug should contact the sponsor first and then Clinical Trials Pharmacy. A copy of the sponsor confirmation should be provided to Pharmacy.
- 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 & study staff 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.

In the event that Clinical trial staff may have COVID19 and/or are unable to come to work:

- Trial 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 trial staff for a particular clinical trial, where permissible staff from other clinical trial units may need to assist to execute the minimum requirements to ensure continued participant safety.
- Trial 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.
- Delegation logs should be reviewed and updated

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

- All data entry reduced and priority will be given to essential SAE and AE reporting
- All protocol amendments (unless directly related to patient safety) may be suspended
- All administrative tasks will be prioritized based on staff's ability to perform such activities
- RGO and HREC submissions for new trials may be delayed
- Data lock timelines may not able to be adhered to

For Austin Health sponsored trials, coordinating site staff should implement contingency plans in respect to the above information and their obligations for safety monitoring.

Communicate your plan with your trial participants

It is critical that trial teams continue to effectively communicate with trial participants on how the pandemic may affect their participation in a trial and what contingencies could be put in place to ensure their safety, wellbeing and as far as possible their continuance on the trial. Where certain trial activities can be conducted remotely, this should be promoted. Ensure that you use lay language. This patient information does not require Ethics approval.

Ethics Committees

- Meetings will be conducted virtually according to the current planned schedule
- All ethics and governance submission will be in electronic format
- Legal documents such as CTRA's, MTAs and RCAs with e-signatures (as opposed to wet inked) are acceptable. E-signatures include Docusign, scanned copy or photo image of the entire signature page of are acceptable.
- Post-approval amendments for Ethics and Governance will continue as usual.

Reporting to the Ethics Committee

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 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 on a 4 monthly basis.

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

Useful resource from the FDA:

Coronavirus (COVID-19) Update: FDA Issues Guidance for Conducting Clinical Trials (Issued 18th March 2020) https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-issues-guidance-conducting-clinical-trials

A **COVID Clinical Trial Governance Group** will be established immediately to support and oversee clinical trial activity at Austin Health and include.

- Chair: Director of Research/ Manager, Office for Research
- Gastroenterology / Hepatology trials
- Cancer Clinical Trials Unit
- ICU Trials
- Neurology trials
- NCRESS trials
- MCRI trials
- Michael Ching (Pharmacy Trials)
- Jenny Horvath (Pathology)
- Radiology
- Manager, Ethics & Research Governance
- Research Governance Manager

Additional support from Office for Research:

The Office staff will support you during this challenging time. If you need any advice, please contact either:

Dr Sianna Panagiotopoulos, Manager, Office for Research

E: research@austin.org.au, Mobile 0419 884 715

Mrs Lisa Pedro, Manager Ethics and Research Governance

E: lisa.pedro@austin.org.au, Mobile 0418 342 209

Website: http://www.austin.org.au/Human_Research_Ethics_and_Governance/

Appendix A

Attach patient label here

RISK ASSESSMENT FOR CORONAVIRUS FOR: PATIENTS ATTENDING CLINICS/DIAGNOSTICS

ONLY self-notifying patients need to be screened

Date:
Location:

PART A: INITIAL QUESTIONS

1. **Are you a PATIENT or a VISITOR?**

2. **If PATIENT, ask: In the last 28 days, have you:**
   - **Been overseas?**
   - **Had any contact with a confirmed case of COVID-19 (novel coronavirus)?**

If answers "YES" to either of the above questions:

- **Place a surgical mask on the patient.**
- **Complete Part B of the Risk Assessment in the relevant area (see flowchart).**

3. **If VISITOR, ask: In the last 14 days, have you:**
   - **Been to a high risk countries (click here for a list of high risk countries)?**
   - **Had any contact with a confirmed case of COVID-19 (novel coronavirus)?**

If answers "YES" to any of the above questions:

It's recommended that they go home for self-quarantine, unless they are required to be present e.g. as the primary carer of a dependant patient such as a child, or as a translator. Please be sensitive and empathetic when informing them of this. Below is a suggested response:

"It's important that we limit the risk of COVID-19 (coronavirus) being spread. As it can take up to 14 days for symptoms to occur, the Department of Health and Human Services is recommending anyone who may be at risk to self-quarantine at home and avoid public spaces. I understand that this may be upsetting for you and you want to be here to support your friend/family, but we need to protect the health of our staff and our patients. If you need more information or have any concerns call the Department's COVID-19 hotline on 1800 675 398."

IMPORTANT:

Record that risk assessment questionnaire has
been completed in the patient's medical record and retain a copy locally.

Attach patient label here

PART B: RISK ASSESSMENT

1. Do you have any of the following symptoms?	**Date first noticed**
☐ Fever	
☐ Cough	
☐ Shortness of breath	
☐ Sore throat	
If YES: place a SURGICAL MASK on the patient	

2. Have you been in or transited through any other country at any time in the last 28 days? ☐ YES ☐ NO		
Please list the countries visited	Date arrived	Date departed
☐		
☐		
☐		
☐		
☐		
When did you arrive back in Australia?		
Date:	Airline:	Flight number (if known):

3. In the last 28 days, have you:		
Had known contact with a confirmed case of coronavirus?	☐ YES	☐ NO
Had known contact with a suspected case of coronavirus?	☐ YES	☐ NO
Visited/Attended/Worked in a healthcare facility/hospital overseas?	☐ YES	☐ NO

4. Risk assessment completed by:	
Name:	Date:
Contact (phone or email):	

➔ GO TO PART C

PART C: NEXT STEPS FOR PATIENTS

1: Travel overseas OR 2: Contact with coronavirus	Symptoms (fever and/or acute respiratory symptoms)	Action
YES	YES	If appears unwell -> surgical mask on patient and follow usual escalation process (e.g. MET call) If does not appear unwell • Surgical mask on patient • Place the patient in Droplet + Contact precautions (see below) • Test for COVID-19 – see Hub for instructions
YES	NO	If travel to **a** high-risk country, OR contact with coronavirus in the last 14 days • Defer care until >14 days after return / contact if appropriate, otherwise provide care using Droplet + Contact precautions (see below). Otherwise, manage as per usual
NO	YES or NO	• Manage as per usual

Droplet + Contact precautions:

- Notify Infection Control
- Isolate to a single room with the door closed
- PPE for staff: surgical mask, protective eyewear, full-length gown, gloves.
- Follow standard Hand Hygiene protocols.

Infection Control contact:

- **Infectious Diseases** on 0401 608 571 (during business hours for Austin Health coronavirus clinical enquiries).
- **For urgent clinical queries after hours**: Contact Infectious Diseases Registrar/Consultant via Switch.
- **Infection Control** on x3434 (8am to 4.30pm, Monday to Friday).