NSW GOVERNMENT Health Sydney Local Health District

SLHD Guidance to Investigators on the conduct of clinical trials and clinical studies during the COVID-19 pandemic

The following guidance relates to all clinical studies including clinical trials and other types of clinical research involving participation of patients or community members.

Contents

Version Number	Purpose/Change	Author/s	Date Published
Version 2.9	Initial document	COVID-19 Response Team	26 March 2020
Version 3	Updates 1. Consideration for on-going studies (Pg 3). 2. Remote monitoring (Pg 7). 3. Consideration for new trials (Pg 10). 4. Additional costs incurred from contingency arrangement during the Pandemic (Pg 10). 5. Human Tissue Act (Pg 11) 6. Updated reference documents links (Pg 14)	COVID-19 Response Team	12 June 2020 & 28 July 2020
Version 4	Updates 1. Remote monitoring and/or auditing requests from authorised personnel who are based within or outside of Australia (Pg 7) 2. Sharing of information without patient consent (Pg 8) 3. Approved platforms for sharing information securely (Pg 7) 4. Live viewing of data using approved video conferencing platforms (Pg 8)	Dr Roy Donnelly Merela Ghazal Professor David Cook	21 October 2021 2 March 2022 15 March 2022

COVID-19 Clinical Trial Response Working Group Members

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14. Ms Merela Ghazal - SLHD Executive Research Manager

A. Considerations for on-going studies

I. Ensuring the safety of trial participants is paramount

Investigators and sponsors should pro-actively consider the procedures within the study protocol, identify those which may require modification in order minimise the risk to participants of being exposed to COVID-19 and agree on the appropriate changes to the protocol.

Participants should be informed about the measures being taken to ensure their safety and the safety of staff in so far as it is possible. They should be explicitly be given the following options:

- continuing to participate in the trial
- suspending their participation, if this is viable, or
- withdrawing from the trial.

Once it has been decided to modify trial protocols and procedures or that the trial can continue as per existing protocol, all participants should be made aware of the situation and of any changes that affect them. This can be by telephone call, SMS or email.

This conversation (or email or SMS exchange) should be file-noted in the medical record. If the participant decides to withdraw from the trial, this withdrawal should be file-noted in the medical record, and the withdrawal form should be signed by the participant when they are next able to visit the trial site. Issues relating to obtaining consent are dealt with in **A (vi) of this document** and in the NHMRC Clinical Trial Project Reference Group Guidelines (reference 2 below).

Investigators and sponsors should also consider the appropriate actions to be taken to minimise harm to those participants whose individual circumstances (e.g. state of health, travel needs, or inability to attend due to internal or external border closures) place them at particular risk.

In deciding on the actions to be taken, investigators and sponsors are encouraged to discuss with the approving HREC the proposed changes (see **C** below). They should also consult the more detailed guidance given by the NHMRC Clinical Trials Reference Group (reference 2 below).

Investigators and sponsors of studies approved by an SLHD HREC should provide to the approving HREC as soon as practical to the appropriate HREC a summary of the actions they are proposing to take (see **C** below).

The SLHD HRECs have introduced mechanisms for expedited review of protocol amendments and protocol deviations made in response to the COVID-19 pandemic (see **C** below).

We do not encourage immediate protocol amendments unless there are concerns for participant (or staff) safety, in which case an expedited review by the HREC Executive is possible for studies approved by an SLHD HREC. If there is concern or uncertainty about this, advice should be sought from the HREC Executive (to be contacted via the Executive Officer).

There will be an increase in protocol deviations. These should be well-documented to enable regulatory and peer review of the trial.
An increase in protocol deviations due to Coronavirus will not necessarily constitute a serious breach. Deviations that do not represent a material risk to participant safety or to the scientific validity of the study may be collated into a consolidated report submitted at the end of the pandemic (or at six-monthly intervals, whichever occurs sooner).

Deviations that are a material risk to participants or to the scientific integrity of the study should be reported expeditiously. The SLHD HRECs have introduced mechanisms for rapidly considering significant protocol deviations made in response to the COVID-19 pandemic (see **C** below).

II. Subject to (I), the scientific validity of the study should be protected to the greatest extent possible

Sponsors and investigators should fully document during the course of the study:

- the reasons for and type of any contingency measures implemented
- the period over which the measures were implemented
- the participants impacted and how they were impacted by the measures

Missing data should be specifically documented and explained in the case report form (CRF).

The impacts on the statistical plan caused by protocol deviations arising from COVID-19 such as missing data, altered follow-up schedules or changed methodologies for measuring study outcomes should be addressed in the amended protocol.

The reasons for deciding to suspend or terminate a study should be fully documented and reported to the HREC (see **C** below).

III. The study should not adversely impact on the ability of the Health System to respond to the COVID-19 pandemic

It is recognised that many clinical studies are embedded within routine care or are carried out in a manner that does not adversely impact on the provision of healthcare.

Studies which may impact adversely on healthcare should be modified, if possible, to minimise their potential impacts. For example, a study bringing participants into health care facilities for follow-up, should consider follow-up by telephone (e.g. tele-health) or by local healthcare, pathology or imaging providers. Similarly, study procedures that require the use of personal protective equipment (PPE) should be modified or deleted from the protocol, if appropriate, to remove the requirement for PPE.

Where the impacts of a study on a site cannot be minimised or may increase as a consequence of COVID-19 related protocol modifications, the sponsor and investigators should discuss with the site whether continuation of the study is justified by the balance between the potential benefits of continuing the study and the potential impacts on the site of the study.

The approving HREC should be informed of the outcome of such discussions. The SLHD HRECs have established mechanisms for facilitating the provision of ethical advice, if requested (see **C** below).

IV. Impacts of the pandemic on study staff

Investigators and sponsors should consider how to minimise risks from the pandemic to study staff, for example, by using tele-health approaches, screening participants for COVID-19 symptoms before permitting them to attend the trial site (mandatory), and by introducing systems to permit study-associated staff to work from home rather than work within a health care facility.

Investigators and sponsors should also consider the potential impact on the study of study staff becoming unavailable, whether due to illness, quarantine or re-assignment (see **A (vii)** below and reference 2).

V. Urgent protocol deviations made to protect participant or staff safety

Investigators and sponsors should take such actions as are required to minimise the risk for participants and staff from COVID-19 and provide regular updates on the consequent protocol deviations to the HREC. As the situation evolves, there will inevitably be further variations to study protocols. Documenting these prospectively and seeking more formal amendments as required will keep the workload manageable.

Urgent Safety Measure (USM) as defined in the NHMRC Report on "Safety monitoring and reporting in clinical trials involving therapeutic goods" (2016) can be implemented prior to notifying the approving HREC in cases of urgency. If there are significant changes to study procedures which impact on the risk-benefit balance for the participant then a USM should be implemented and the Sponsor, HREC and, where appropriate, the TGA should be notified of them promptly and certainly within 72 hours (see **C** below and reference 2).

Deviations from the protocol that the sponsor and investigator agree do not have a material impact on the safety of the participant, such as changes to procedures leading to the use of tele-health instead of face to face clinic visits, or the use of a courier to deliver investigational product (where appropriate) to a participant's home should not constitute a USM and hence do not require expedited reporting (but see **A(x)(1)** and reference 2) for proposed changes in the supply and the dispensing of investigational products). These non-urgent changes to the protocol schedule or investigational plan should be reported to the HREC in a consolidated report at the end of the pandemic or at six-monthly intervals (whichever occurs sooner).

VI. Informing participants of changes to study procedures and obtaining their consent

Participants must be informed of changes to the study protocol that represent low or negligible risks to participants (as defined in the National Statement 2018, see below). This can be done verbally and does not require signed consent though the site should document the discussion in the medical record.

If there is no concern of an increased risk or inconvenience of trial participation, reconsent should not be required. Participants should be given the options of continuing or withdrawing from a trial or suspending their participation as discussed under section A.1 of this document.

It is recognized that in some trials, the risks associated with COVID-19 (which should be discussed and managed with each participant) are primarily due to delivery of standard care (e.g. providing treatments, documenting response to treatment for ongoing care etc).

If the sponsor requires written consent, or the change constitutes a material increase in risk to the participant, then written consent should be obtained retrospectively at a time that is safe and convenient for the participant.

As a rule, changes to consent procedures should be sent, prior to implementation, to the approving HREC for approval. The SLHD HRECs have established expedited review processes to facilitate this (see **C** below).

Deviations from the informed consent procedures that do not deviate from the spirit of the approved protocol by the approving HREC should be notified as Protocol Deviations via consolidated lists at the end of the pandemic or six-monthly.

Participants who do not attend clinic visits or complete other trial activities may be reminded that these are required; however, if a patient declines or actively refuses to participate in trial activities, then their decision should be respected and they should be considered to have withdrawn from the trial. These participants should be informed that their decision will not affect their ongoing treatment or participation in future clinical trials (see reference 2).

Additional detailed guidance on consent issues arising from conducting clinical studies during the COVID-19 epidemic is provided in the NHMRC CTPRG Guidelines (reference 2 below).

Always consider the rights of participants to be informed of changes to their care and to consent to these changes.

VII. Ensuring continuity of supervision and staffing of the study

Sponsors and investigators should proactively plan mechanisms for mitigating the effects on the trial of quarantining or illness of the Principal Investigator or study staff.

In the event that the Principal Investigator or sub-investigator are unable to exercise their duties because they are in quarantine or ill, the person/people taking over responsibility

for the conduct of the study and for the safety of the participants should be notified to the approving HREC within 14 days, where possible. Their Curriculum Vitae should be provided to the HREC, if this has not been previously provided. Existing delegations should still be followed, if they exist.

VIII. Monitoring

Sponsors and investigators should collaborate to reduce monitoring visits through the use of information technology or delay such visits until after the end of the pandemic. Where a physical monitoring visit is agreed to be essential to the integrity of the study, the monitor(s) should be screened for symptoms of COVID-19 prior to the visit and occupy an office isolated from study staff and patients/participants.
During the pandemic, traditional on-site monitoring has been difficult to coordinate for reasons such as

- staffing limitations
- site access restrictions
- travel restrictions.

It is recognised that off-site monitoring may continue to be a preferred method by some sponsors even as the pandemic subsides. However, remote operations that overly increase the burden of trial site staff are discouraged. Units are therefore encouraged to negotiate suitable compensation for their time to coordinate remote auditing and monitoring activities.
If onsite monitoring or auditing is not feasible or if remote monitoring or auditing is strongly preferred by study sponsors, the sponsor and the institute must take necessary steps to maintain patient confidentiality protocols whilst conducting remote audits or monitoring. Consideration needs to be given to ensuring access takes place in an appropriate area where people who are not authorised could view sensitive data. The device/platform through which eMR is accessed must be an official device/platform from the sponsor, or an SLHD approved platform. File share requests must be emailed to official email addresses of authorised personnel, personal email addresses must not be used by either party.

Remote review of source documents should be documented with the same level of detail as on-site monitoring activities, and any resulting actions to address issues identified from the remote monitoring or auditing should be consistent with procedures and processes described in the study monitoring plan.

I. **Monitoring and/or auditing requests from authorised sponsor personnel (including those who are located overseas):**
Where the ethics approved Participant Information Statement and Consent Form has included the disclosure of the participant's information locally or overseas to authorised sponsor monitors for the purposes of trial monitoring, units may use the following:

1. NSW Health endorsed - Accellion SFT/Kiteworks (Secure file sharing is recommended)

2. Sponsor recommended platform. The platform and the relevant security arrangements must have been approved by the local Ethics Committee as part of the study approval.

Units are encouraged to de-identify data where possible, however, identifiable information may be disclosed where the consent has provided such authority via the relevant secure platforms.

Printing or downloading of any records is discouraged and should be disabled within the system through appropriate access restrictions.

II. **Sharing of data without Participant Consent:**
If participant consent is not possible or feasible, **fully deidentified** data may be shared for the purposes of monitoring and auditing with approval from the local Ethics Committee as part of the study approval via the NSW Health endorsed - Accellion SFT/Kiteworks platform, or platforms endorsed by sponsors which meet appropriate security requirements.

III. **Live viewing of data using approved video conferencing platforms:**
Sharing of identifiable source data via password protected conferencing platforms such as Zoom and Microsoft teams for visual confirmation of records is not encouraged unless there are no more secure alternatives available. If necessary, the Participant Information Statement and Consent form should allow for disclosure via this means. If this method is used, proper precautions must be taken to ensure only authorised recipients can visualise the participant information and that the information is not photographed or otherwise copied unless this is allowed for in the Participant Information Statement.

IX. Reporting to the TGA

The TGA has included guidance in the NHMRC CTPRG Guidelines (reference 2 below) on reporting protocol deviations and amendments. These guidelines should be consulted for detailed advice.

It is important to note that:

1. Researchers, sponsors, institutions, and HRECs should consult and adhere to existing guidance for safety monitoring and reporting published by NHMRC and the TGA https://www.nhmrc.gov.au/about-us/publications/safety-monitoring-and-reporting-clinical-trials-involving-therapeutic-goods
2. Any proposed modifications to standard practice should be discussed between the relevant parties and authorised, if appropriate, by the responsible party.
3. Any incidents associated with the attendance at a clinic (or other relevant context) of a participant known, or later discovered, to be symptomatic should be promptly reported as an adverse event or safety issue, as relevant, in accordance with existing guidance.
4. Variations to CTN trials such as changes to existing therapeutic goods, addition of therapeutic goods or addition of sites and those variations that are not responsive to COVID-19 will continue to require notification to the TGA.

X. Issues relevant to particular changes to study protocols

I. Continuation of the delivery of trial medication.

The Sponsor and Investigator should ensure that the proposed mechanism of supply of the investigational product(s), for example, delivery by courier to the participant's home:

- Is consistent with the storage requirements of the product(s)
- Is compliant with relevant Commonwealth, State and LHD regulations and procedures
- Ensures the participant has consented (verbally at a minimum) to disclosure of their name and address to the courier
- Does not lead to a breach of participant confidentiality
- If it is proposed that the participant should pay the cost of the courier this will require HREC approval

The SLHD Clinical Trials Pharmacy can be contacted for advice on the acceptability of any proposed changes to supply of investigational products.

II. Withdrawal of treatment with study product(s)

Sponsors and investigators should consider whether additional safety monitoring is required following the withdrawal of a participant from a study in which they are receiving an active intervention.

III. Suspending recruitment while continuing existing participants

This may be appropriate where participants may be gaining a benefit from their on-going participation that outweighs any potential for increased exposure to COVID-19 for participants or staff attributable to the study.

IV. Amendments related to COVID-19 testing or analysis

Where testing is mandated by the site, or for routine care, then a protocol amendment is not required, even if the testing occurs during study visits.

A protocol amendment is required if the outcomes of the testing will be used by the Sponsor or Investigators for a research objective. It should be treated as an Urgent Safety Measure and reported to investigators, approving HREC and the TGA within 72 hours.

V. Eligibility of participants with COVID-19 to remain in the study

Investigators and sponsors should consider how the protocol will manage participants with COVID-19.

Will they be withdrawn? If so, what follow-up should be required to ensure their safety, in particular, if they have been on active therapy.

If they are not withdrawn, what measures should be introduced to ensure their safety, the safety of the study staff and of the community?

How will the conduct of the study be affected by withdrawals due to COVID-19? Will they be replaced? How will COVID-19 associated discontinuations be treated in the statistical analysis of the study?

In all cases, the handling of participants and potential participants who are suspected or known to have COVID-19 should comply with the applicable Commonwealth, State, and SLHD guidelines.

XI. Additional costs incurred as a result of contingency arrangements during the COVID -19 Pandemic

Study participants should not be expected to pay for any costs associated with their participation in clinical trials, even if they will be reimbursed in the future. It is preferable that the site and the sponsor come to an arrangement with the service provider to bill the site or the sponsor directly for any services rendered such as pathology services, courier services etc.

B. Considerations for new studies

Any research study looking to recruit participants who are patients under the management of RPA Virtual Hospital, must be reviewed by the RPAH Virtual Hospital Research Steering Committee and approved by the Chief Executive as a pre-requisite to ethics, governance and SLHD Executive approval process.

I. Studies relevant to the COVID-19 pandemic

Consistent with the guidance from the NHMRC CTPRG (reference 2) and NSW Health (reference 1), the SLHD HRECs have established facilitated processes for considering new studies relevant to the COVID-19 epidemic (see **C** below).

Investigators and sponsors considering submitting new studies relevant to the COVID-19 pandemic are advised to:

- Engage proactively with the HREC
- Address in the protocol the potential impact on participant safety of the study
- Address in the protocol the potential impact on the health system of the study
- Address in the protocol the potential impact on the safety of study staff of the study
- Outline mechanisms for mitigating the effects of illness or quarantine of the investigator or of key study staff.

The Research Office has established an eConsent system using REDCap that is equivalent to a written consent where required for HREC approved or in compliance with legislative or policy requirements. Meaningful interactions between the participant, family and clinician and/or researcher are important components of obtaining informed consent, notwithstanding whether a 'wet-ink' or electronic signature is used.

In some circumstances, a verbal consent process may be approved by the HREC. However, researchers need to be aware that the Human Tissue Act mandates written consent where

researchers are collecting additional tissue (including blood) purely for the purpose of the research (that is, where the tissue was not otherwise collected for the purpose of clinical care). The recommended eConsent process satisfies the requirements of the Human Tissue Act for written consent for collection of tissue purely for research. See below regarding separate rules applying to the use of tissue for research.
Details are available on
https://www.slhd.nsw.gov.au/rpa/Research/eConsent.html

Consent Under Human Tissue Act for *Use* of Tissue and COVID-19 Research
An amendment to the Human Tissue Act now allows the use of Human Tissue that has been lawfully collected (such as for clinical care) for research purposes without consent upon satisfying the following two criteria:

- The use of human tissues for research has been approved by the Secretary of Health and;
- The research is required in connection with managing or monitoring the risks to public health arising from COVID-19

The research must still be approved by a HREC which may require consent depending upon the circumstances.
A letter to the Secretary of Health should be drafted and should include the following information;

- That the research team are seeking a waiver for the use of tissue for COVID-19 research.
- A description of how it meets the National Statement requirements for a waiver, with additional reference to the COVID-19 issue and the risk to public health.
- A statement should be made about how the diagnostic test will address the COVID-19 pandemic.

II. Studies that are not relevant to the COVID-19 pandemic

The SLHD HRECs will continue to consider new studies that are not relevant to COVID-19.

They will use their standard processes for these and will adhere to the published closing dates for submission of studies and meeting dates.

Starting of any new non-COVID-19 clinical trials is subject to approval of the Executive/Chief Executive and decisions made by the NSW Ministry of Health.

Investigators and Sponsors should be aware, that the load of COVID-19 related amendments and protocols as well as the re-assignment of key HREC and RGO staff may lead to significant delays in the consideration of studies that are not related to COVID-19. The SLHD HRECs and RGOs will do their best to ensure that this is not the case. They seek Investigators' and Sponsors' understanding and patience if they are unable to do so.

Submissions should address in the protocol, in addition to the usual requirements mandated by GCP:

- the potential impact on participant safety of the study commencing during the pandemic

- the potential impact on the health system of the study commencing during the pandemic
- the potential impact on the safety of study staff of the study commencing during the pandemic
- Whether a participant in this study who subsequently is infected with SARS-CoV-2 would be precluded from entering a clinical trial of therapy for COVID-19
- whether the trial is intended to commence start before pandemic stops or not

Proponents of new studies, whether related to COVID-19 or not, should consult the relevant sections of the NHMRC CTPRG Guidance and NSW Health Guidance (see references 1 and 2).

C. Facilitated HREC processes for dealing with COVID-19 related submissions

The SLHD HRECs are holding out-of-session meetings. RPAH HREC meet every Monday (commenced 30 March 2020) while Concord HREC convene on an ad-hoc basis. Research units should check the Research Offices websites for up-to-date information and submission requirements. A dedicated webpage for COVID-19 can be found on the Research Ethics and Governance Office websites.

D. Purpose and intended audience of this guidance document

This document is to provide guidance to investigators carrying out studies within SLHD sites or carrying out studies that are under the auspices of SLHD HRECs. In responding to these guidelines, investigators are encouraged to collaborate closely with the sponsor of the study and with the sites in which they are operating.

E. Suggestions for improvement and updated versions

It is intended to regularly update this guidance in response to the issues thrown up by the pandemic and to suggestions and comments made by investigators, sponsors and other stakeholders.

Please send by email any comments you may have to David Cook, Chair of the SLHD COVID-19 Clinical Trial Response Working Group (David.cook@sydney.edu.au) copying in Ms Merela Ghazal, SLHD Executive Research Manager (merela.ghazal@health.nsw.gov.au).

F. Recommencing clinical trials

The emergence of the COVID-19 pandemic in early 2020, led to a pause/suspension on some non-COVID-19 research with increased priority placed on COVID-19 studies. With the current positive trends indicating that the pressures on the health system are easing in respect of COVID-19, paused, suspended and new clinical trials may be considered to gradually resume or commence.

The decision on whether to restart a paused/suspended study, or commence a new study, rests with the study sponsor, principal investigator, HREC, RGO and the SLHD Executive team.

In restarting a paused study or in the start-up of new studies, certain preconditions should be taken into consideration:

Safety: Clinical trials should only recommence or start when safe to do so.

- Safety of study participants and personnel is of paramount importance.
- Matters to reconsider in restarting new trials are as follows:

1. Safety considerations such as risk of exposure to COVID-19 and measures to mitigate this.
2. Government guidance on social distancing, restart of work, and travel.
3. NSW Health and SLHD policies in respect of COVID-19.

Site Readiness: The pace of restart and the commencement of new studies should be commensurate with capacity and readiness of SLHD.

- Assessing the continued availability of the clinical investigator/sub-investigators to provide oversight of the trial and properly assess and manage safety issues that may emerge.
- Assessing the continued availability of trained staff that could be available to handle the expected tasks
- Assessing the availability of adequate resources for clinical trial activities, including consideration for Personal Protective (PPE) stock in the current risk status. Refer to the following links for further advice:
  - http://cec.health.nsw.gov.au/__data/assets/pdf_file/0009/595827/Amber-Alert_Moderate-Transmission-FAQs-24-July-2020-Final.pdf
  - http://internal.health.nsw.gov.au/communications/covid-19/documents/Infection-Prevention-Control-Response-Escalation-Framework.pdf
- Assessing the capacity of supporting departments, e.g. pharmacy, pathology, radiology etc. to support clinical trial units.

Study Viability: Only studies that are still viable should restart/start.
Some studies that have been paused or have not yet started may no longer be viable, for scientific, clinical, financial or practical reasons. It would be unethical and inefficient to restart/start studies that are no longer viable.

G. Supplementary material

I. Definitions of negligible and low risk

National Statement (2018) 2.1.6

Research is 'low risk' where the only foreseeable risk is one of discomfort.
Where the risk, even if unlikely, is more serious than discomfort the research is not low risk.

National Statement (2018) 2.1.7

Research is 'negligible risk' where there is no foreseeable risk of harm or discomfort; and any foreseeable risk is no more than inconvenience. Where the risk, even if unlikely, is more than inconvenience the research is not negligible risk.

II. Other sources of Guidance

i. NSW Health Guidance Document COVID-19 and Clinical Trials for Sponsors Sites and Researchers – 9 September 2020

https://www.medicalresearch.nsw.gov.au/covid-19-clinical-trial-guidance/

ii. Australian Government Department of Health - Covid 19: Guidance on clinical trials for institutions, HRECs, researchers and sponsors (9 April 2020).
https://www1.health.gov.au/internet/main/publishing.nsf/Content/Clinical-Trials

iii. FDA Guidance on Conduct of Clinical Trials of Medical Products during the COVID-19 Pandemic. Guidance for Industry, Investigators, and Institutional Review Boards (updated 30 August 2021)

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-guidance-conduct-clinical-trials-medical-products-during-covid-19-public-health-emergency

Contains useful examples that supplement the advice in this document and the NSW Health Guidance Document

iv. Guidance from the UK NHS Health Research Authority (12 October 2021)

https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/covid-19-guidance-sponsors-sites-and-researchers/

v. Guidance from the UK Medicines and Healthcare products Regulatory Agency (MHRA; updated 16 November 2021)

https://www.gov.uk/guidance/managing-clinical-trials-during-coronavirus-covid-19

vi. EU Guidance (updated 10 February 2022)

https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/guidanceclinicaltrials_covid19_en.pdf

vii. Initial TGA Guidance on reporting COVID-19 protocol breaches and amendments

Note: also consult the guidance in the NHMRC Guidelines (reference 2 above)

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Dear Prof Cook,

Thank you for your enquiry. We are closely working with other relevant departments on providing a guidance soon.

At this stage, the TGA is providing below advice to the Clinical trial sponsors.

The TGA, as part of the Department of Health, understands that the coronavirus outbreak (COVID-19) may adversely impact clinical trials in Australia.

In recognition of the impact of COVID-19 on trial variations, the TGA is advising that:

- Trial sponsors do not need to submit variations in the following instances:
  - Where the variation is due to COVID-19 and
  - Where the variation would not normally incur a fee (such as changes to the trial start/finish, number of participants etc.)

- At this time, variations would still be required where:
  - The variation is not related to COVID-19
  - The variation incurs a fee (such as changes to existing therapeutic goods, addition of therapeutic goods or addition of sites)

Patient safety remains paramount. Clinical trial sponsors will need to consider with the relevant HREC what steps need to be taken to ensure uninterrupted supply of the investigational medical product (and any other products used in the trial) to participants. In addition, if a clinical trial needs to be temporarily halted, researchers will need to contact the approving HREC to discuss the management of the suspension of the trial.

The TGA is closely monitoring the evolving situation to respond to issues as they arise. During this time, enquires regarding COVID-19 will be responded to by the TGA as a priority. There is no expectation of delay in Clinical Trial Notification review timelines and we will continue to process CTNs within our regular 5-7 business days timeframe at this stage.

viii. National Institute for Health Research (NIHR)
A framework for restarting NIHR research activities which have been paused due to COVID-19
https://www.nihr.ac.uk/documents/restart-framework/24886