Guidance Note: Protocol Deviations occurring in Clinical Trials approved by the Human Research Ethics Committee of Tasmania (HREC Tas)

It is the responsibility of the Principal Investigator to ensure that all clinical trials are conducted in accordance with the terms set out in the application approval letter, any subsequent amendment approval letters and in accordance with the *National Statement on the Ethical Conduct Human Research* (NHMRC 2023).

DEFINITIONS

For the purposes of this guidance note, **protocol** means the current approved document that outlines the research procedures. This is usually a formal protocol document that describes the background, rationale, objectives, design, methodology, statistical considerations, and organisation of a clinical trial.

A **protocol deviation** is any change, non-compliance, or departure from the approved protocol. Protocol deviations may be minor or major. **Minor protocol deviations** do not carry significant ethical or administrative consequences. **Major protocol deviations** are those that affect participant's rights, safety, or wellbeing and/or the accuracy and reliability of the study data. Any protocol deviations that affects participant safety must be reported. Protocol deviations may result from the action of a participant or researcher.

Examples of minor protocol deviations

- Visit non-compliance (for example a study visit is conducted outside of the required timeframe or a procedure is missed) and there are no safety concerns;
- Incorrect execution of the consent form (for example participant did not date their signature);
- Participant declines to complete scheduled research activities.

Examples of major protocol deviations:

- Use of unapproved recruitment procedures;
- Randomisation of an ineligible participant;
- Use of an unapproved version of the Participant Information and Consent Form;
- Visit non-compliance (for example a study visit is conducted outside of the required timeframe or a participant monitoring visit is missed) and there are safety concerns;
- Loss of laptop computer that contained identifiable information about participants;
- Incorrect execution of the consent form (for example consent form was signed by someone other than an approved person (e.g. someone not named on the ethics application).

The sponsor (if applicable) and the Human Research Ethics Committee (HREC) may consider a protocol deviation presented in advance of the event acceptable, for example if a participant will miss a study visit due to holidays.

REPORTING REQUIREMENTS

Minor protocol deviations do not need to be reported to the HREC at the time they occur. All minor deviations must be recorded in the study file and reported to the sponsor (if applicable), and to the HREC at the time of the annual report.

Refer to 'Templates' under the 'Help' tab of ERM, for a template protocol deviation tracking log. For sponsored clinical trials, this log will usually be provided by the sponsor.

Major protocol deviations must be reported to the HREC and the sponsor (if applicable) as soon as possible.

All protocol deviations (major or minor) must be recorded in a protocol deviation tracking log and submitted along with the annual report to the HREC each year.

Protocol deviations that occur at other Australian or international sites do not need to be reported to the University of Tasmania HREC, unless the deviation results in a change to the protocol, in which case should be submitted as an amendment submission via ERM.

PROCESS

For major protocol deviations:

1. Login to ERM.
2. Select the relevant project.
3. Select the 'Create Sub-form' from the 'Actions' panel on the left-hand side. You must have permission to 'Create all sub-forms' to see this button.
4. Choose the *Human Ethics Protocol Deviation Form – Provisional*, followed by the green 'Create' button.
5. Click on 'Start Here'.
6. Complete the questions on the form as required.
7. Click 'Submit' from the 'Actions' panel on the left-hand side. The deviation form will then be submitted to the appropriate HREC for review.

For all protocol deviations:

Record all protocol deviations in a protocol deviation tracking log as they occur and upload the log with the annual report to the HREC each year via ERM.

***Please note**:* If any changes to the project are required following the protocol deviation, an amendment submission should be submitted via ERM.

Relationship to other processes, procedures or guidelines

- Any protocol deviation that meets the definition of a reportable Significant Safety Issue (SSI) must be submitted as per the NHMRC guidance: Safety monitoring and reporting in clinical trials involving therapeutic goods (November 2016).
- Any protocol deviation that may be considered a breach of the Australian Code for the Responsible Conduct of Research, or a University Research Policy, or may be considered Research Misconduct will be referred to the Tasmania University's Managing Allegations of Research Misconduct Procedure (or relevant process for non- University projects).

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