Western Research

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Guidance Document	Application Guidelines for Multi-phase Research and Open Label Extensions
Effective Review	HSREB
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The Health Sciences Research Ethics Board (HSREB) reviews research protocols via an online application in the Western Research Ethics Management system. This allows the protocol as it was conceived to be reviewed but also ensures that important elements around procedures, data handling, risks, recruitment, and consent are specifically outlined as requested in the application. WREM also ensures complete information is given to the HSREB and organizes study documentation for review and approval.

For multi-phase research or research involving multiple methodologies and or populations, the distinction of when one, versus multiple, applications are required can be nuanced. Certainly, a separate WREM application is required for each protocol. **One application cannot accommodate multiple protocols.**

For non-clinical research with a single protocol, it is acceptable to seek approval for a single protocol outlining multiple phases or components. However, it is also acceptable and often preferable to submit a separate WREM application for each phase. This facilitates the application being clear and thus a timely review. When a researcher submits multiple WREM applications for a related course of study, they *can* be reviewed at the same time and measures are taken to link the applications so that the context is provided for reviewers. When at all possible, a single Ethics Specialist is assigned to all related files even if they are not submitted at the same time.

When considering whether or not to submit multiple applications, please consider the burden on the researcher to explain separately and in an itemized way the procedures, data handling, risks, population, and consent for EACH component. This can be challenging, but not impossible, in one application**. If each phase is not sufficiently clear in the initial submission or populations are deemed to require different risk-benefit considerations, the HSREB can request separate applications. These may need to be reviewed consecutively rather than concurrently.**

Similarly, amendments that propose an additional protocol or are of a scope deemed to be outside of the initial objectives of a study will require a new WREM application.

Considerations specific to Open Label Extension Studies (OLEs)
Pharmaceutical research often includes an open label extension (OLE) study. This occurs when patients participating in double blind placebo-controlled trials of new medications are invited, on completion of the initial trial, to take the study drug for some further period. Patients are openly given the active substance at this stage, regardless of their assignment in the initial trial.

If an OLE is integrated into the initial trial design within the same protocol for initial review, both/multiple phases can be submitted as one application. **The HSREB supports and**

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encourages a separate Informed Consent Form (ICF) for the OLE. However, there will be consideration for a single consent including the OLE if there is sufficient justification to do so. In such instance the applicant must also provide evidence that the trial has robust mechanisms for safety monitoring and sufficient interim analysis prior to proceeding to the OLE.

If the OLE is not planned at the time of the initial application, for the purpose of HSREB review/approval, the main study and OLEs are two separate studies and should be submitted separately with separate consents.

OLE studies generally have different objectives, methodology, benefits and risks, participant populations and recruitment processes, and different information/consent documentation requirements. There are also concerns regarding participants who had been randomized to placebo in the RCT who will, in the OLE, be subjected to open label medication. There is a greater need for monitoring at first dose(s). The HSREB examines OLE studies carefully because individual participants may be invited to participate in the OLE without knowing their treatment status in the primary study (e.g., active drug or placebo), and before aggregate data about efficacy and safety have been fully analyzed. This means that participants previously doing well on placebo or low doses of the drug will be enrolled in the OLE on active medication and the participant may be given a higher dose than they were previously taking.

The HSREB is concerned about the possible undue influence to participate in the clinical trial with the understanding of potential continued access to free medication particularly if it is offered at the beginning of the primary study. This requires special consideration.

These issues are of sufficient concern to require the protocol, SAEs and other issues associated with the OLE to be reviewed and monitored separately from the primary study should they not be able to be fully considered at one time in the initial submission.

Revision History

October 29, 2026	Allowance of single ICF in certain instances opposed to always requiring separate consents. Update Ethics Officer terminology to Ethics Specialist.