

# The Office of Human Research Ethics

The University of North Carolina at Chapel Hill

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## The Lineberger Protocol Review Committee Policy and Procedures

### Introduction

The Protocol Review Committee, or PRC, is a standing, multidisciplinary, peer-review committee of the UNC Lineberger Comprehensive Cancer Center.

The committee's job is to enhance the quality of clinical cancer research at UNC by evaluating research protocols and providing constructive feedback to investigators and maintaining scientific oversight of the conduct of clinical research.

It includes a rotating group of faculty physicians from Hematology, Oncology, and other disciplines; UNC Biostatistics faculty; UNC social scientists; specialized ad hoc members; and patient advocates.

#### **The PRC's mandate is to:**

- ensure the scientific merit of the proposed research
- ensure patient safety parameters of proposed studies and protocol amendments.
- monitor study accrual and recommend closure of under-performing trials.

### What Does the PRC Review?

#### **The PRC reviews any study that:**

- recruits from the UNC Health Care clinical settings for cancer patients; or
- receives funding from a cancer agency, foundation, or other cancer-related group; or
- focuses on cancer or on a risk factor for cancer.

This includes a wide range of study types from low-risk observational studies that recruit UNC cancer patients to high-risk treatment studies, and the range of studies in between.

#### **The PRC reviews:**

- Investigator Initiated Trials (IITs), whether UNC initiated the trial or is a participating site
- Pharmaceutical sponsored trials
- Studies managed by another institution
- Cooperative group and other externally peer reviewed studies funded and supported by the National Cancer Institute

## The PRC does not review:

- cancer-related studies that do not have direct interaction with subjects,
- cancer-related retrospective studies involving review of medical records or tissue analysis, or
- studies unrelated to cancer or cancer risk factors.

## What are the PRC's Review Criteria?

The PRC assesses protocols to ensure that institutional resources are being used effectively, and that activation of national protocols conforms with the research aims of UNC. The committee judges the acceptability of protocols based on several factors:

- Background data justifying the proposed research
- Scientific design and merit
- Risk/benefit ratio
- Biostatistics
- Feasibility
- Resource use

## Types of PRC Reviews Summary

Like the IRB, the PRC evaluates new studies, protocol amendments, and renewals through expedited, administrative, or full board review depending on the study type. For example, interventional treatment trials undergo full board review. Observational, health services research trials typically undergo expedited review.

## New Studies in Detail

All studies require:

- Signoff by an appropriate disease group leader.
- Signoff by a biostatistician for studies whose Sponsor is UNC Lineberger  
Submission of a clinical protocol and
- Submission of the Investigator Brochure if the study is a Phase I, II, or III study of a non-FDA approved drug

During review, the PRC categorizes studies by Risk level as minimal, moderate, or high.

- **Minimal risk** ratings are typically assigned to nutritional, behavioral, psychosocial, diagnostic, and other non-therapeutic studies.
- **Moderate** ratings are typically for studies involving industry or cooperative group sponsored trials with appropriate data and safety monitoring plans, or investigator-initiated single-site Phase II or III studies that use FDA-approved agents.

- **High** ratings go to all investigator-initiated trials involving an investigational agent all Phase I investigator-initiated trials, and all Phase II and III investigator-initiated multi-center trials

Moderate and High-Risk Studies are then given a Complexity Rating, which accounts for:

- use of a healthcare provider with specialized training
- an unusual route of administration
- admission for intensive monitoring required beyond standard of care
- collection of biological samples
- Pharmacokinetic (PK) sampling, and
- The number of sites for LCCC multicenter trials.

The UNC Lineberger Monitoring team uses the Risk ratings to guide determination of the frequency of monitoring of UNC Lineberger IITs.

The UNC Lineberger Data and Safety Monitoring Committee uses the complexity ratings to guide determination of frequency of review.

## Amendments

The PRC reviews study amendments depending on the significance of the proposed changes as well as the type of study and study Sponsor.

For IITs, pharma, and other institution studies: significantly changing the study design such as adding a new disease group, cohort, substudy, or treatment modality as well as changing the primary objective or endpoint of the study will qualify for PRC amendment review.

Specifically for IITs, significantly changing the statistical section and/or adding a collection of new or additional biomarker samples will qualify for PRC amendment review.

Cooperative group studies are not required to submit for PRC amendment review.

## Renewals

Typically, the PRC conducts **annual** reviews of on-going studies that are:

- **Not yet Open to Accrual**, but six months or more have passed since the PRC's Initial review;
- **Open to Accrual**; or
- **Closed to Accrual**, but research-related interaction/intervention continues with subjects.
- **Currently On Hold or Suspended.**
- **Cooperative Group studies** (e.g., Alliance), but only if the number of subjects accrued during the previous year is less than 40% of the annual accrual goal

However, a renewal can receive approval with a six-month re-review when there are concerns about low accrual.

The PRC stipulates a number of subjects to be accrued within the six-month re-review timeframe.

If the study does not meet the PRC's request, the PRC can consider the study for administrative closure. A study can also receive an administrative closure determination due to lack of compliance.

## Summary

In summary, the PRC is an important partner in the overall Human Research Protections Program at UNC. Their contributions are similar to those of the Scientific Review Committee. They help prioritize participant well-being by assuring sound research design and adequate safety monitoring. The PRC's risk-based and complexity-based review framework supports appropriate resource allocation and use, and provides an extra layer of oversight that IRB members can rely on to help them determine that the 111 Criteria for Approval are met.

Thanks for watching!