

Notice to the Extramural Community:
Policy related to Phase III Clinical Trials

Background

Clinical trials (<http://www.nlm.nih.gov/services/ctclintrial.html>) range from small, first-in-human studies (Phase 0/I) to larger trials of activity (Phase II) or efficacy (Phase III) (<http://www.nlm.nih.gov/services/ctphases.html>). These trials may be related to prevention, treatment, screening, symptom control, and behavior modification. Multi-modality approaches are frequently involved (i.e., surgery, radiation, systemic treatments, imaging). NCI has traditionally provided support for all phases of trials and interventions via grants and cooperative agreements (R03, R21, R01, P01, U01, UM1, and U10). Historically, the majority of early phase trials have been conducted under R03, R21, R01, P01, U01, and UM1 mechanisms. Most Phase III trials have been conducted under the U10 mechanism, with a limited number of phase III trials performed under R01, P01, and U01 mechanisms.

Due to the complex nature of chemoprevention, symptom control, and treatment-related Phase III trials, NCI believes it is no longer appropriate to support these trials under the R01 and P01 investigator-initiated grant mechanism. Most Phase III clinical trials testing these interventions cannot be completed from protocol development to enrollment, follow-up and final analysis within the five-year funding cycle associated with R01 and P01 mechanisms. As the success of competing type 2 R01 and P01 applications cannot be guaranteed, commitment to Phase III trials of interventions that will take longer than five years is impractical. For these reasons, NCI has determined that a more appropriate mechanism for Phase III intervention studies expected to take longer than five years is the National Clinical Trials Network (NCTN), formerly known as the Cooperative Groups, where these trials can be closely monitored for rates of enrollment, clinical performance, and regulatory compliance in keeping with their goal, in most cases, to establish a new standard of clinical care.

Some Phase III trials that do not involve medical interventions (drugs, surgery, radiation, or imaging) may still be considered for funding under the R01 or P01 mechanisms if solid evidence can be provided to assure their completion (conception to final analysis) within five years. Examples of Phase III trials that might meet these criteria and for which investigators might still apply via R01 or P01 applications include:

1. Public health interventions, such as studies that test the efficacy of a psychosocial, pharmacologic, psychopharmacologic, behavioral, educational or lifestyle, or health services intervention to improve cancer prevention or cancer treatment efficacy (e.g., interventions for smoking cessation, vaccine uptake, immune function, screening behavior, or treatment adherence), as they are not viewed as cancer medical intervention studies, or
2. Phase III comparative effectiveness research (<http://www.nlm.nih.gov/hsrinfo/ce.html>) if it involves only behavioral or health systems research, or
3. Studies that test the efficacy of a psychosocial, psychopharmacologic, behavioral, health services, educational or lifestyle intervention, or of drugs, surgery, radiation therapy, or medical devices to address physical symptoms or other adverse consequences of cancer (e.g., nausea or pain) and its treatment (e.g., depression, social function, or caregiver adaptation).

These trial types have shorter term end-points and might be successfully completed within a five-year funding period.

Alert to the Extramural Community to the Following Action by NCI

NCI will no longer accept R01 or P01 applications, starting with the xxxxx receipt dates, for Phase III (efficacy) trials that test therapeutic or imaging modalities in clinical trials. NCI will continue to accept R01 or P01 applications for trials that are limited to public health interventions, comparative effectiveness research, and other psychosocial, behavioral, and related interventions to address consequences of cancer (see examples above) provided they can be completed entirely within the 5-year grant cycle. Ongoing Phase III efficacy clinical trials/studies currently supported by NCI in the grant portfolio are permitted to be supported as part of a competitive renewal grant.