Placebos (HRPP 3.13)

Description:

This policy describes UNMC's requirements for IRB review and approval of clinical trials that utilize placebos.

Definitions:

Placebo: an inactive substance or treatment that may resemble an active medication or treatment but has no therapeutic value.

Randomization: the assignment of subjects to different treatments, interventions, or conditions based on chance, rather than by design of selection.

Use of a Placebo:

Use of a placebo is ethically justified under certain conditions.

The following are recognized circumstances in which placebo use may be ethically permissible:

- **No standard therapy exists**
  - This is currently no established standard of care or recognized effective intervention for the condition being studied
- **Standard therapy is ineffective**
  - The existing standard treatment has been shown to be no more effective than no treatment
- **Standard therapy has significant toxicity**
  - The standard treatment may be clinically effective, but is associated with substantial toxicity
- **Standard therapy is unavailable**
  - Due to factors such as resource limitations or drug shortages, the standard treatment is not accessible to the patient population involved in the research
- **Methodological necessity with ethical safeguards**
  - There are scientifically sound reasons to use a placebo, and the participants who receive placebo are not subject to additional risks as a result of not receiving the intervention

Study Design Considerations:

When a placebo is used in a clinical trial, the **investigator must demonstrate**, and the **IRB must find**, that appropriate safeguards are in place to minimize risks and ensure ethical study conduct.

Risk Minimization Requirements:

- The risk associated with placebo is minimized. Acceptable procedures to reduce risk may include, but are not limited to:
    - Frequent and careful monitoring for worsening of the subject's underlying condition
    - Early withdrawal criteria for subjects who exhibit clinical deterioration or insufficient improvement
    - Prompt intervention or treatment, including re-initiation of effective therapy, if clinically indicated
    - Exclusion criteria for participants who are at increased risk of harm from placebo non-response
    - Cross-over design, allowing all participants to eventually receive the investigational intervention
    - Oversight by an independent Data and Safety Monitoring Board (DSMB) to ensure ongoing safety and ethical integrity
- The investigational intervention must offer the potential for at least equivalent direct benefit to the participant compared to the current standard of care

Informed Consent Requirements:

For **clinical trials using a placebo**, the informed consent process and document must include:

- A **clear statement that a placebo will be used,** with a lay explanation such as: *"A placebo is a pill or injection that looks like the treatment but has no medicine in it."*
- The **scientific rationale for using a placebo,** described in accessible language
- A **description of the risks** associated with non-treatment, including the potential for worsening of the subject's condition or disease
- A **withdrawal plan** outlining how subjects will be removed from the study if their condition deteriorates or fails to improve within predefined parameters