

**Department:** UAMS Institutional Review Board  
**Policy Number:** 17.12  
**Section:** Special Populations  
**Effective Date:** July 31, 2002  
**Revision Date:** April 15, 2004

**SUBJECT: Terminally Ill Patients**

In many contexts, research on terminal illness and its treatment requires the involvement of terminally ill patients when alternative populations for study do not exist or when involving alternative populations would be ethically unjustifiable. Two important reasons for concern regarding research involving terminally ill persons are: (1) they tend to be more vulnerable to coercion or undue influence than healthy adult research subjects; and (2) research involving the terminally ill is likely to present more than minimal risk.

Terminally ill patients are those who are deteriorating from a life-threatening disease or condition for which no effective standard treatment exists. It is generally considered unacceptable to ask such persons to participate in research for which alternative, not similarly burdened, populations of subjects exist. Nevertheless, it may often be necessary to involve terminally ill patients in research concerning their disease and its treatment. Further, terminally ill persons should not be excluded from research in which they may want to participate simply because of their status. Terminally ill individuals are a vulnerable population of research subjects, and, therefore, require additional protection against coercion and undue influence [45 CFR 46.111(b)]. If an IRB regularly reviews research involving the terminally ill, it should include among its members one or more individuals knowledgeable about and experienced in working with these subjects [45 CFR 46.107f].

With the appearance of HIV, concerns have emerged about circumstances under which persons with serious and life-threatening conditions may have access to research drugs through expanded access programs. The FDA's Parallel Track program and Treatment IND regulations seek to address these concerns. The IRB have a role both in considering circumstances in which terminally ill persons are appropriately excluded from research because they are a vulnerable group, and in providing persons who have no therapeutic alternatives the opportunity to receive the possible benefits of experimental interventions.

**DEFINITIONS**

**Expanded Availability:** Policy and procedure that permits individuals who have serious or life-threatening diseases for which there are no alternative therapies to have access to investigational drugs and devices that may be beneficial to them. Examples of expanded availability mechanisms include Treatment INDs, Parallel Track, and open study protocols.

**Therapeutic Intent:** The research physician's intent to provide some benefit to improving a subject's condition (e.g., prolongation of life, shrinkage of tumor, or improved quality of life, even though cure or dramatic improvement cannot necessarily be effected.) This term is sometimes associated with Phase 1 drug studies in which potentially toxic drugs are given to an individual with the hope of inducing some

improvement in the patient's condition as well as assessing the safety and pharmacology of a drug.

**Phase I Trials:** It is important to distinguish between risks that may be justified by anticipated benefits for the research subjects and risks associated with procedures performed purely for research purposes. A particularly difficult issue relating to research involving terminally ill patients arises in connection with the conduct of Phase 1 drug trials in which the drugs involved are known to be particularly toxic (e.g., a new form of cancer chemotherapy). In some of these studies, any benefit to the subject is, at best, highly unlikely. Despite the "therapeutic intent" of the investigators to benefit the subject, subjects may in fact experience a decline in health status, no improvements in terms of quality of life, or lengthened life for only a short time. It is extremely important that prospective subjects be clearly informed of the nature and likelihood of the risks and benefits associated with this kind of research. The challenge to the investigator and the IRB is to provide patients with an accurate description of the potential benefits without engendering false hope.

**Group C Drugs:** The FDA and the National Cancer Institute (NCI) developed a special category of drugs called "Group C." Group C drugs may be provided by oncologists to appropriate cancer patients through protocols outside the controlled clinical trial prior to the drug approval. In 1987, the FDA initiated a regulation establishing the treatment investigational new drug application (Treatment IND), and in 1992, instituted a policy providing for a "parallel track" mechanism [21 CFR 312.34]. Under a Treatment IND protocol, eligible patients have access to investigational new drugs intended to treat serious or life-threatening diseases; Parallel Track protocols enable persons with AIDS or HIV-related diseases who cannot participate in clinical trials to have access to investigational drugs.

## **IRB CONSIDERATIONS**

The IRB should be satisfied that the nature, magnitude, and probability of the risks and benefits of the research have been identified as clearly and as accurately as possible. Special attention should be paid to the consent process, both in terms of the accuracy of the information to be provided and the manner in which consent is sought. As a general rule, accurate information concerning eligibility for participation (*i.e.*, diagnosis and prognosis), treatment options, and risks and benefits should be conveyed clearly and in a manner that will not either engender false hope or eliminate all hope.

The IRB must also consider including other information the patient might find relevant to making an informed decision to participate. For example, subjects should be told whether or not participation in the study is a condition for treatment at the institution; any costs to the patient of the research should be stated explicitly. The IRB should consider whether any payment might constitute an undue enticement, particularly if the subject population is economically disadvantaged. Patients should be provided with relevant information well in advance of making a decision about participation, and consultation with others such as family members, close friends, clergy, or medical consultants should be encouraged.