Clinical Research Shared Service Standard Operating Procedure

SOP 103-ADM Clinical Trials and Clinical Research Conducted at AZCC

Approval signature: [Signature]
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Purpose:
The Arizona Cancer Center (AZCC) is designated as a Comprehensive Cancer Center and governed by local policies and procedures, state and federal regulations for the conduct of clinical research involving human subjects. Clinical research conducted at the AZCC consists of national group studies (e.g., SWOG, ECOG, COG), external reviewed institutional studies, internal institutional studies, AZCC initiated/industry sponsored and industry initiated/sponsored clinical trials. This SOP describes the specific types of clinical trials that may be conducted at the Arizona Cancer Center and the general process flow for conduct of clinical trials.

References:
• ICH GCP 4.8.10 Guidance for Industry
• 21 CFR Part 50.20 General requirements for informed consent
• The Cancer Centers Branch of the National Cancer Institute; Policies and Guidelines Relating to the Cancer Center Support Grant (September 2004).
• All SOPs are applicable to this SOP.

Authors:
Revised by SOPRC.

Target Audience:
Individuals participating in clinical research programs at the Arizona Cancer Center.

Tools:
• SOP 101-ADM How to Write and Format an Arizona Cancer Center (AZCC) Clinical Research Standard Operating Procedure

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- SOP 102-ADM Review and Approval process of Arizona Cancer Center (AZCC) Clinical Research Standard Operating Procedures

**Definition of Terms:**
- **Behavioral Science Committee (BSC)**
- **Clinical Trials Office (CTO):** Individuals responsible for the regulatory documentation completion and distribution for sponsored projects as part of the Clinical Research Shared Service at the Arizona Cancer Center.
- **Dose Limiting Toxicity (DLT)**
- **Human Subjects Committee (HSC) (U of A IRB)**
- **Human Subjects Protection Program (HSPP):** The University of Arizona (U of A) Human Subjects Protection Program is the overall program that incorporates the Institutional Review Boards.
- **Institutional Biosafety Committee (IBC):** An institutional oversight committee for approving clinical trials involving gene therapy.
- **Institutional Review Board (IRB) or Western Institutional Review Board (WIRB):** An independent body constituted of medical, scientific, and non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trial protocol and amendments and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.
- **Maximum Tolerated Dose (MTD)**
- **Scientific Review Committee (SRC):** The SRC is charged with performing peer review of the scientific design of research studies. In most general terms, any cancer-related scientific study involving human tissue or subjects using Cancer Center resources must be reviewed by the SRC.

**Clinical Trials, Protocol Types and Phases Requiring Institutional Oversight Committee Approval**

**Non-Intervention studies:** Ancillary, Companion, or Correlative Studies

**Screening, Early Detection, or Diagnostic:** trials directly testing the efficacy of devices, techniques, procedures, or tests for earlier/more accurate detection or diagnosis of disease.

**Supportive Care:** studies in which an intervention is used to improve the comfort and quality of life for the patient.

**Epidemiologic/Observational:** studies among cancer patients and healthy populations that involve no intervention or alteration in the status of the participants (e.g., surveillance, risk assessment, environmental and behavioral studies including Quality of Life (QOL) studies, etc.)

**Prevention intervention:** clinical trials for the modulation of cancer risk and inhibition of cancer progression using nutrition, dietary or chemoprevention interventions.

**Therapeutic Intervention:** Clinical trials with therapeutic intent using drugs, radiation, surgery, and/or biological agents.
Protocol Types:

**Phase I:** Typically the first human clinical exposure to an investigational product(s) and often are referred to as toxicity studies. These are the first phase of clinical evaluations following animal research of an investigational product. Phase I studies investigate the pharmacodynamics, pharmacokinetics and toxicity of the investigational product. Dose escalation may also be a component of a Phase I study. This early clinical experience will begin to provide evidence of human tolerance to the product. The major objective of a Phase I study is to determine the maximum tolerated dose (MTD) as well as identifying the dose limiting toxicity (DLT). Experience from Phase I studies will directly influence future clinical strategy and testing. Efficacy is not determined for a Phase I trial; therefore no exceptions should be made for subject eligibility.

**Phase I/II:** A Phase I/II study is designed to overcome some of the limitations (wide range of tumor types and heavily pretreated subjects) of a Phase I study in determining antitumor activity of an investigational product. In a Phase I/II study the MTD is determined in a group of patients with the same disease and thereby may provide a more accurate measurement of antitumor activity.

**Phase II:** Phase II clinical trials are intended to evaluate safety and effectiveness of an investigational product for a given disease or group of diseases. A secondary objective is often to further define toxicity. Phase II studies may also include pharmacokinetics and dose ranging. These are typically well-controlled studies to assess response rates. Phase II studies sometimes are split into subgroups: Phase IIa (earlier Phase II studies) and Phase IIb (later Phase II studies).

**Phase III:** The major objective of a Phase III study is to compare the efficacy of at least two treatments. Typically it is a comparison of the current standard of care versus one or more experimental treatment arms. This comparison should be done using a prospective randomized clinical trial although comparison with a historical control may be necessary. It is a large well-controlled clinical study of 100s to 1,000s of subjects. Phase III studies include safety, efficacy, response rates, survival and quality-of-life evaluations.

**Phase IV:** Phase IV clinical studies are post-marketing studies for commercially available drugs that may be conducted to expand "off-label" use and to further assess toxicity data.

**Pilot Study:** A study to determine the feasibility of a proposed treatment or procedure. A few subjects are treated in a predefined, specific manner in order to determine the feasibility of conducting a larger study.

**Safety Issues:**
Clinical research involving human subjects must conform to generally accepted scientific principles. The clinical trials should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interests of the study subject must always prevail over the interests of science and society. The protection of subjects who participate in a clinical trial is the responsibility of the investigator,
other clinical trials personnel (RNs, Clinical Research Coordinators, etc.), IRB, Biosafety Monitoring and regulatory agencies.

**General Process Steps:**

1) New and/or potential trials are reviewed and discussed at team meetings.
2) Protocols and clinical studies are developed and drafted by the physicians, other clinical and basic science research personnel and study sponsors.
3) Protocols are submitted to CTO and routed for review to include resource requirements, study design and statistical power, pharmacy requirements and budgeting.
4) Regulatory documents and protocols are completed and submitted to the appropriate study sponsor and oversight committees, SRC, IRB and/or IBC.
5) After review and approval by committees, additional study personnel are assigned, site initiation visit is conducted, and the study is activated for accrual.
6) The study continues to be active until enrollment targets are met as long as there are no safety issues and continued renewal (IRB) is maintained.
7) While the study is active, it is internally and/or externally monitored.
8) At the conclusion of the study, audits may be conducted and a close out visit is held.
9) Data analysis is performed and manuscripts written and submitted.