Purpose:
This SOP describes the steps taken to organize and prepare the Arizona Cancer Center (AZCC) for all clinical studies subject to investigational new drug (IND) regulations for drugs and biologics during all investigational phases of development. It describes the steps followed by the AZCC from the time a sponsor, including sponsor-investigator for investigator-initiated studies, selects the site for a clinical study until a study close-out visit is completed.

References:
- January 1988 Guidelines for the Monitoring of Clinical Investigations
- November 2003 International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline
- 21 CFR 312.50 General Responsibilities of Sponsors.
- 21 CFR 312.60 General Responsibilities of Investigators.
- 21 CFR 312.66 Assurance of IRB Reviews.
- All SOPs are applicable to this SOP.

Authors:
Revised by SOPRC.

Target Audience or Responsibilities:
Individuals participating in clinical research programs at the Arizona Cancer Center, and Southern Arizona Veterans Administration Health Care System.
Tools:
- Example of Site Evaluation (Prestudy) Visit (SEV)
- Example of Site Initiation Visit (SIV)
- Example of Study Close-out Visit
- Glossary of Terms azcc\azccnas1\ctagroupSOPS

Contacts:
- Arizona Cancer Center (AZCC): Clinical research site located at 3838 N. Campbell Avenue, Tucson, Arizona 85724; phone number: (520) 694-9083. AZCC Clinical Trials Office located at 1515 N. Campbell Avenue, Tucson, Arizona 85724; phone number: (520) 626-9008.
- Premiere Oncology of Arizona: 9023 E Desert Cove Avenue, Ste. 101, Scottsdale, Arizona 85260; phone number: (480) 860-5000.
- Southern Arizona Veterans Administration Health Care System (SAVAHCS): A satellite clinical research site located at 3601 S. 6th Avenue, Tucson, Arizona 85723; phone number: (520) 792-1450.
- Southern Arizona Veterans Administration Health Care System Research & Development Committee (SAVAHCS RDC): 3601 S. 6th Avenue, Tucson, Arizona 85723, phone number: (520) 629-1824.

Definition of Terms:
- Confidentiality Disclosure Agreement (CDA): A confidentiality or non-disclosure agreement protects confidential information shared between a study sponsor and investigator. The Confidant agrees to treat such information as confidential information of the Sponsor. As the importance of the confidential information increases, so does the relative complexity of the Agreement.
- Contract: A written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters. The protocol may serve as the basis of a contract. The financial aspects of a clinical trial protocol are documented in an agreement between the sponsor and the investigator/ institution.
- Contract Research Organization (CRO): A person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.
- Data and safety monitoring board (DSMB): An independent committee whose membership includes, at minimum, a statistician and a clinical expert in the area being studied. Responsibilities of the DSMB are to: ensure that risks associated with participation are minimized to the extent possible, ensure the integrity of the data, and stop a trial either if safety concerns arise or as soon as its objectives have been met.
- OnCore: Database used to store protocol and patient data at the Arizona Cancer Center.
- Protocol: A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. Throughout the ICH GCP Guidelines, the term "protocol" refers to protocol
and protocol amendments.

- **Protocol Submission Form:** A form that summarizes a new protocol for review/approval by the study team.

- **Resource Review:** Routing form with the attached protocol is sent out for protocol review, accommodation account set up and department budgets.

- **Site Evaluation Visit (SEV):** Sponsor-initiated visit before site selection to determine if investigators and staff are qualified to conduct a particular study in terms of previous experience conducting similar research, adequate number of potential subjects, staff willingness to fulfill regulatory obligations, adequate numbers of trained staff and adequate facilities and equipment to perform study. Prestudy visits are recommended, but not always required, especially if the study site has performed studies in the past for the specific company sponsoring the trial.

- **Site Initiation Visit (SIV):** Sponsor visit at the beginning of a study to ensure that research staff is knowledgeable with drug mechanism of action, anticipated side effects, protocol procedures, and associated Case Report Forms (CRFs). The study initiation visit occurs after the sponsor and study team have committed to proceed with the study, and all needed clinical supplies are available or en route.

- **Sponsor/Investigator:** An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a subject. The term does not include any person other than an individual (e.g., it does not include a corporation or an agency). The obligations of a sponsor/investigator include both those of a sponsor and those of an investigator.

- **Study Close-out Visit:** Thorough review of the regulatory documents will be made by a sponsor representative to compare CRFs and sponsor-to-site documentation. Records are maintained per protocol guidelines.

**Safety Issues:**
Prior to enrolling the first subject, all regulatory and institutional requirements must be met, and preparations for protocol procedures must be complete. Additionally, the research staff and others involved in recruitment, selection of subjects and enrollment must receive appropriate training.
**Process Steps:**

**Note:** "Sponsor" includes sponsor/investigator for investigator-initiated studies.

1) Sponsor contacts IRB Coordinator or physician for interest in protocol participation. The sponsor then forwards Confidentiality Disclosure Agreement (CDA) to IRB Coordinator for investigator's signature. IRB Coordinator returns original signed document to sponsor and requests a Protocol Synopsis.

2) Protocol synopsis is reviewed and discussed at team meeting.

3) If the team agrees that the study should be activated, the Protocol Submission Form is completed and signed by the team leader.

4) A Site Evaluation (Prestudy) Visit is scheduled by CTO for the Sponsor to assess the site and speak with the PI and/or other research team personnel.

5) If the site is approved by the Sponsor, the complete protocol, Investigator's Brochure, consent(s), regulatory documents and any other study materials are sent by the sponsor to the IRB Coordinator.

6) A copy of the protocol is forwarded for budget and contracting negotiation to the Contracts and Grants Administrator and other resource reviewers (Research Nursing Manager, Investigational Pharmacist, Lead Clinical Research Coordinator) and any additional personnel (i.e., pathology, radiation oncology, in-patient pharmacy, nuclear medicine) as required by the protocol.

7) IRB Coordinator (or CTO personnel) creates OnCore record and pending study file. The protocol and Investigator's Brochure are attached in OnCore.

8) The IRB Coordinator submits the Interdepartmental Billing Form to pay IRB fees to the Arizona Cancer Center Business Office.

9) The IRB Coordinator retains the Protocol Submission Form and Interdepartmental Billing Form to be submitted with other study materials to the Scientific Review Committee.

10) The IRB Coordinator prepares the protocol submission for Committee (SRC, IBC, HSC) review and approval. The following documents are prepared:
   - Project Approval Form (complete full length version PAF for local IRB submission, abbreviated version PAF for WIRB submission);
   - Informed Consent Form(s);
   - PHI Authorization.

11) The IRB Coordinator (or CTO personnel) attach the Project Approval Form, consenting instruments, study protocol, study Investigator's Brochure, signed Protocol Submission Form, approved Interdepartmental Billing Form, summary of previous study IND reports (if supplied by sponsor), and any other protocol tools received for study conduct to the pending study file in OnCore. When the file is complete, it is submitted electronically to the Scientific Review Committee (SRC). Receipt of the submission is electronically acknowledged by the Scientific Review Committee.

12) The SRC reviews the protocol and an Outcome Report is sent electronically to the PI and the IRB Coordinator. The Committee may have questions or request revisions or clarifications. Responses are made to the Committee by the PI/IRB Coordinator. Correspondence between the PI, IRB Coordinator, and SRC committee is entered into OnCore and a hard copy is made for filing in the regulatory binder.
13) Upon approval of the SRC, the IRB Coordinator forwards a hard copy submission packet, including any revisions made in response to the SRC review, PAF with original signatures, consenting instruments, protocol, Investigator's Brochure, and signed Interdepartmental Billing Form to the IRB. Some protocols may require additional committee reviews/approvals (i.e., Institutional Biosafety, Radiation Safety, DSMB, project-specific reviews).

14) Following review of the project, the IRB corresponds with the PI/IRB Coordinator with questions, concerns, or requests for revisions or clarifications. Responses and revised documents are re-submitted to the IRB as requested and entered into OnCore by the IRB Coordinator (or CTO personnel) and a hard copy is made for filing in the regulatory binder.

15) If the study is being submitted to WIRB, after the submission to WIRB is approved by the local IRB, the IRB Coordinator will submit the study electronically to WIRB. Submission will include the appropriate WIRB Submission document (either for a study which has been previously reviewed and approved by WIRB, or for the initial submission of a study to WIRB), local IRB approval, consenting documents (or templates supplied by the sponsor), required regulatory documents (i.e., Form FDA 1572, medical licenses, and CVs), and the protocol and Investigator's Brochure. If the study has not been previously approved by WIRB, see WIRB instructions for submissions.

16) When final approval is received from either the local IRB or WIRB, the approval letter(s), and stamped consenting instruments are sent (by hard copy or e-mail) to the IRB Coordinator. Electronic copies are entered into OnCore by the IRB Coordinator (or CTO personnel). Copies are forwarded (by e-mail) to the Sponsor, members of the research team, investigational pharmacist and other personnel/services as required by the protocol. The team members are also notified that copies of all of these materials are attached in OnCore so that they may access them at any time. A copy of the protocol, approval letter, and currently approved stamped consents are filed in binders located in the clinic consult room by the research team.

17) After SRC approval, the Regulatory Specialist submits the required regulatory documents to the Sponsor and distributes regulatory documentation to the study team (Refer to SOP 112-ADM Clinical Trial Documentation Distribution). The Regulatory Specialist, if necessary, will also prepare the Form FDA1572 which will be submitted to WIRB.

18) All study documents are filed in a regulatory binder.

19) If study will be conducted at SAVAHCS, refer to VA policies and guidelines on conduct of clinical trials. Refer to Section 12200.5: Requirements for the Protection of Human Subjects in Research on Veterans Administration.

20) The IRB Coordinator confirms that the contract has been finalized; CTO can schedule a Site Initiation Visit.

21) The Site Initiation Visit is conducted by the Sponsor and includes a review of the protocol, and specific training in protocol procedures as required of the PI and each team member. After the SIV has been completed, the Sponsor will authorize shipment of study drugs/supplies, and the study is officially open to accrual. This action is
Study Closure and Close-out Visit
The study may be closed due to completion of the study (as determined by the protocol procedures and sponsor), at the sponsor’s discretion for safety reasons, or by the SRC due to lack of accrual. Once all local subjects are off-study (no longer receiving treatment or being followed for any reason) and the sponsor is no longer requesting information regarding study data (queries), a close-out visit by the sponsor occurs to complete and finalize study documentation between the sponsor and the PI/study site.

1) The Clinical Research Coordinator schedules the study close-out visit.
2) The IRB Coordinator, Regulatory Specialist and CRC communicate with the sponsor and prepare all clinical binders and documents, and regulatory binders for final review.
3) The sponsor requests submission and/or updates for any outstanding data, pharmacy documentation, IRB and/or regulatory documents. These are submitted as requested.
4) The PI, CRC, Investigational Pharmacist, Regulatory Specialist and IRB Coordinator meet with the sponsor during the close-out visit to confirm all outstanding documentation is complete and that there are no questions outstanding. Once all documentation is complete, the sponsor will send a termination letter to the IRB Coordinator confirming that all documentation for the study is complete.
5) When the termination letter form the sponsor is received, the IRB Coordinator will submit a “Concluded” CRF/PRF to the IRB/WIRB. After final approval is received, recorded in OnCore and a copy sent to the sponsor, the study will be considered “Concluded.”
**Example: Site Evaluation (Prestudy) Visit Checklist**

The Site Evaluation (Prestudy) Visit is coordinated by the CTO between interested sponsors/pharmaceutical companies and investigator(s). A tour of UMC-North facilities (e.g., pharmacy, drug storage location, source document files/storage, treatment area) is conducted. In addition, potential sponsors may want to discuss the contracting process and meet with the investigator(s).

- Receive request to schedule meeting from investigator or sponsor.
- Prepare SEV file folder/label. Insert and complete Event Planner Worksheet.
- Obtain contact information for investigator(s), sponsor and participants on Event Planner Worksheet:
  - name
  - phone number(s)
  - e-mail address
  - date of contact
  - using worksheet and other appropriate tools, coordinate date/time availability of investigator and sponsor
  - reserve meeting room (optional)
- Send participants confirmation of meeting time/place via Outlook; add information to CRSS shared calendar.
- Enter SEV information into crss on AZccnas1 SIV, SEV, CDA Feasibility Qs.doc folder spreadsheet.
Example: Site Initiation Visit (SIV) Checklist

The Site Initiation Visit is coordinated by the CTO personnel following assignment of research personnel and confirmation that all required approvals and regulatory documents have been obtained and copies retained in the regulatory binder/file.

Potential participants:

- Investigator(s)
- Sponsor representative(s)
- Contract Research Organization representative(s)
- Investigational Pharmacist
- Research Nurse Coordinator
- Clinical Research Coordinator (CRC)
- Regulatory Specialist
- Research Technician (as dictated by protocol)
- Contracts and Grants Administrator (optional)
- Data & Safety Monitoring Board Coordinator (optional)
- QC/QA Coordinator (optional)
- Southern Arizona Veterans Administration Health Care System research staff, as appropriate

☐ Receive request to schedule meeting from investigator/sponsor/CRO representative.
☐ Prepare and complete SIV Event Planner Worksheet.
☐ Obtain contact information for investigator, sponsor and participants on Event Planner Worksheet.
  - name
  - phone number(s)
  - e-mail address
  - date of contact
☐ Identify required study participants. Enter study-specific personnel assignments in OnCore protocol contacts information screen.
☐ Prior to SIV, distribute latest approved version of protocol and Investigational Brochure (as necessary) to assigned research staff as soon as possible.
☐ Using worksheet and other appropriate tools, coordinate date/time availability of investigator, sponsor and/or CRO representative.
☐ Verify with Contracts and Grants Administrator that budget has been negotiated/finalized and contract has been signed/fully executed.
☐ *Check CTO calendar(s) for meeting date/time conflicts (monitor visits, participant work schedules, and established meetings). Enter information in CRSS shared calendar.
☐ Reserve meeting room/s.
☐ Send participants confirmation of meeting time/place via Outlook; add information to CRSS shared calendar.
☐ Enter SIV information into crss on AZccnas1 SIV, SEV, CDA Feasibility Qs.doc folder spreadsheet.
☐ Reserve requested equipment. Media Tech: 626-0151; CTO maintains, conference phone, etc. Add information to CRSS shared calendar.
☐ Prepare and distribute final agenda as soon as possible.
☐ Provide sign-in log if no study-specific log is provided.
☐ At close of meeting, check with visitor(s) for necessary assistance.
☐ Return materials and equipment to proper location.
☐ Confirm drug availability and/or receipt.
☐ Confirm receipt of lab supplies.
☐ After sponsor’s authorization, update OnCore status to “Accrual Open.”
Example: Study Close-out Visit

At time of Study Close-out, a thorough review of the regulatory documents will be made by a sponsor representative to compare CRFs and sponsor-to-site documentation. Records are maintained per protocol guidelines.

- Receipt of IRB conclusion letter (optional).
- Clinical Research Coordinator (CRC) schedules date/time to meet with study monitor.
- All outstanding regulatory documentation and Case Report Forms are complete and available for review.
- All data queries received to date have been resolved to the extent possible.
- Study drug is prepared for return or disposed of at site per sponsor instructions. (Refer to SOP-201 PHM Handling of Investigational Drugs.)
- All other unused study-related materials are returned or destroyed as directed by sponsor.
- Investigator meets with a sponsor representative regarding close-out items.