4. PARTICIPANT ENROLLMENT

4.1 Initiation of a New Study

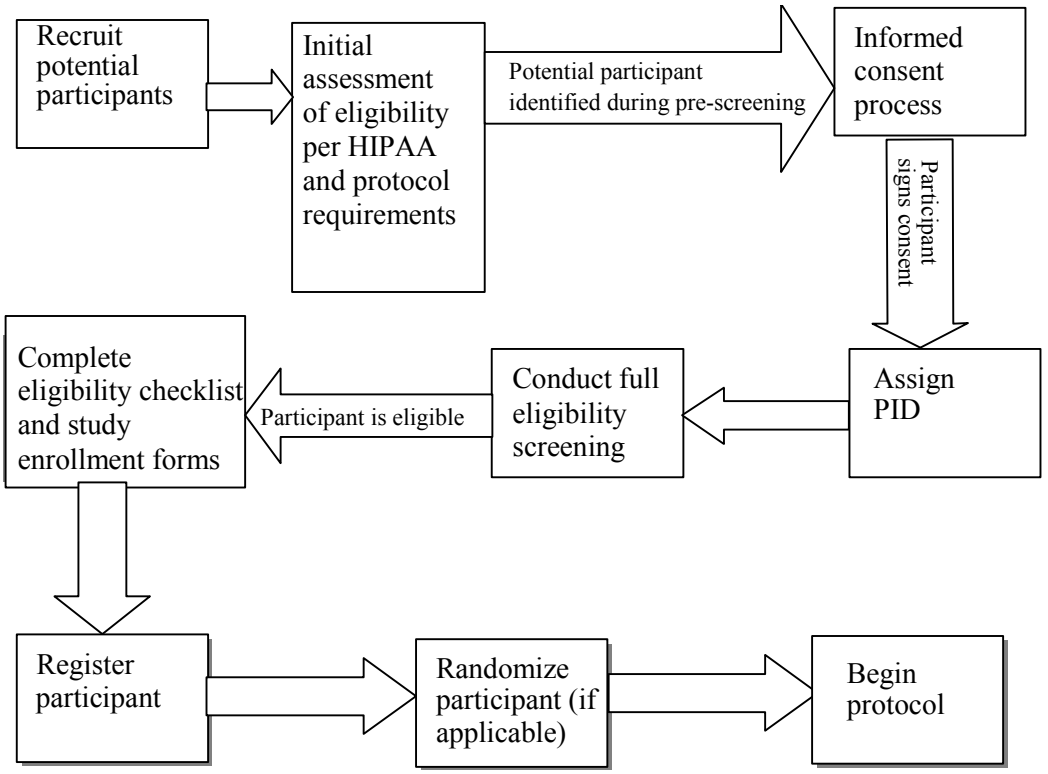
Prior to initiating a new Phase I or II study, qualified site staff are responsible for the implementation of a number of tasks that will contribute to a successful completion of a clinical trial. The PI, Study Coordinator, and other research staff will work within existing systems within the institution in order to accomplish a successful launch of a new study. The following is a list of key items necessary for study staff to implement at the beginning of each study protocol:

- Obtain DCP approval of clinical protocol, informed consent, CRF, Biomarker Methods Validation Report (if applicable), and Data and Safety Monitoring Plan;
- Submit all required regulatory documents and other requested documents to DCP;
- Assure that for all DCP-sponsored IND trials: 30-day waiting period following FDA submission of IND with no clinical holds placed by the FDA;
- Receive IRB approval and send letter/documentation to DCP and the DCP Regulatory Contractor;
- Obtain an executable contract with the lead organization;
- Receive adequate study agent supply on site;
- Have approved CRFs present and available for use;
- Determine whether a site initiation visit by the CRA from the DCP Monitoring Contractor, DCP staff, and involved study site staff (as required by DCP) will be conducted prior to the beginning of study approval;
- Prepare a Site Personnel Signature/Delegation Log;
- Have available copies of the DCP/IRB-approved informed consent forms and recruitment materials for the research team to provide to potential participants;
- Develop procedures for CRF completion, data entry, and a mechanism to prepare study progress reports;
- Record procedures for the collection, shipping, and processing of laboratory specimens required by the protocol; and
- Develop a Participant Identifier (PID) logbook and screening log.

4.2 The Enrollment Process

When required by DCP, the enrollment process may begin once the initiation visit has taken place and the site is prepared logistically to conduct the study (see Figure 4-1). The initiation visit can take place when DCP has given final study approval and the appropriate IRB has granted approval. Enrollment refers to the tasks that each site undertakes to initiate participant accrual beginning with recruitment and followed by a review of potentially eligible participants.

FIGURE 4-1. Participant Enrollment Process



4.2.1 Participant Recruitment

Recruitment for DCP chemoprevention trials will occur in different ways depending upon the particular study, research site, and creativity of assigned recruitment staff. Some potential participants may be recruited through primary care and specialty practices such as dermatology or urology. Other potential participants may be reached through oncology clinics. General media or specific outreach methods can be used to recruit members of the public. Each site is responsible for developing a

recruitment plan, recruitment materials, and methods to retain study participants as necessary. All participant recruitment materials must be approved by DCP and the IRB prior to their use.

In developing site-specific recruitment strategies, it is important that site staff be sensitive to the culture, personal beliefs, and current life circumstances of potential participants that could influence their decision to participate on a chemoprevention clinical trial. For example, potential participants may want to take a more active role in their health care and/or receive regular medical attention, or they may want to assist in the gathering of medical knowledge. They may also worry about perceived and/or real side effects, payment issues, and being viewed as "guinea pigs." The process of informed consent begins with the recruitment phase of a study.

4.2.2 Initial Evaluation of Participant's Eligibility Using the Inclusion/Exclusion Criteria

A general assessment of the participant's potential eligibility should be made to determine if further eligibility screening is warranted. Tests and procedures to confirm eligibility can be done only after the participant has signed the informed consent form.

4.2.3 Obtaining Informed Consent

Every effort must be made to protect the rights of the study participants. An investigator may not involve a participant in research (including tests to evaluate eligibility) unless the investigator or his or her representative has obtained a signed DCP and IRB-approved informed consent document. An investigator should obtain informed consent only under circumstances that provide the prospective participant sufficient opportunity to consider whether or not to participate.

NOTE: Participants who are minors or who cannot make their own health care decisions will need a legal representative to provide consent. Assent requirements may also apply. For further information on assent requirements, consult your local institution and/or state regulations.

Obtaining informed consent is more than obtaining a signature on a form. It is a process designed to:

- Provide the participant with current and ongoing information about the study;

- Ensure that the participant understands the information that has been presented and has an opportunity to ask questions;
- Discuss the participant's rights as outlined in the consent form;
- Grant the participant the opportunity to agree or disagree to take part in the study;
- Allow the participant the opportunity to freely withdraw from the study in the future; and
- Permit the participant the opportunity to allow or refuse to have his or her biologic samples stored and used for future research.

NOTE: During a site monitoring visit, the CRA will check the date the participant or legal representative signed the informed consent, as well as whether that signature was obtained on or before the date(s) that any screening or other study-related procedures were conducted. The CRA will also review the date an informed consent form was approved by the IRB and will determine whether a participant's signature was obtained only IRB approval.

4.3 Assigning a Participant Identification Number

Once a participant has been identified as potentially eligible for enrollment in the study and has signed an informed consent document, the participant will be assigned a unique identifier sometimes referred to as a Participant Identifier (PID). Depending on the funding mechanism of the clinical center, the staff, will develop a strategy for providing this PID, or it will be provided by DCP. Once a participant has been assigned a PID number, that number never changes. If the participant is enrolled in future stages of the study, he or she will retain that PID number. If the participant does not enroll, that PID number will not be reassigned. The PID logbook that contains the participants' names and their assigned PID numbers must be kept in a locked, secure place with access limited to appropriate study personnel.

NOTE: DCP will comply with the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule in order to protect the privacy of research participants. Please refer to the following website for more information: http://www.hhs.gov/ocr/hipaa/.

4.4 Determining Eligibility

Once a participant is identified as a potential candidate for a study and has signed the informed consent document, the screening (or pre-entry) assessment to fully evaluate and confirm eligibility begins. This eligibility evaluation may include laboratory and/or clinical tests. The results of

the tests help determine whether the participant satisfies the inclusion/exclusion criteria of the protocol. All screening evaluations are performed prior to the participant's registration.

All participants who undergo screening for a study must be recorded in a study-specific screening log. If a participant is found to be ineligible or otherwise does not enroll in the study, the reason for this must be stated in the log.

Participants who sign the informed consent document, but who are not eligible for the study due to the inclusion or exclusion criteria, must be told why they cannot participate in the clinical trial. This explanation is often provided by the Research Nurse or Study Coordinator. The reason(s) for ineligibility must be recorded in the participant's study chart and should include a note indicating the participant understood the rationale for exclusion.

After eligibility has been determined, the protocol-specific eligibility checklist must be completed to document that the participant fulfills the inclusion/exclusion criteria of the protocol. If the participant meets the criteria of the protocol, the study enrollment form will be completed and the participant will be ready for registration.

NOTE: During a site monitoring visit, the CRA will check the Eligibility Checklist CRF against the source documentation. The CRA may also ask to review the screening log while on site.

4.5 Registering/Randomizing Participants

The mechanism for officially registering and randomizing participants onto a DCP study will vary depending upon the protocol. The person responsible for randomizing participants and study staff to be blinded to study agent also will differ with each protocol. Details for registering/randomizing participants should be found in the protocol. For example, if a pharmaceutical company is involved in the study and is assigned randomization responsibilities, site staff may be required to call or fax the eligibility and enrollment forms to that company. Likewise, if several sites are involved in the study and the statisticians at the lead organization are responsible for randomization, all sites will send eligibility and enrollment information to the lead organization's statisticians. In other instances, the research pharmacist at the site may be responsible for implementing the randomization process. DCP does not perform the function of registering and randomizing participants. Therefore, it is critical that site staff assess eligibility criteria carefully, as eligibility may be checked only at the time of the annual site monitor visit. During

site monitoring visits, participant eligibility will be one of the main items assessed by the CRA or by other designated monitoring staff.