2. DCP ORGANIZATIONAL OVERVIEW, DESCRIPTION OF PREVENTION TRIALS, AND SUMMARY OF CONTRACTOR RESPONSIBILITIES

2.1 Overview

The goal of the National Cancer Institute (NCI) is to achieve a future where all cancers are controlled or eliminated, by stimulating and supporting research and its application. NCI is leading the world in defining the standard of cancer care and prevention. The Institute has six divisions, each specializing in a different aspect of cancer research. The Division of Cancer Prevention (DCP) is a growing, dynamic matrix organization committed to evidence-based cancer prevention research. The goals are to advance biomedical science, strengthen preventive medicine, and improve public health. Research is carried out through the positive, interactive efforts of all DCP staff dedicated to the success of the Division's activities.

2.2 Prevention Trials

Cancer prevention science seeks methods to reduce the risk, or chance, of developing cancer. Because carcinogenesis can take decades to manifest, it also provides time and opportunity to inhibit, retard, or reverse the process of carcinogenesis with lifestyle changes or the use of chemopreventive agents. Cancer prevention trial participants may have varying degrees of cancer risk. Participants may be at average risk or they may have some known risk factor or combination thereof, such as prior history of cancer, family history of cancer, inborn genetic mutation, or environmental exposure.

There are three types of trials: screening trials, control trials, and intervention trials. Intervention trials generally take one of two forms. Behavioral studies focus on finding out whether actions people take, such as exercise or smoking cessation, can prevent cancer. *Agent studies* focus on examining whether taking certain medicines, vitamins, minerals, or food supplements (or a combination of them), can prevent cancer.

- **Screening Trials:** The goals of screening trials are to develop tools for detecting cancer or pre-cancers before an individual becomes symptomatic and to see if early detection and treatment of disease improves the outcome. Screening can include:

  - Imaging tests (e.g., x-rays) that produce images of internal organs and tissues in the body;

  - Biological tests of the blood, urine, and other bodily fluids and tissues to find indicators of disease processes; and

  - Genetic tests that look for inherited genetic markers linked to certain types of cancers (e.g., BRCA1 gene mutation).

- **Control Trials:** A cancer-control trial assesses the effect of an intervention on cancer symptoms, side effects of cancer treatment, or the participant's quality of life. As with other clinical trials supported by DCP, the intervention can be pharmaceutical, nutriceutical, dietary, or behavioral.

- **Chemoprevention Trials:** Chemoprevention trials may be Phase I, Phase II, or Phase III studies.

  - Phase I chemoprevention trials are the first studies in people which evaluate how new agents should be given (by mouth, applied to the skin), how often, and what dose is safe. A Phase I trial usually enrolls only a small number of patients, sometimes as few as a dozen. DCP also administers a pre-clinical program (Rapid Access to Prevention Intervention Development Program) to foster cancer prevention agent development and move promising agents into early clinical trials.

  - Phase II chemoprevention trials are conducted in larger groups of participants who are at high risk for certain cancers. These continue to study the safety of the agent and begin to evaluate how well the new agent works; usually by measuring the agent's effect on biomarkers at the genetic, molecular, or tissue level. In other words, these studies do not aim to prove a decrease in cancer incidence, but rather to show an agent's effect on ongoing pre-cancerous processes. Phase II studies usually focus on a particular type of cancer. Frequently these trials are conducted using a placebo-controlled group.

  - Phase III chemoprevention trials are conducted either in populations at high risk for specific cancers or in participants from the general population. These studies test new agents, a combination of agents, or a new surgical procedure in comparison to the current standard or to a placebo. A participant will usually be assigned, at random, to the investigational group, to the standard group, or placebo. Phase III trials often enroll large numbers of participants and may require 5-10 years to reach the study end-point. Phase III trials may be conducted at physicians' offices, clinics, hospitals, or cancer centers nationwide.

2.3 DCP Organization

Peter Greenwald, M.D. is the Director of the Division of Cancer Prevention, and Leslie Ford, M.D. is the Acting Deputy Director and Associate Director for Clinical Research. DCP is organized into a matrix of eleven groups, seven Foundations of Prevention Research Groups, and four Organ System Research Groups. The Protocol Information Office (PIO) is the coordinating office for Cancer Prevention Studies. Linda Parreco, R.N., M.S. is the head of the PIO. All protocol activity from protocol development to final report submission is coordinated through the PIO. The PIO works closely with the Organ System Research Groups, the Chemopreventive Agent Development Research Group (CADRG), and the Community Oncology and Prevention Trials Research Group (COPTRG) to facilitate the research process for Principal Investigators conducting cancer prevention trials. The DCP Matrix Organizational Chart is shown as Figure 2-1 on page 2-4 and displays the organization of the division. A list of names, addresses, and telephone numbers of DCP staff are in Appendix A.

2.4 Prevention Protocol Management

There are three primary areas of protocol management:

- Protocol Development;
- Regulatory Affairs; and
- Study Site Monitoring.

DCP has enlisted the support of several contractors to assist with these activities. CCS Associates in Mountain View, California assists with protocol development and regulatory affairs and the Westat Team manages the study site monitoring, data management, and informatics activities.

The CCS Associates contractor is responsible for assisting the PIO, Research Group personnel, and study site staff with protocol development and management of regulatory issues during the conduct of a study. CCS Associates provides technical assistance with drafting, revising, and managing IND packages, and DCP sponsored New Drug Application (NDA) documents. Regulatory documents will be described in Chapter 5, Study Record Maintenance.

The Westat Team consists of staff with clinical trials monitoring experience, clinical trials data management experience, and clinical trials database informatics experience. Over the 5-year contract, the Westat Team will:

- Enhance the existing database, DCP Enterprise System Knowledgebase (DESK), and develop software applications to collect, analyze, and report the study data;
- Standardize site monitoring processes; and
- Provide consistent education and training to site staff about the conduct and management of clinical research trials.

A glossary of terms in Appendix B is provided to assist with definitions of DCP prevention terminology.

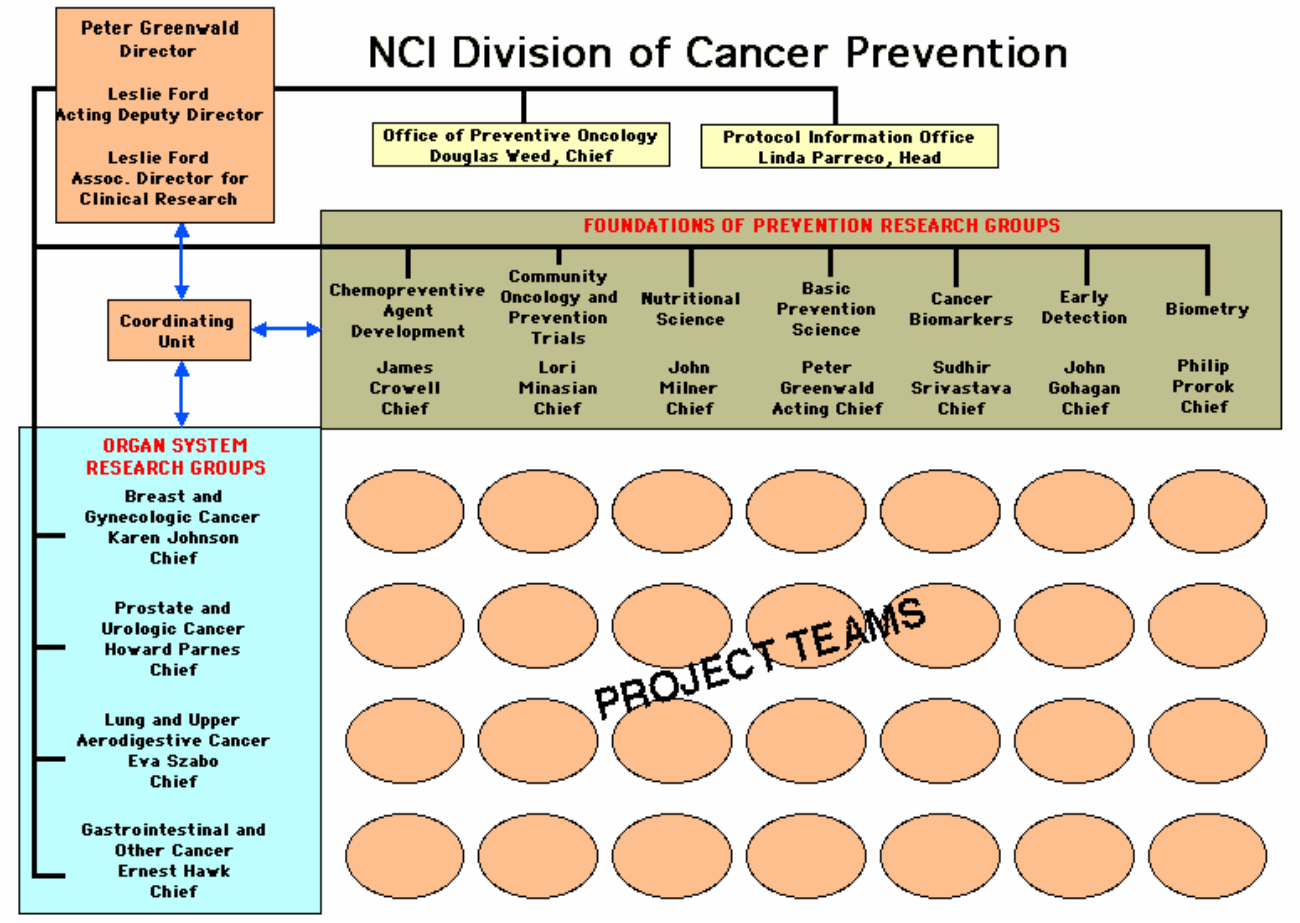

Figure 2-1. DCP Matrix Organizational Chart