National Cancer Institute Community Oncology Research Program (NCORP)

Program Guidelines

Revised May 2018

Division of Cancer Prevention
and
Division of Cancer Control and Population Sciences

National Cancer Institute

National Institutes of Health

Table of Contents

PART 1: OVERVIEW OF THE NATIONAL CANCER INSTITUTE COMMUNITY ONCOLOGY RESEARCH PROGRAM (NCORP).....6

I. Introduction.....6
A. Purpose and Content of Guidelines.....6
B. Background, Overview, and Purpose of NCORP.....7
C. Goal, Scope and Strategy of NCORP.....7
D. Organization of Key Components of NCORP.....7
E. Interactions with Other NCI-Supported Programs.....7
1. National Clinical Trials Network (NCTN).....7
2. NCI NCTN Biospecimen Banks.....7
3. NCI Cancer Trials Support Unit (CTSU).....8
4. NCI Central Institutional Review Board (CIRB).....8
5. Research Programs of the Center to Reduce Cancer Health Disparities (CRCHD).....9
6. NCI Advisory & Scientific Committees.....10

II. Types of Research in NCORP.....11
A. Cancer Prevention Research.....11
B. Cancer Screening Research.....11
C. Post-Treatment Surveillance Research.....11
D. Cancer Control Research.....11
E. Cancer Care Delivery Research.....12
F. Cancer Treatment Trials.....12
G. Health-Related Quality of Life Sub-Studies.....12
H. Correlative Science Sub-Studies.....12
I. Biospecimen Collection.....12
J. Cancer Disparities Research.....12

III. NCORP General Management, Operating and Funding Principles.....13
A. General Management.....13
B. NCORP Operating Principles.....13
1. Access to NCORP Trials & Crediting for Patient Accrual to Trials.....13
2. Submission of Data and Biospecimens.....14
3. Use of the NCI Central Institutional Review Board.....14
4. Processes for review and approval of Non-NCORP funded Study Proposals using NCORP Infrastructure.....14
5. Collaborations Among Research Bases and with Other Organizations on Clinical Trials/Studies.....17
6. Compliance.....17
C. NCORP Network Funding Principles.....18
1. Grant Funding for Key Components of NCORP.....18
2. Funding for Research Bases.....18

2.1 Total Budget 18
2.2 Core Budget 18
2.3 Cancer Care Delivery Research Budget 18
3. Funding of Sites for Cancer Control, Prevention, Treatment & Imaging Clinical Trial Data Collection/Management & Biospecimen Collection 19
4. Funding of Sites for Cancer Care Delivery Research 20
5. Program Income for Key Components of NCORP 21

IV. Terms & Conditions of Award for Cooperative Agreements for NCORP Key Components 22
A. General Terms and Conditions of Award for All Key Components of NCORP 22
1. General Programmatic Responsibilities 22
2. Dispute Resolution 22
B. Specific Terms and Conditions of Award for the Key Components of NCORP 23
1. Specific Awardee Rights & Responsibilities - NCORP Research Bases 23
1.1 Clinical Trial and Cancer Care Delivery Development Program 23
1.1.1 Overall Responsibilities for Cancer Control, Prevention and Cancer Care Delivery Clinical Research 23
1.1.2 Overall Research Strategy for Disparities Research Studies 23
1.1.3 Scientific Research and Administrative Committees 24
1.1.4 Young Investigator Mentoring/Training 25
1.1.5 Communications Support 25
1.1.6 Publications 25
1.1.7 Data Rights 27
1.2 Membership Affiliation(s) 27
1.3 Operational Management 28
1.3.1 Governance, Organizational Structure, Policies & Procedures, and Membership 28
1.3.2 Conduct of Cancer Control, Prevention and Care Delivery Research Studies 29
1.3.3 Quality Assurance and Onsite Auditing 35
1.3.4 Financial Management 38
1.3.5 Legacy Studies 39
1.4 Program for Collaborations and Participation in Collective Management 39
1.5 Compliance with Federal Regulations for Clinical Research & Resource Sharing Plans 39
1.5.1 Office for Human Research Protection (OHRP) Assurances 39
1.5.2 IRB Review of NCORP Studies by Member Institutions/Sites 40
1.5.3 Assurance of Appropriate Informed Consent by Member Institutions/Sites 40
1.5.4 Inclusion of Women, Minorities, and Children in Clinical Research 41
1.5.5 Data and Safety Monitoring Policy and Plans 41
1.5.6 Resource Sharing Plans 42
1.5.7 Education on the Protection of Human Subjects and Good Clinical Practice 42
1.5.8 Other Federal Regulations 43
1.6 Conflict of Interest Policy 43
1.7 Special Requests for Use of NCORP Infrastructure Services 43
2. Specific Awardee Rights & Responsibilities – NCORP Community Sites 44
2.1 Definition, Eligibility, and Accrual Threshold 44
2.1.1 Definition of an NCORP Community Site 44
2.1.2 Annual Accrual Threshold 44
2.2 Overall Responsibilities for Community Sites 44

2.2.1 Scientific Leadership & Contribution to NCORP Activities....44
2.2.2 Young Investigator and Leadership Mentoring/Training....45
2.2.3 Operational Management (Governance/Organization, Institutional Support, Components)....45
2.2.4 Use of the NCI Central Institutional Review Board....46
2.2.5 Study Operations – Conduct of Studies and Data Management....47
2.2.6 Quality Assurance and Onsite Auditing....47
2.3 Site Responsibilities....48
2.4 Compliance with Federal Regulations for Research....48
2.4.1 Inclusion of Women, Minorities, and Children in Clinical Research....49
2.4.2 Resource Sharing Plans....49
2.4.3 Education on the Protection of Human Subjects and Good Clinical Practice....49
2.4.4 Other Federal Regulations....49
2.5 Conflict of Interest Policy....50
3. Specific Awardee Rights & Responsibilities – NCORP Minority/Underserved Community Sites....51
3.1 Definition, Eligibility, and Accrual Threshold....51
3.1.1 Definition of an NCORP Minority/Underserved Community Site....51
3.1.2 Annual Accrual Threshold....51
3.2 Overall Responsibilities for Minority/Underserved Community Sites....51
3.2.1 Scientific Leadership & Contribution to NCORP Activities....51
3.2.2 Young Investigator and Leadership Mentoring/Training....52
3.2.3 Operational Management (Governance/Organization, Institutional Support, Components)....52
3.2.4 Use of the NCI Central Institutional Review Board....53
3.2.5 Study Operations and Data Management....54
3.2.6 Quality Assurance and Onsite Auditing....54
3.3 Site Responsibilities....55
3.4 Compliance with Federal Regulations for Research....55
3.4.1 Inclusion of Women, Minorities, and Children in Clinical Research....56
3.4.2 Resource Sharing Plans....56
3.4.3 Education on the Protection of Human Subjects and Good Clinical Practice....56
3.4.4 Other Federal Regulations....56
3.5 Conflict of Interest Policy....57
C. NCI/DCP and DCCPS Staff Responsibilities....58
1. NCI Responsibilities Related to NCORP Research Bases....70
1.1 Coordination of National Priorities....58
1.2 Scientific Resource for NCORP Research....58
1.3 Scientific and Administrative Program Directors Activities....58
1.4 Attendance at Meetings of NCORP Research Base....59
1.5 Data and Safety Monitoring Boards (Data Monitoring Committees)....59
1.6 Coordination of Resources to Enhance Accrual/Completion of NCORP Studies....60
1.7 Study/Trial Closure....60
1.8 Quality Assurance and Onsite Auditing....61
1.9 Data Management and Analysis Review & Use of Standard NCORP Tools and Services 62
1.10 Program Review, Strategy Sessions, and Federally Mandated Requirements....63
2. NCI Responsibilities Related to NCORP Community Sites and Minority/Underserved Community Sites....64

2.1 Scientific and Administrative Program Directors & Activities 64
2.2 Review of Clinical Trials and Other Studies in NCORP Network for Crediting 64
2.3 Onsite Auditing 64
2.4 Data Management and Access 65
2.5 Investigational Drug Management 65
2.6 NCORP Community or Minority/Underserved Community Site Organizational Changes 65
2.7 Program Review and Federally Mandated Requirements 65
D. Joint Responsibilities (Key Components NCORP, NCI/DCP and NCI DCCPS) 66
1. General Study Development and Conduct 66
1.1 Data and Safety Monitoring Boards (Data Monitoring Committees) 66
1.2 Development of Collaborative Trials and International Trials 67
2. Network-Wide Common Services, Tools, and Resources 68

V. Budget Levels for Per Case Management Funding & Budget Adjustments for NCORP 69

VI. Changes in Principal Investigator(s) for Any Key Component of NCORP 69

VII. Changes in Awardee Institution for Any Key Component of NCORP 69

VIII. Appeals Process for Decisions Regarding Study Proposals and Types of Studies Performed by NCORP 69
A. Decisions on Study Proposals 70

IX. Other NCI Administrative Considerations 70
A. Program Staff Administration of NCORP 70
B. Senior Program Specialist for NCORP 70
C. NCI Office of Grants Administration (OGA) 70
D. Miscellaneous Budgetary Considerations 71
1. Carryover Requests 71
2. Requests for Non-competing Supplemental Funding 71

X. Appendix 73
I. NCI/DCTD/DCP Policies for the NCTN/NCORP Programs (URLs to Websites) 73
II. Other Important NIH/NCI URLs, Federal Citations, List of Abbreviations and Key Definitions 74

Part 1: Overview of the National Cancer Institute Community Oncology Research Program (NCORP)

I. Introduction

A. Purpose and Content of Guidelines

These Guidelines for the National Cancer Institute Community Oncology Research Program (NCORP) have been developed by staff of the Division of Cancer Prevention (DCP) and the Division of Cancer Control and Population Sciences (DCCPS), NCI. Because NCORP is an integral part of the overall National Clinical Trials Network (NCTN), these NCORP Guidelines have been developed in collaboration with staff of the Division of Cancer Treatment and Diagnosis, Cancer Therapy Evaluation Program (DCTD/CTEP). DCP and DCCPS have also collaborated in the creation of these Guidelines with the Center to Reduce Cancer Health Disparities (CRCHD), the Office of Grants Administration (OGA) and the NCI Division of Extramural Activities (DEA), as well as with the advice of members of the extramural scientific community. The purpose of these Guidelines is to describe the NCI's terms, conditions and expectations for NCORP grantees and investigators, and the National Institutes of Health (NIH) staff who are involved with NCORP. They are intended to encourage a multi-disciplinary, comprehensive, community-based network that will: 1) design and conduct cancer prevention, control, and care delivery clinical research studies; 2) enhance patient and provider access to cancer treatment and imaging trials conducted under the reorganized NCTN; and 3) integrate disparity research questions into clinical trials and cancer care delivery research.

This Guidelines document is divided into five parts as described below *(Parts 2 – 5 are available on the password protected NCORP Portal accessible by NCORP grantees)*:

Part 1 – Overview of NCORP
This part describes NCORP and its policies and procedures, including the Terms and Conditions of Award. Separate sections are devoted to cancer prevention, control and care delivery research, the main research components comprising the program.

Part 2 – Guidelines for Submission of Annual Research Performance Progress Report (RPPR)
This part describes the annual progress report to be submitted using the Research Performance Progress Report (RPPR) via the eRA Commons.

Part 3 – Guidelines for Development of Concepts, Protocols, and Amendments for NCORP Cancer Prevention, Control, or Care Delivery Clinical Research Studies
This part describes the procedures for submitting and review of concepts, protocols and amendments.

Part 4 – Guidelines for Approval of NCORP Organizational Changes
These guidelines provide information regarding preparation of correspondence and submission of all the required documentation when preparing for organizational changes.

Part 5 – Appendices
This part contains reference materials and other documents relevant to the policies and procedures associated with NCORP.

A variety of other rules and regulations affect NCORP (e.g., NIH grants policy, policies of the Office of Human Research Protections). Guidelines in this document are intended to cover

NCI/DCP's special requirements for NCORP and to supplement NIH and U.S. Department of Health and Human Services (DHHS) policies. These Guidelines, as well as the policies of all awardees under NCORP, must adhere to NCI, NIH, and DHHS policies. Grantees should contact the NCORP Director if they believe these Guidelines conflict with other applicable Federal policies in order to resolve any apparent discrepancies in the interpretation of these Guidelines.

B. Background – See RFA for additional information

C. Overall Goal and Scope of NCORP – See RFA for additional information

D. Organization of Key Components of NCORP

The NCORP Network is comprised of 3 components: (1) NCORP Research Bases; (2) NCORP Community Sites; and (3) NCORP Minority/Underserved Community Sites.

Each of these key components have separate RFA in which they are described. See specific RFAs for additional information

E. Interactions with Other NCI-Supported Programs

In addition to the three key components that are listed above and will be directly funded by NCORP, other NCI grant and contract supported Programs and their awardees as well as NCI Advisory Committees will have important supporting roles in carrying out the research objectives of NCORP. Thus, NCORP awardees will be expected to interact as appropriate with such entities/programs as NCTN, NCI NCTN Biospecimen Banks, the NCI Cancer Trials Support Unit, the pediatric and adult NCI Central Institutional Review Boards, research programs of the Center to Reduce Cancer Health Disparities, and NCI Advisory and Scientific Committees including the NCI Scientific Steering Committees.

1. National Clinical Trials Network (NCTN)

NCORP Community Sites and Minority/Underserved Community Sites are expected to accrue to NCTN treatment trials. NCORP Research Bases grant funding should not be used to develop or conduct treatment and imaging trials.

2. NCI NCTN Biospecimen Banks

The advent of powerful molecular technologies and the emergence of targeted therapeutics have opened the door to developing more effective and, in some cases, individualized treatment of patients with cancer aimed at specific cancer-related pathways. Understanding risk and mechanisms of disease related symptoms and treatment related toxicities may be enhanced by specimen collection in conjunction with NCORP studies. Development of effective interventions, based on comprehensive analysis of critical pathways of cancer initiation and progression, requires access to biological specimens from patients treated in prospective studies. High-quality biological specimen banks containing uniformly collected specimens from such studies along with validated clinical and outcome data are essential for development and delivery of new diagnostic and predictive tools to guide the use of targeted therapies. In particular, key components of NCORP conducting phase 3 clinical trials are uniquely positioned to provide high-quality biologic specimens associated with detailed information regarding method of diagnosis (screen-detected versus symptomatic), treatment histories, recurrence data, and careful follow-up from patients over long periods of time.

NCORP Research Bases are encouraged to consider conducting ancillary/correlative studies. Such studies may be amenable to funding through the Biomarker, Imaging, and Quality of Life Studies Funding Program (BIQSFP) or alternative funding (e.g., AHRQ, PCORI) mechanisms but the studies must be reviewed and approved by DCP before protocol initiation.

The infrastructure needed to ensure the collection of high-quality, well annotated human specimens from NCTN treatment studies is funded and administered by DCTD through the NCTN Cooperative Agreement awards. Review of research project requests for use of biospecimens banked from NCORP trials is also administered by DCTD through the NCTN Program.

RFA-CA-14-501 (2015 – 2020) supports a harmonized NCTN banking network for four adult and pediatric NCTN Groups (https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-14-501.html). A Research Base may request funding under NCORP to cover costs for staff/personnel to coordinate activities with the associated tumor banks for its clinical trials/studies.

3. NCI Cancer Trials Support Unit (CTSU)

The Cancer Trials Support Unit (CTSU) is a service of the National Cancer Institute's (NCI) Cancer Therapy Evaluation Program (CTEP) developed to provide administrative support for phase 3 and select phase 2 clinical trials conducted by the NCTN Program, select NCORP cancer prevention, control and care delivery research, and other NCI-supported clinical trial programs. It is strongly encouraged that the CTSU be utilized for all NCORP clinical trials. It is anticipated that use of the CTSU will become a future requirement for all of NCORP cancer prevention, control and screening/post-treatment surveillance trials by the end of the initial six-year funding cycle.

The CTSU provides the following support for NCORP:

- Facilitates access to trials conducted by NCORP;
- Provides 24/7 centralized, web-based, patient enrollment via the Open Patient Enrollment Network (OPEN), supported by Research Base membership rosters and institutional review board (IRB) approvals provided via the Regulatory Support Services (RSS); and
- Provides support for the Common Data Management System (CDMS), including remote data entry, and helps to harmonize procedures and policies related to operational aspects of trial conduct across NCORP.

More information regarding the CTSU, including other services and new initiatives, is available at: http://www.ctsu.org.

4. NCI Central Institutional Review Board (CIRB)

The NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research (NOT-OD-17-076) became effective on January 25, 2018. In compliance with this policy, the NCI Central IRB (NCI CIRB) is the sole IRB of record for all sites conducting clinical trials through the NCORP and NCTN networks and is responsible for study review (initial review, amendments, continuing reviews, recruitment materials, unanticipated problems and serious or continuing noncompliance) and approval of local context considerations.

To comply with the NIH policy:

- All NCORP sites must be enrolled in the CIRB as of the date of their award.
- All new NCORP protocols will be opened under the CIRB.
- All CIRB-enrolled sites must open all new studies under the CIRB.
- Patients on CIRB-approved protocols who are followed by local IRBs must be transferred to the CIRB within a timeframe to be specified in the new NCTN and NCORP grants (12-18 months). This transfer is initiated by the local site via the filing of a Study Specific Worksheet through the CIRB Local Context Review Process.
- Legacy NCORP protocols (e.g. CCOP studies opened before 2/1/2015 and CCDR studies opened before 6/1/2016) currently conducted under the oversight of local IRBs will complete accrual and follow-up under their existing IRB arrangements. NCI

anticipates that most of these trials will be completed before the Common Rule compliance date of January 20, 2020.

All NCORP sites will comply with the conditions of their Federal-Wide Agreement (FWA) and the CIRB Standard Operating Procedures.

5. Research Programs of the Center to Reduce Cancer Health Disparities (CRCHD)

CRCHD initiates, conducts, integrates, and engages in collaborative research studies with NCI Divisions, Offices and Centers, and other NIH Institutes and Centers. These collaborations promote cancer health disparities outreach, research, training, and identify new and innovative scientific opportunities to improve cancer outcomes in communities experiencing an excess cancer burden. CRCHD's cancer disparities outreach and research programs include the Partnerships to Advance Cancer Health Equity (PACHE), National Outreach Network, and a portfolio of cancer disparities researchers and trainees in basic, behavioral, clinical, translational, and population-based science that are supported by the Continuing Umbrella of Research Experiences (CURE).

PACHE enables partnerships between institutions serving racial/ethnic and/or underserved communities with cancer health disparities and NCI-designated Cancer Centers (CCs) to increase the participation of these institutions in cancer research and research training. PACHE is also designed to increase the involvement and effectiveness of NCI-designated Cancer Centers (CCs) in developing effective research, education, and outreach programs to encourage diversity among competitive researchers and reduce cancer health disparities.

The National Outreach Network (NON) is a network of Community Health Educators (CHEs) embedded within NCI's cancer disparities outreach and research programs. Working through CHEs, NON seeks to enhance NCI's ability to develop and disseminate culturally appropriate, evidence-based cancer information that is tailored to the specific needs and expectations of diverse racial, ethnic, and underserved communities.

The Geographical Management of Cancer Health Disparities Program (GMaP) seeks to strengthen regional capacity dedicated to advancing cancer health disparities research, training, and community education and outreach. GMAP leverages the strengths of its regional hubs by facilitating collaboration, communication, information exchange, resource sharing, and training opportunities among GMaP members within each geographic area and with participating NCI programs.

In addition, the CURE program offers unique training and career development opportunities to increase diversity in the cancer and cancer health disparities research workforce. Students and researchers from middle school through junior investigator levels, are provided with competitive funding opportunities at all stages of their education and career, thereby increasing the portfolio and diversity of cancer and cancer disparities researchers.

The benefits of interacting with the outreach, research and training programs of CRCHD to NCORP include access to diverse racial, ethnic and underserved communities with established clinical and community-based partnerships. Additionally, these collaborations and partnerships will enhance the integration of a disparities focus within NCORP, and increase opportunities to identify, design, and develop research questions and interventions aimed at reducing cancer disparities. In parallel, these activities will educate the oncology community about disparities in access to care and cancer care outcomes, as well as effective strategies to reduce barriers to participation in clinical trials and improve patient involvement in their cancer care. Lastly, there will be enhanced opportunities for eligible early stage investigators conducting research, receiving mentorship, and offer additional disparities-focused clinical research collaboration potential within NCORP.

More information regarding the CRCHD, including its diverse research and outreach programs, is available at: http://crchd.cancer.gov.

6. NCI Advisory & Scientific Committees

The NCI Advisory and Scientific Steering Committees associated with clinical trials and translational research activities funded by the NCI are described briefly below. Information on these Advisory Committees is available at: http://ccct.cancer.gov/committees/overview and information on the NCI Scientific Committees is available at: http://transformingtrials.cancer.gov/steering/overview. The NCI Coordinating Center for Clinical Trials (CCCT) is the administrative organization overseeing the activities of these Committees. General information on CCCT is available at: http://ccct.cancer.gov/about/overview.

NCI Clinical Trials and Translational Research Advisory Committee (CTAC)

The NCI Clinical Trials and Translational Research Advisory Committee (CTAC) is an external oversight committee, governed by the provisions of the Federal Advisory Committee Act that advises the NCI Director on the NCI-supported national clinical and translational research enterprises, including both intramural and extramural research. CTAC evaluates the clinical trial portfolio across the NCTN and NCORP, the review decisions of the NCI Scientific Steering Committees (e.g., NCI disease and non-disease-specific Steering Committees, and Clinical Imaging Steering Committee), and the overall trial portfolio for gaps and balance among the different disease areas and modalities. Committee members include leading authorities in clinical trials and translational research. The CCCT Director serves as the Executive Secretary for CTAC and the CCCT staff facilitates operations. General information on CTAC is available at: http://deainfo.nci.nih.gov/advisory/ctac/ctac.htm.

NCI Scientific Steering Committees (SSCs)

The NCI Scientific Steering Committees strive to enhance the NCI's entire clinical trials enterprise through implementation of prioritization and scientific quality initiatives under the purview of the NCI Clinical Trials and Translational Research Advisory Committee (CTAC). General information on the NCI Steering Committees is available at: http://transformingtrials.cancer.gov/steering/overview.

The NCI SSCs are composed of leading cancer experts and advocates from outside the Institute and NCI senior investigators who meet regularly to:

- evaluate concepts for scientific merit and feasibility;
- enhance patient advocate and community oncologist involvement in clinical trial design and prioritization; and
- convene Clinical Trials Planning Meetings to identify critical questions, unmet needs, and prioritize key strategies.

The NCI SSCs most relevant to the work of NCORP are the Symptom Management and Quality of Life Scientific Steering Committee, the Cancer Prevention Scientific Steering Committee, and the Cancer Care Delivery Research Scientific Steering Committee.

The Symptom Management and Quality of Life Steering Committee evaluates symptom management intervention clinical trial concepts conducted through NCORP for scientific merit and provides expertise to review quality of life studies embedded within treatment trials.

The Cancer Prevention Steering Committee evaluates innovative cancer prevention, screening and surveillance concepts.

The Cancer Care Delivery Research Scientific Steering Committee evaluates all NCORP concepts related to cancer care delivery research for scientific merit and feasibility of CCDR in the community setting.

NCI Clinical and Translational Research Operations Committee (CTROC)

The Clinical and Translational Research Operations Committee (CTROC), an internal NCI advisory committee composed of representatives from NCI Divisions, Offices, and Centers involved in NCI-supported clinical trials and translational research provides strategic oversight for NCI clinical trials and translational research programs and infrastructures, including informatics. The Committee reviews clinical trials and translational research programs proposed by Divisions, Centers, and Offices to coordinate efforts Institute-wide. CTROC also oversees and approves applications under the Biomarker, Imaging, and Quality of Life Studies Funding Program (BIQSFP) to support integral and integrated biomarker, imaging, and quality of life studies as well as Cost-Effectiveness Analysis (CEA) proposals which are associated with Research Base clinical trial concepts approved for conduct under NCORP that are eligible for BIQSFP funding. Information on the BIQSFP is available at: http://biqsfp.cancer.gov/.

II. Types of Research in NCORP

The primary goal of NCORP research is to develop and conduct cancer prevention, control, and screening/post-treatment surveillance trials and health-related quality of life (HRQOL) and cancer care delivery studies with prominent involvement of community oncologists, other specialists, and the populations they serve. An equally important focus of NCORP is an emphasis on trials/studies in minority and underserved populations. Randomized controlled trials of interventions are of highest priority for NCORP.

A. Cancer Prevention Research

Cancer prevention research is defined as clinical evaluations of the effectiveness of interventions for the purpose of reducing the risk for developing cancer (including but not limited to chemopreventive agents, surgical interventions, and lifestyle modifications). In select circumstances, observational studies may also be considered by the Program.

B. Cancer Screening Research

Cancer screening research is defined as clinical evaluations of methods for the early (pre-symptomatic) detection of cancer and precancerous lesions. In select circumstances, observational and longitudinal studies may also be considered by the Program.

C. Post-Treatment Surveillance Research

Post-treatment surveillance research is defined as clinical evaluations of methods for earlier detection of cancer recurrence. In select circumstances, observational studies may also be considered by the Program.

D. Cancer Control Research

Cancer control research is defined as clinical evaluations of interventions to improve patients' quality of life and/or to treat symptoms arising from cancer or toxicities arising from cancer therapy as well as ways to improve continuing, palliative, and end-of-life care. In select circumstances, pilot, observational and natural history studies may also be considered by the Program to inform the development of future randomized controlled trials. In addition, studies to understand mechanisms of symptoms and toxicities are encouraged.

E. Cancer Care Delivery Research

Cancer care delivery research is a multidisciplinary science that seeks to improve clinical outcomes and patient well-being by intervening on patient, clinician, and organizational factors that influence care delivery.

F. Cancer Treatment Trials

NCORP Research Bases are not funded to design or implement cancer treatment trials. However, NCORP Community sites and Minority/Underserved Community sites are expected to accrue participants to cancer treatment trials designed and conducted under the NCTN Program.

G. Health-Related Quality of Life Sub-Studies

NCORP Research Bases are funded to develop hypothesis-driven HRQOL studies embedded in NCTN treatment or imaging trials as secondary endpoints to inform the primary endpoints in the trials. These secondary endpoints are usually measured by patient-reported outcomes that provide critical data for patient/clinician treatment decisions and acceptance of new therapies.

H. Correlative Science Sub-Studies

The patient, provider and organizational information accumulated in the course of NCORP clinical trials/studies provide the Research Bases with unique opportunities to address scientific questions about molecular genetics, epidemiology, pathology, and other topics that pertain to cancer prevention and control (e.g., risk assessment, premalignant lesions, toxicities of therapy) and cancer care delivery research (e.g., patient report outcomes, clinical decision-making). Such investigations can add considerable strength to a Research Base's total scientific program and are encouraged. While integral or integrated studies associated with a phase 3 or large, randomized phase 2 trial may be eligible for financial support through the Biomarker, Imaging, and Quality of Life Studies Funding Program (BIQSFP) at: http://biqsfp.cancer.gov/, a variety of other funding mechanisms – including investigator-initiated grants (R01s, P01s), Cooperative Agreements and industry, foundation or other government funding for discrete projects (U01s, U19s) may also be appropriate for funding correlative science sub- studies, especially those ineligible for BIQSFP funding.

I. Biospecimen Collection

Although NCORP supports the collection of biospecimens in conjunction with clinical studies and cancer care delivery studies conducted by the Research Bases, direct funding for correlative science studies using those specimens outside of BIQSFP and/or specific NCI/DCP approved administrative supplements for specific studies is not provided under or in association with NCORP. Access to biospecimens collected in conjunction with an NCORP study for research will be guided by the appropriate review process (see Section IV.B.1.5.6.2 of these Guidelines) regardless of the funding source used for the collection or storage of the biospecimens.

J. Cancer Disparities Research

NCORP cancer disparities research incorporates the unique needs of diverse populations such as adolescents and young adults (AYAs), and the elderly; racial and ethnic minorities; sexual and gender minorities; and rural residents into studies and takes steps to enhance participation of these groups within clinical trials and other human subjects research. Research seeking to understand and address cancer disparities should be integrated across all focus areas as appropriate, including both studies focused exclusively on disparities and the inclusion of disparities-related aims in studies with a broad focus.

III. NCORP General Management, Operating and Funding Principles

A. General Management

Direct programmatic oversight of NCORP is provided by the NCI Division of Cancer Prevention (DCP) and its programs. The Chief of the Community Oncology Prevention Trials Research Group (COPTRG), DCP, NCI is the Director of NCORP. The CCDR Scientific Lead, a member of the Healthcare Delivery Research Program (HDRP), Division of Cancer Control and Population Sciences (DCCPS), provides guidance and oversight related to cancer care delivery research performed within NCORP. The Director and CCDR Scientific Lead work with the DCP Senior Program Specialist, Program Directors, and program management staff to oversee the key components of NCORP. For cancer care delivery research-related tasks, NCI/DCCPS Program Directors will provide project management support as needed.

NCI/DCP and DCCPS staff involved with NCORP also work closely with NCI staff from the Division of Cancer Treatment and Diagnosis (DCTD), especially program staff within the Cancer Therapy and Evaluation Program (CTEP) for the National Clinical Trial Network (NCTN), to manage NCORP as NCORP Community Sites and Minority-Underserved Community Sites participate directly in the clinical trials of the NCTN and NCTN Groups. NCI/DCP and DCCPS staff involved with NCORP also works closely with NCI staff from the Center to Reduce Cancer Health Disparities (CRCHD) to facilitate the integration of cancer disparities research questions into clinical trials and cancer care delivery studies and to participate in the review of concepts. General information on DCP, DCCPS, DCTD, and CRCHD is available from the NCI public website at the URLs listed below:

- NCI Division of Cancer Prevention (DCP): http://prevention.cancer.gov/
- NCI Division of Cancer Control and Population Sciences (DCCPS): http://cancercontrol.cancer.gov/
- NCI Division of Cancer Treatment and Diagnosis (DCTD): http://dctd.cancer.gov/
- NCI/DCTD Cancer Therapy Evaluation Program (CTEP): http://ctep.cancer.gov/
- NCI Center to Reduce Cancer Health Disparities (CRCHD): http://crchd.cancer.gov/

B. NCORP Operating Principles

The purpose of the NCORP is to provide standing support for a consolidated and integrated national Network that conducts cancer prevention, control and care delivery research on an ongoing basis. In NCORP, Research Bases will collaborate with each other and with NCI to achieve the research objectives of NCORP based on operating principles that stress harmonization of procedures used by the individual Research Bases and their member institutions/sites. This includes the use of standard tools and services for the conduct of cancer prevention, control and care delivery clinical research studies to ensure that NCORP trials/studies are developed and conducted as efficiently as possible and with collaboration and coordination among the Research Bases and other NCI-supported program and investigators.

1. **Access to NCORP Trials & Crediting for Patient Accrual to Trials** (Does not apply to care delivery studies)

   Research Bases' non-NCORP member institutions/sites will be able to enroll patients/participants to NCORP cancer prevention, control and screening/post-treatment surveillance clinical trials led by their affiliated NCORP Research Bases and those posted on the CTSU irrespective of affiliations. NCORP Community Sites and Minority/Underserved Community Sites will be able to credit adult and AYA trial treatment

enrollments to any NCTN Group to which they belong. Pediatric trial treatment enrollments will be credited to the pediatric NCTN Group. Enrollments to prevention, control and screening/post-treatment surveillance trials through CTSU may be credited by the Community Site to any of its affiliated NCORP Research Bases, based on their crediting rules. It is anticipated that non-NCORP affiliates of institutional members of a particular Research Base will follow the crediting decision of the main member for a particular trial; however, that is at the discretion of the Research Bases through their membership rules.

Note: International sites (i.e., non-U.S. sites) that are members of NCORP Research Bases may not be able to participate in all NCORP studies because of special regulatory issues specific to the country of the international member. The Research Base must specify any potential restrictions related to enrollment from international members prior to trial activation. For trials being conducted under an NCI/DCP IND, this information must be reviewed and approved by NCI prior to trial activation.

2. Submission of Data and Biospecimens

All data must be sent by the institutions/sites participating in a trial directly to the NCTN Group that is leading the NCTN trial, or to the NCORP Research Base that is leading the NCORP trial or study unless an exception is approved by NCI to accommodate the needs of a specific trial/study. Biospecimens will be collected and sent to the NCTN Group or NCORP Research Base trial-specific biobank and/or laboratory.

3. Use of the NCI Central Institutional Review Board

The NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research (NOT-OD-17-076) became effective on January 25, 2018. In compliance with this policy, the NCI Central IRB (NCI CIRB) is the sole IRB of record for all sites conducting clinical trials through the NCORP and NCTN networks and is responsible for study review (initial review, amendments, continuing reviews, recruitment materials, unanticipated problems and serious or continuing noncompliance) and approval of local context considerations.

To comply with the NIH policy:

- All NCORP sites must be enrolled in the CIRB as of the date of their award.
- All new NCORP protocols will be opened under the CIRB.
- All CIRB-enrolled sites must open all new studies under the CIRB.
- Patients on CIRB-approved protocols who are followed by local IRBs must be transferred to the CIRB within a timeframe to be specified in the new NCTN and NCORP grants (12-18 months). This transfer is initiated by the local site via the filing of a Study Specific Worksheet through the CIRB Local Context Review Process.
- Legacy NCORP protocols (e.g. CCOP studies opened before 2/1/2015 and CCDR studies opened before 6/1/2016) currently conducted under the oversight of local IRBs will complete accrual and follow-up under their existing IRB arrangements. NCI anticipates that most of these trials will be completed before the Common Rule compliance date of January 20, 2020.

All NCORP sites with comply with the conditions of their Federal-Wide Agreement (FWA) and the CIRB Standard Operating Procedures.

4. Processes for review and approval of NCORP Studies Receiving Additional Support

All cancer prevention, control and care delivery clinical research studies to be conducted within NCORP must be through a Research Base. There are different approval processes required if the study is supported by Federal or by non-Federal sources.

Federally Funded Studies (e.g., NIH, AHRQ, DOD)

Federally funded studies are not required to undergo Steering Committee concept review because they have already undergone peer review. Such studies may come to the attention of NCORP Research Bases and NCI Program Directors without full consideration of feasibility, potential overlap with open or planned studies, and/or fit within NCORPs research scope. Making necessary adjustments can create delays in study implementation that are inconsistent with the goals of clinical trial stewardship established by the NIH. (http://jamanetwork.com/journals/jama/fullarticle/2553888?guestAccessKey=554e0981-9434-45f2-b122-d0e673cd1182).

Thus, in order to promote the efficient and equitable use of resources in the initiation, implementation, and completion of research studies, the following guidelines outline the process for submitting research grant applications (e.g. R series, P01s) that propose to use the NCORP network for study implementation. These guidelines describe the required process for coordinating communication between NCORP Research Bases and their respective NCI NCORP Program Directors, as well as the review and approval requirements for conducting research through the NCORP network. **NOTE: A study cannot be submitted simultaneously as a concept to the NCI and an investigator initiated grant for peer review if they are funding the same activity.**

Because NIH Institutes and NCI Divisions differ in their approach to handling applications and funded grants, there are some variations in process as follows:

- Cancer Control (including Symptom Science) Prevention & Screening: The Program Directors in the NCI Division of Cancer Prevention (DCP), Community Oncology and Prevention Trials Research Group, are responsible for the scientific oversight for cancer control/symptom science applications and funded grants using the NCORP network. Some grants outside of NCI are monitored in conjunction with Scientific Program Directors in other NIH Institutes. At the time of submission, applicant(s) may request assignment of their grant application to the NCI and to a specific NCI NCORP Program Director. (For more information go to: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-008.html). By doing so, the application can be more easily/directly/quickly brought to the attention of the interested/involved NCI Program Director after it has been received, logged-in, and assigned to the NCI.

- Cancer care delivery research: The primary Scientific Program Director for all cancer care delivery research applications and funded grants will be the person with the most relevant scientific expertise within any NCI Division, NIH Institute, or other federal agency. Staff in the NCI Division of Cancer Control and Population Sciences Healthcare Delivery Research Program will serve as a liaison and monitor progress on these grants. Applicants, Research Bases and NCI staff should work together well in advance of submission to establish the appropriate relationships. NIH applicants are encouraged to request assignment of their application to the appropriate Scientific Program Director. (For more information go to: (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-008.html)

Prior to submission of a research grant application

Interested investigators are required to contact NCI (NCORP) Program Directors or the Research Bases to determine if the concept is within the research scope of the program. Investigators contacting the NCORP Program Directors in either the Division of Cancer Prevention or the Division of Cancer Control and Population Sciences will be directed to the Research Base that is best suited for the concept and provide contact information. When the initial contact is with an NCORP Research Base, the Research Base notifies their assigned NCORP Program Director of an investigator's intent to submit a research grant application to a federally funding agency **at least four weeks prior to submission.**

Regardless of the first point of contact, the NCORP Research Base should provide the NCORP Program Director a brief abstract describing the study aim(s), study population, and a statement of rationale for use of the NCORP network. The NCORP Program Director will provide feedback regarding: 1) the feasibility of conducting the study within the network, 2) potential scientific overlap with existing studies, and 3) confirmation that the study fits within the cancer control/prevention, symptom management, care delivery or disparities NCORP research scope. In advance of submitting the grant application, it is expected that the PI and Research Base have communicated with NCORP sites regarding interest and participation in the study.

Post study section review and award

The study will be submitted as a protocol to NCI DCP Protocol Information Office (PIO) via a Research Base **within 90 days of receipt of the Notice of Award or start of Project Period (as indicated on the Notice of Award); whichever is later**. This 90-day requirement will apply to studies that are funded after April 1, 2017. Therefore, as soon as the Summary Statement is released (usually within 6-8 weeks after completion of the review) the investigator should contact the Scientific Program Director assigned to the grant as well as the NCORP Program Director for the Research Base that will be submitting the protocol to discuss next steps. Communication with the NCORP Program Director and Scientific Program Director is critical during this time, particularly if the grant is supported by a Federal Agency, NIH Institute or Center other than NCI. Inability to meet the 90-day submission time frame may result in forfeiture of access to the NCORP Network.

The full protocol will undergo review by the NCI Protocol Review Committee. Once the full protocol is approved by the NCORP Protocol Review Committee and NCI Central IRB, the PI and Research Base may proceed with conducting the federally funded study within NCORP

Non-Federally Funded NCORP Studies, Applications and Letters of Intent (LOI) - (e.g. PCORI, American Cancer Society, Leukemia and Lymphoma Society)

The following process is used to request use of the NCORP Network to implement studies supported by non-Federal funders. The process supports coordination of communication, review, and approval requirements between NCI and the non-Federal funder. The NCI has established communications with some non-Federal funding organizations to accommodate their respective review processes.

Application planning and/or Letter of Intent (LOI)

Interested investigators are required to contact NCI (NCORP) Program Directors or the Research Bases to determine if the concept is within the research scope of the program. Investigators contacting the NCI Program Directors will be directed to the Research Base that is best suited for the LOI or concept and provide additional information. When the initial contact is with an NCORP Research Base, the Research Base notifies their assigned NCORP Program Director of an investigator's intent to submit a research grant application or LOI to a non-federally funding agency or organization **at least four weeks prior to submission.**

The NCORP Research Base or investigator should provide the NCORP Program Director a brief abstract describing the study aim(s), study population and a statement of rationale for use of the NCORP network. The NCORP Program Director will provide feedback regarding: 1) the feasibility of conducting the study within the network, 2) potential scientific overlap with existing studies, and 3) confirmation that the study fits within the cancer control/prevention, symptom management, care delivery or disparities NCORP research scope.

When an LOI is selected to be submitted as a full application. The NCORP Program Director will be notified that an application is being submitted and updated on any changes/revisions to study design. All of this must take place at least four weeks before submission of a full application.

Post award

If the application is approved for funding by the non-Federal sponsor, there are two additional steps required to conduct the research within the NCORP infrastructure.

1. The NCORP Research Base shall submit a concept to the NCI DCP Protocol Information Office (PIO) for scientific review by an NCORP Steering Committee or the NCORP Concept Review Committee.
2. If the concept is approved, the NCORP Research Base will then submit a full protocol to the NCI DCP Protocol Information Office (PIO) for review by the NCORP Protocol Review Committee **within 90 days.**

Once the full protocol is approved by the NCORP Protocol Review Committee and NCI Central IRB, the Research Base may proceed with conducting the non-federally funded study within NCORP.

5. Collaborations Among Research Bases and with Other Organizations on Clinical Trials / Studies

Research Bases are encouraged to collaborate with other Research Bases and with other NCI-funded programs and investigators (e.g., NCI-designated Cancer Centers, Early Phase Cancer Prevention Consortium, Early Detection Research Network, Center to Reduce Cancer Health Disparities, NCI Cancer Research Network, R01 and P01 investigators). These collaborations may include advancing research ideas from pilot studies to phase 3 trials, joint-participation and sharing of evidence-based practices in cancer care delivery and disparities research studies and other research endeavors. Research addressing common research questions such as specific toxicities and populations are areas where collaboration is especially encouraged. These efforts could include but are not limited to setting standard definitions, identifying common data elements, developing mutual outcome measures and collecting data across the network in a consistent manner. Research Bases are encouraged to engage investigators with expertise in these areas and to collaborate with each other and with other NIH institutes and other federal agencies in research to address gaps in understanding the biology of toxicities and symptoms which prevent the development of interventions as well as the use of comparative effectiveness and patient-reported outcomes in assessing toxicities and symptoms, and designing trials/studies to improve clinical practice

6. Compliance

Researchers have an obligation to take appropriate steps to protect both the integrity of science and the human subjects who participate in research studies. Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human subjects. Research Bases as well as all other key components of NCORP are required to comply with this standard as it provides public assurance that the rights, safety, and well-being of study participants are protected, and that study data are credible. Information on GCP standards in FDA-regulated Clinical Trials is provided at: http://www.fda.gov/oc/gcp/default.htm. Good Clinical Practice Guidance Document: https://ctep.cancer.gov/branches/ctmb/clinicalTrials/docs/good_clinical_practices.pdf

The integrity of study data is a function of the entire process of data collection and analysis. Research Bases as well as the other key components of NCORP need detailed Quality Control and Quality Assurance plans and systems to assure protocol adherence in

the administration of protocol-prescribed interventions and observational studies and the uniform collection of data. Vigilance to detect honest errors, whether systematic or random, as well as data falsification, is especially important.

NOTE: In concordance with NCI CTEP guidelines, NCORP will not issue or approve any waivers for protocol deviations. If a change to an NCORP-approved protocol is necessary, the Study Chair may submit an amendment to the protocol. Please see the following URL for further information:
http://ctep.cancer.gov/protocolDevelopment//policies_deviations.htm

C. NCORP Network Funding Principles

1. Grant Funding for Key Components of NCORP

The allowable costs under the Cooperative Agreements for each of the key components of NCORP are described within the NIH Grants Policy Statement located at: https://grants.nih.gov/policy/nihgps/index.htm. In general, the funds can support costs associated with personnel (e.g., staff hired to support grant, research base scientific and administrative committee leaders, principal investigators for specific studies, etc.), travel, appropriate equipment, and other operational costs related to the conduct of clinical trials/studies; however, costs for patient recruitment (allowed for CCDR studies), patient care and laboratory tests are generally not allowed under the grant funding for NCORP, however, support may be considered on a case by case basis. Support for patient recruitment may be requested for underserved or underrepresented populations in clinical research.

2. Funding for Research Bases

2.1 Total Budget

The budget of a Research Base is divided into two parts: (1) a core budget which includes costs for cancer prevention, control and screening/post-treatment surveillance clinical trials as well as HRQOL studies embedded within treatment and imaging trials and (2) a cancer care delivery research budget.

2.2 Core Budget

The core budget has two elements: (1) infrastructure costs for developing, conducting and analyzing NCORP clinical **trials and HRQOL studies and (2) costs for reimbursing member** institutions/sites that are not funded as a NCORP Community Site or Minority/Underserved Community Site (hereinafter referred to as "non-NCORP institutional members") for data collection and management and biospecimen collection associated with subject enrollment to NCORP clinical trials and HRQOL studies ("per case management" costs). The total cost infrastructure budget is dependent on the projected accrual to clinical trials and HRQOL studies led by the Research Base. The total cost per case management budget is dependent on projected accrual by the Research Base's non-NCORP institutional members to the clinical trials and HRQOL studies that it leads as well as to those led by other Research Bases that the non-NCORP institutional member is expected to credit to the applicant Research Base.

2.3 Cancer Care Delivery Research Budget

The cancer care delivery research budget has two elements: (1) costs for the scientific and statistical leadership, data systems/informatics and management infrastructure necessary to develop, conduct and analyze cancer care delivery research studies ("infrastructure costs") and (2) costs to cover study operations, statistical analysis, data management, quality control, study monitoring and auditing

for studies led by the Research Base ("study-specific costs"). No per case management costs for non-NCORP institutional members should be budgeted as only NCORP Community Sites and Minority/Underserved Community Sites will be funded to participate in cancer care delivery research studies.

3. Funding of Sites for Cancer Control, Prevention, Treatment & Imaging Clinical Trial Data Collection/Management & Biospecimen Collection

NCI federal funding for institutions participating in all NCORP trials/studies to cover the costs related to data collection/management and biospecimen collection associated with enrolled patients ("per case management funding") is provided in one of three ways:

- Grant funding (i.e., dollar value/credits) from NCI to NCORP Community Sites and Minority/Underserved Community Sites

- Grant funding from NCI to NCORP Research Bases which then contract with their non-NCORP institutional members via purchase service or subcontract agreements on a "per-case" basis.

- Grant funding from NCI or another federal source (e.g., NHLBI) awarded to the NCORP Research Bases which then pay the NCORP Community Sites, Minority/Underserved Community Sites and their non-NCORP institutional members on a per-case basis.

In keeping with the need for collaboration across NCORP, funding for cancer control, prevention, and care delivery collection/management and biospecimen collection is provided in a consistent manner for institutions/sites that enroll patients on NCORP studies. For NCORP Community Sites and Minority/Underserved Community Sites, each cancer control, prevention, treatment and imaging clinical trial approved by NCI will be assigned a credit value by NCI/DCP (Care delivery studies are not assigned credits. See Section 4 below for care delivery study funding principles). Credits will be based on the complexity of the intervention, the amount of data management required, and the duration of follow-up. In general, the final amount of funding for cancer treatment, prevention, control and large-scale trials will be itemized on the funding sheet. Health-related quality of life, advanced imaging studies, molecular screening and biospecimen collection are considered "ancillary studies and will receive a variable credit per accrual based on the dollar value reimbursement rate determined by CTEP and/or DCP and the dollar amount paid per estimated credit in the Notice of Grant award. The credit is claimed one time by NCORP Community or Minority/Underserved Community Site grantees against the grant year in which the participant was enrolled on the protocol.

NCORP Community Sites and Minority/Underserved Community Sites that are assigned an estimated accrual credit target of 200 or more credits in their initial award and in subsequent budget periods will receive a "high performance" per case management funding dollar amount (also referred to as high performance intervention for this category of NCORP grantee). NCORP Community Sites and Minority/Underserved Community Sites that are assigned an estimated accrual credit target of less than 200 credits annually will receive a "standard" per case management funding amount for accruals to the base intervention. Funding amounts will be provided on each trial-specific funding sheet. All applicants must provide a justification for the amount requested based on actual costs to be incurred. The credits used to determine budgets/funding for NCORP Community Sites and Minority/Underserved Community Sites were and will continue to be based on accrual to all NCTN and NCORP trials regardless of which NCORP Research Base is credited with the accrual by the enrolling site. "Ancillary" credits will not count toward achievement of the 200-accrual credit threshold.

Any separate, non-NCI/DCP funding (i.e., funding not provided under the Cooperative Agreements of NCORP) or any NCORP funding provided as a separate administrative supplement that is dispensed by a Research Base to cover costs associated with patient enrollment on NCORP trials/studies that it leads ("Special Per Case Management Funding") must be provided to all qualified institutions/sites that participate in the relevant NCORP trial/study regardless of which Research Base the enrolling institution belongs to and/or credits with the patient accrual. This principle is considered an essential feature of NCORP and the Terms and Conditions of Award as it is fundamental to ensure fairness for work performed across the NCORP Network.

3.1 Per Case Management Funding Categories for Clinical Trials (Does not include cancer care delivery studies)

The various funding categories for NCI/DCP supported studies are described below.

- **Prevention**: Funding to cover data management and follow-up for subjects enrolled in prevention trials (chemoprevention, secondary prevention) aimed at reducing cancer risk, incidence and mortality. Research Bases can request support for recruitment of non-cancer patients on a study-by-study basis.

- **Cancer control:** Funding to cover data management for patients enrolled in interventional or observational cancer control research studies aimed to reduce the morbidities associated with cancer and its treatment as well as improving the quality of life of individuals undergoing treatment or with a history of cancer.

- **Screening/Post-treatment surveillance:** Funding to cover data management for patients enrolled in screening or post/treatment surveillance studies (e.g., imaging, biomarkers).

- **Treatment:** Funding to cover data management and follow-up for patients enrolled in a treatment trial that undergo the study intervention and/or randomization.

- **Health-Related Quality of Life**: Funding to cover data management for patients enrolled in HRQOL studies embedded in treatment or imaging trials as secondary endpoints including those using patient-reported outcomes.

- **Advanced Imaging:** Funding to cover data management for subjects enrolled in advanced imaging studies

- **Molecular Screening:** Funding to cover data management costs for patients enrolled on a trial that require specific screening with informed consent as part of the trial (e.g., investigational molecular test of their tumor) and who do not subsequently undergo the study treatment/intervention and/or randomization because of the screening results.

- **Biospecimen Collection Per Case Management Funding:** Funding to cover biospecimen collection and any associated biospecimen management costs for subjects enrolled on studies which require biospecimen collection and for subjects who agree to participate in optional biospecimen collections associated with trials. This category of funding would not be expected to be given in association with molecular screening per case funding except in unusual circumstances.

4. Funding of Sites for Cancer Care Delivery Research

Funds awarded for Cancer Care Delivery Research (CCDR) are restricted and may not be used for any other purpose without the written prior approval of the National Cancer

Institute (NCI). These funds are not eligible for carryover under the expanded authorities without the written prior approval of the NCI.

NCORP Community and Minority/Underserved Community Sites must have at least one affiliate site participating in cancer care delivery research studies. Any affiliate or sub-affiliate of an NCORP site rostered with a CTEP ID is eligible for participation in approved CCDR studies.

In the competing and non-competing applications, a separate CCDR detailed budget and justification is required (with direct, indirect, and total cost for CCDR broken out) that reflects the projected expenses associated with sustainable CCDR study participation and anticipated CCDR activities in the next grant year. In non-competing years, CCDR budget requests may exceed the previously approved amount.

CCDR budgets may include the following elements:

- Costs for overall scientific and management leadership and coordination for research program
- Costs for study coordinator and research staff responsible for patient recruitment, accrual, and data monitoring
- Costs for components and subcomponents for CCDR study implementation and accrual at their location.

5. Program Income for Key Components of NCORP

Under the Cooperative Agreement grants awarded for all key components of NCORP, awardees are allowed to accept funds from non-governmental sources to support NCORP research that is not supported in part or in full by the NCI (e.g., additional funding supplementing the NCI/DCP basic intervention funding, support for correlative science studies associated with trials/studies conducted under NCORP, nonprofit foundation support for cancer care delivery research). Awardees also are allowed to receive and use funds from other governmental funding mechanisms (e.g., R01s) related to the specific research study. NCORP studies using alternative funding must still be reviewed and approved by NCI. These funds are considered "Program Income" and must be reported under the Terms and Conditions of Award for the key components of NCORP unless they are exempted under the NIH grant policy for program income available at: https://grants.nih.gov/policy/nihgps/index.htm. These funds are considered a valuable resource to help further the research objectives of the entire Program. Nevertheless, the Cooperative Agreements for NCORP always define the operational principles under which the awardees must function to ensure the independence of the research conducted regardless of whether program income is or is not available for specific clinical trials/studies conducted by NCORP.

IV. Terms & Conditions of Award for Cooperative Agreements for NCORP Key Components

A. General Terms and Conditions of Award for All Key Components of NCORP

See RFA for additional information

1. General Programmatic Responsibilities

The awardees' programmatic responsibilities for the conduct of the research supported under the Cooperative Agreement for each of the key components of NCORP are described in the documents listed below and any subsequent modifications to these documents:

NCI Community Oncology Research Program (NCORP) Guidelines (i.e., "these Guidelines") https://ncorp.cancer.gov/resources/applicants/guidelines.pdf

NCI/CTEP Investigators Handbook (Manual for Participants in Clinical Trials of Investigational Agents Sponsored by the Division of Cancer Treatment and Diagnosis, NCI) https://ctep.cancer.gov/investigatorresources/docs/InvestigatorHandbook.pdf

Guidelines for Monitoring of Clinical Trials for Cooperative (i.e., Network) Groups, CCOP Research Bases, and the Cancer Trials Support Unit (CTSU) https://ctep.cancer.gov/branches/ctmb/clinicalTrials/monitoring_coop_ccop_ctsu.htm

Specific portions of these documents, as enumerated in the Funding Opportunity Announcement for each of the key components of NCORP (as well as in specific sections of these NCORP Guidelines), are incorporated by reference as program-specific Terms and Conditions of Award.

Programmatic responsibilities for the individual key components of NCORP, for NIH Staff and joint responsibilities are described in detail under "Specific Cooperative Agreement Terms & Conditions of Award for the Key Components of NCORP" located in Section IV.B of these guidelines.

2. Dispute Resolution

Any disagreements that may arise in scientific or programmatic matters (within the scope of the award) between award recipients and the NIH may be brought to Dispute Resolution, except for areas of dispute that are already addressed by the appeal process within the Terms and Conditions of Award for decisions regarding approval of study proposals and the types of studies supported by NCORP as described in **Part 1 – Section VIII** of these Guidelines.

For other scientific and programmatic matters that are not covered by the appeals process, a Dispute Resolution Panel composed of three members will be convened. It will have three members: a designee of the Network Group representatives on the NCORP Leadership Management Committee chosen by them without NIH staff voting, one NIH designee, and a third designee with expertise in the relevant area who is chosen by the other two. In the case of individual disagreement, the first member may be chosen by the individual awardee. The appeals process and this special dispute resolution procedure do not alter the awardee's right to appeal an adverse action that is otherwise appealable in accordance with PHS regulation 42 CFR Part 50, Subpart D (http://www.ecfr.gov/cgi-bin/text-idx?rgn=div5&node=42:1.0.1.4.23).

B. Specific Terms and Conditions of Award for the Key Components of NCORP

1. Specific Awardee Rights & Responsibilities - NCORP Research Bases

See RFA for additional information

1.1 Clinical Trial and Cancer Care Delivery Development Program

1.1.1 Overall Responsibilities for Cancer Control, Prevention and Cancer Care Delivery Clinical Research

It is the responsibility of the NCORP Research Base to develop and articulate an overall research strategy related to cancer prevention, control, screening/post-treatment surveillance and health-related quality of life. This includes clinical evaluations of the effectiveness of interventions for the purpose of reducing the risk for developing cancer (including, but not limited to, chemo-preventive agents, surgical interventions, and lifestyle modifications); development of risk assessment models; methods for the early detection of cancer and management of precancerous lesions (i.e., screening) or for the earlier detection of cancer recurrence (i.e., post-treatment surveillance); interventions to improve patients' quality of life and/or to treat symptoms arising from cancer or toxicities arising from cancer therapy; and ways to improve continuing, palliative, or end-of-life care. Such studies are aimed at reducing cancer incidence, morbidity, mortality, and cancer disparities through the identification, testing, and evaluation of effective and appropriate strategies and interventions.

It is the responsibility of the Research Base awardee, in accordance with its constitution, bylaws, policies, and procedures, to develop the details of the research design, including definition of objectives and approaches, planning, implementation, analysis, publication of results, interpretations, and conclusions of the studies. The Research Base awardee is responsible for statistical leadership for NCORP clinical trials, including developing the statistical research design and analysis plan, statistical analysis, appropriate interim monitoring plans, interpretations, and conclusions in regard to study data.

The Research Base is also responsible for all aspects of data management. It must have Standard Operating Procedures (SOPs) covering all aspects of data management, study monitoring, and data analysis for NCORP trials. The SOPs should include plans for training NCORP investigators and Clinical Research Professionals (CRPs) at member participating sites and Study Chairs and Study Teams about their responsibilities for data management and study monitoring. The Research Base must also have the appropriate facilities and equipment, especially with respect to information technology, to provide for complete data management for all aspects of NCORP trials.

1.1.2 Overall Research Strategy for Disparities Research Studies

NCI defines "cancer health disparities" as "differences in the incidence, prevalence, mortality, and burden of cancer and related adverse health conditions that exist among specific population groups." Populations of specific interest include AYA, and the elderly; racial and ethnic minorities; sexual and gender minorities; and rural residents. Disparities research questions must be an identifiable component of a Research Base's research strategy and should be integrated across all NCORP research focus areas, study types and care settings, as appropriate. Research seeking to understand and address health disparities can include both studies focused exclusively on disparities and the inclusion of disparities-related aims in studies with a broad focus.

The most desirable studies will be those that undertake one or more of the following:

- Studies to enhance participation of racial/ethnic and other populations underrepresented in research.
- Studies that address determinants of disparities (e.g., social factors, health care system factors, co-morbidities, genomics) that disproportionately affect outcomes for racial/ethnic and underserved populations.
- Studies that address disparities related to care and outcomes of the more serious, prevalent cancers and cancer related problems which persist in racial/ethnic minorities and other underrepresented populations.

1.1.3 Scientific Research and Administrative Committees

The Research Base is responsible for establishing scientific and administrative committees for cancer control, prevention and care delivery research studies and developing a process for the selection of leadership for these committees. The Research Base should ensure that committees involve appropriate representation from relevant stakeholders, including a range of clinical experts, behavioral, disparities and health services researchers, community representatives, and patient advocates. The Research Base is responsible for establishing clear operating principles and procedures for committees and facilitating their operations by arranging meetings and establishing and maintaining electronic communication tools.

Scientific Research Committees: Scientific research committees are defined as committees that function primarily to develop and oversee the conduct of clinical trials and HRQOL and cancer care delivery research studies within a defined strategy (e.g., cancer prevention and control; observational research)

The primary responsibilities of the scientific research committees are to develop study concepts and oversee protocol development and study conduct for approved studies. Through these processes, feasibility of accrual and other types of participation will be considered; including minority/underserved accrual and participation will be addressed. Further, the Committees will work with NCORP disparities/underserved committees to help develop/inform the Research Base's overall research strategy including research questions addressing cancer health disparities.

Correlative science studies, especially integral and integrated studies, are increasingly central to the interpretation of clinical trials data, particularly for studies of molecularly targeted agents. Scientific research committees play a key role in the development and conduct of correlative science studies associated with Research Base protocols. Funding for integrated and integral correlative science studies is not provided by the NCORP award (except in exceptional circumstances via an administrative supplement by NCI/DCP for a specific study) but may be applied for via the Biomarker, Imaging, and Quality of Life Studies Funding Program (BIQSFP). Information on the BIQSFP is available at: http://biqsfp.cancer.gov/. Other sources of funding may be sought for correlative science studies that are not eligible for BIQSFP funding (e.g., other NCI and NIH grant funding, industry funding); however, the study must still be reviewed by NCI.

Study Monitoring by Scientific Committees & Study Teams: The primary responsibility for study monitoring resides with the Study Chair, Study Statistician, and other members of the study team that help develop and oversee conduct of a specific study. The relevant scientific research committee is responsible for assuring that the study team is satisfactorily meeting its responsibilities for study monitoring.

Administrative Committees: Administrative committees for clinical trials are defined as committees that provide essential core service functions to help effect other aspects of the Research Base's research strategy (e.g., Membership, Auditing, Clinical Research Professionals (CRPs), Conflict of Interest). Administrative committees responsible for cancer

care delivery research also provide essential core services and could include cancer registrars, hospital administration, and financial managers.

1.1.4 Young Investigator Mentoring/Training

The Research Base is responsible for having a mentorship program to involve young investigators from diverse populations and across interdisciplinary backgrounds in cancer prevention, control, screening, and cancer care delivery research and to help train them eventually to take on leadership responsibilities for trials/studies, and/or committees.

1.1.5 Communications Support

The NCORP Research Base is responsible for organizing and disseminating information about the Research Base's scientific activities and major changes in administrative policies and procedures to its members through annual or biannual meetings that review the Research Base's progress, establish priorities, and plan future activities. Additional meetings among Research Base members and meetings with NCI staff may be held as needed. Relevant Research Base responsibilities for meetings include: (a) arranging for appropriate meeting space and accommodations for attendees; (b) developing and distributing meeting agendas; and (c) preparing summaries as appropriate after each meeting for Research Base members and NCI staff.

The Research Base is responsible for establishing routine communication between itself, member sites participating in its studies, and, where applicable, the Cancer Trials Support Unit (CTSU), to facilitate protocol development and study conduct and monitoring. Relevant communication methods include website postings, e-mail, teleconferences, and video-conferences.

1.1.6 Publications

The NCORP Research Base is responsible for ensuring timely preparation and submission of all Research Base publications for peer review. **Research Bases must adhere strictly to the publication policy described below in these Terms and Conditions of Award.**

Acknowledgement of NCI Support and Scope of Publication Policy: Publication or oral presentation of work done via the Research Base's Cooperative Agreement requires appropriate acknowledgment of NCI support. The definition of publications for this Cooperative Agreement includes NCORP Research Base abstracts, press releases, print-media articles/manuscripts, electronic media articles/presentations, letters, etc., related to findings and results from NCI-sponsored studies. All NCORP Research Base publications must reference the NCI protocol title in the manuscript or abstract title whenever relevant to the publication. When appropriate, NCI Program Directors should also be included as co-authors on NCI funded research.

Publication Timelines: Timely publication of NCORP Research Base findings is central to the mission of the Research Base and is a primary means by which the Research Base's accomplishments can be evaluated. Timely presentation of a study's findings and results is especially important when a DMSB recommends the public release of this information. Timely presentation of cancer care delivery research study findings and results is especially important when related to public policy and clinical practice standards.

It is expected that preliminary results of major phase 3 trials and large definitive care cancer delivery studies will be presented at a scientific meeting within 6 to 8 months of completion of the study analysis (if not sooner based on the relevance of the results). It is a requirement under the Terms of Awards that a full manuscript on the study results be prepared and submitted for publication in the peer-reviewed literature (not as an abstract) within 1 year of the availability of the primary study results based on the completion date of

the study recorded in the U.S. National Library of Medicine database, clinicaltrials.gov. Exceptions to this policy must be approved in writing by the NCORP Director. These timelines may be modified in the future by NCI institute-wide requirements that are in development.

It is also a requirement of these Terms of Award that the results of all NCORP studies be submitted as required by the Food and Drug Administration Amendments Act (FDAAA) Section 801 to comply with the rules defined for inclusion of clinical trial information in clinicaltrials.gov.

Pre-Publication Review:

- For cancer care delivery research publications associated with NCI-sponsored NCORP Research Base studies, the NCORP CCDR Scientific Lead must receive a copy of the manuscript or abstract 30 days in advance of publication. No review or comments will be provided unless specifically requested by the Research Base; this is simply a confidential notification. Review timing for publications other than abstracts or manuscripts should be discussed with appropriate NCI/DCCPS staff. No pre-publication review is required for NCORP clinical trial publications.

- All press releases issued by the NCI and/or the Research Base on primary study findings and results require review by NCI, NIH, and DHHS. Pre-review timing for press releases on study finding and results must be discussed with and approved by the NCORP Director and CCDR Scientific Lead for all cancer care delivery research studies. Research Bases are encouraged to send drafts of press releases on other topics to NCI for pre-review and/or pre-release notice.

- In addition to the requirements listed above, Research Bases should consider carefully whether any findings from clinical trials or cancer care delivery research studies that are pending reporting/publication may have major impact for public health or public policy. If there is the potential for major impact for public health or public policy, the Research Base must inform NCORP Director and CCDR Scientific Lead and work closely with NCI to ensure that the information is released to the public in as timely a manner as possible and in a manner to ensure appropriate communication about the results, including how they may affect other ongoing trials and the treatment of patients on those trials, public policy or current clinical practice.

Post-Publication Reporting & Submission to NIH Manuscript System:

- In their competitive Type 1 or Type 2 and non-competing Type 5 applications, Research Bases must report publication references for major clinical trial results and important associated studies to demonstrate the scientific accomplishments of their research strategy. Only references for the manuscripts for key findings should be reported. Copies of manuscripts cannot be submitted as part of the research plan or as appendix material.

- The NIH Public Access Policy ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central *upon acceptance for publication*. To help advance science and improve human health, the Policy requires that these papers are accessible to the public on PubMed Central no later than 12 months after publication. More information about this policy or the submission process is available on the NIH Public Access Policy website at: http://publicaccess.nih.gov/.

1.1.7 Data Rights

The NCI will have access to all data generated under this Cooperative Agreement and may periodically review the data. The awardee will retain custody and primary rights to the data consistent with current DHHS, Public Health Service (PHS), and NIH policies. Pharmaceutical and biotechnology companies will have access to all data generated under DCP Collaborative Agreements; however, the companies may contract directly with the Research Base for access to non-Clinical Data Update System (non-CDUS) data and reports. With respect to cancer care delivery research, external funding agencies and investigators that use the NCORP network to support scientific studies will have access to data from studies funded external to the network (e.g., PCORI and non-profit foundations).

Awardees will retain custody of and have primary rights to the data and software developed under these awards, subject to Government rights of access consistent with current DHHS, PHS, NIH, and NCI policies and within the limits of any accepted binding NCI/NIH collaborative agreements with biotechnology and pharmaceutical partners and as governed by NCI-approved Data Sharing Plans and NCI-approved review for use of biospecimens collected in association with NCORP trials/studies.

1.2 Membership Affiliation(s)

There are two types of NCORP Research Base Member Sites: NCORP Community and Minority/Underserved Community Sites and non-NCORP institutional members. An NCORP Community Site is defined as a consortium of community hospitals and/or oncology practices, which may or may not be formally affiliated in a healthcare system, that accrues participants to cancer control, prevention, treatment and care delivery clinical trials and related studies designed and conducted by NCORP Research Bases. The consortium may also include primary care and other providers. A Minority/Underserved Community Site is defined as a consortium of community hospitals and/or oncology practices, a public hospital, or academic medical center that has a patient population comprising at least 30% racial/ethnic minorities or rural residents and accrues participants to cancer control, prevention, treatment and cancer care delivery clinical trials and related research studies designed and conducted by NCORP Research Bases. Non-NCORP institutional members may be academic institutions and/or associated affiliate members.

The Research Base is responsible for establishing, maintaining and monitoring all its members (i.e., NCORP Community and Minority/Underserved Community Sites and non-NCORP institutional members) that participate in NCORP trials/studies and credit the Research Base with patient accrual. The Research Base must have a "real time", comprehensive, consolidated roster of all its members with their relevant CTEP institution codes, associated investigators and research staff. NCORP rosters are initiated within NCORP-SYS which is communicated to the CTSU Regulatory Support System (RSS) and approved by the Research Base for auditing, financial management and crediting of enrollment purposes.

NCORP Research Bases must establish guidelines for NCORP Community and Minority/Underserved Community Site awardees and non-NCORP institutional members to affiliate (i.e., become members). A Research Base must have established affiliation agreements with all member sites participating in that Research Base's Network.

A Research Base is responsible for providing a portfolio of clinical trials and cancer care delivery research studies, a significant portion of which are feasible to implement in the community setting, are of scientific interest and address the clinical needs of the participating sites' populations. Further, a Research Base must provide adequate resources (training, education, data management etc.) for the participating sites to implement the studies. A Research Base will require a minimum number of clinical trial accruals by the participating sites that reflect their available studies and resources to conduct them.

1.3 Operational Management

1.3.1 Governance, Organizational Structure, Policies & Procedures, and Membership

An NCORP Research Base is responsible for coordinating study proposals, protocol development, protocol submission, study conduct, performance reporting, quality assurance including quality control and study monitoring, protocol amendments/status changes, and adherence (where applicable) to requirements regarding investigational agent management as well as all federal regulations.

The Research Base is responsible for specifying the mix of funding available for a trial/study that it leads prior to trial/study activation (where applicable) as well as for providing information in a timely manner on appropriate modifications in funding on the trial/study during the course of accrual.

Specific responsibilities of the Research Base include the following:

Governance: The Research Base is under the leadership of a "designated" Chair elected by the Research Base's membership, who coordinates all the scientific and administrative decisions related to Research Base-funded activities and the Research Base's institutional members. The Multiple Principal Investigator (PI) option is encouraged for the Research Base award given the team science approach of the research effort. Information on the Multiple PI Option is available at http://grants.nih.gov/grants/multi_pi/index.htm. If this option is used, the Research Base should designate a "Contact PI" among the multiple PIs. The designated Research Base Chair (or Contact Principal Investigator under the Multiple PI option) is also responsible for all grant-related activities and for communication about these activities with the appropriate NCI/DCP staff.

Organizational Structure, By-laws, and Standard Operating Procedures: The Research Base is responsible for development and maintenance of an organizational structure for the Research Base and its members/sites, including a Constitution and By-laws. The organizational structure of the Research Base should be established with clear and appropriate staff roles and reporting responsibilities, especially with respect to the role and reporting responsibilities of the Research Base Chair (who must also be listed as key personnel in the Research Base application and award). The Research Base is also responsible for the preparation and maintenance of Standard Operating Procedures (SOPs) that cover all aspects of its activities.

The organizational structure should include the Scientific Research and Administrative Committees that the Research Base will need to support its research objectives as well any Executive Committee(s) that the Research Base elects to establish. There should be clearly defined term limits and succession/transition plans for the senior leadership of the Research Base and for the leadership of its committees. Terms for the key scientific leadership positions of a Research Base (e.g., designated Research Base Chair, Committee Chairs, etc.) should be limited to encourage participation by new investigators and to ensure a diversity of views over time. The process for filling elected positions for scientific leadership positions should be well described in the By-laws of the Research Base along with details of any exceptions to term limits.

The Research Base shall designate Study Chair(s) for each proposed concept/protocol. The Study Chair will have the appropriate experience and training to guide the study. The Research Base is responsible for assuring the Study Chair meets Federal and local regulatory guidelines and accordingly, can fulfill the requirements of a Study Chair. The Research Base is responsible for establishing policies and procedures for the development and submission of NCORP Research Base study concepts and protocols through the NCI DCP Protocol Information Office (PIO) for review and approval. The Research Base is also responsible for

assembling appropriate study teams for protocol development and for overseeing conduct of approved studies.

Study concepts and protocols should be developed, submitted, and implemented in accordance with NCORP policies. Research Base SOPs should include timelines for the development of concepts and protocols from initial submission of the concept to NCI through study activation. The SOPs should also include mechanisms for monitoring the performance of the Research Base and Research Base committees and investigators in adhering to these timelines, as well as corrective action plans outlining steps to be taken when these timelines are not met. These timelines should meet the following NCORP requirements: 1) concept receipt to approval: 120 days; 2) protocol authoring: 90 days; 3) protocol review and approval: 175 days; 4) protocol approval to activation: 90 days for a total target timeline goal equaling 475 days. To accommodate additional time required for potential revisions, an extra 50-days has been added to the total target timeline to create an absolute deadline of 525 days. Prior to the 525-day deadline, requests for an extension with justification may be submitted in writing to the DCP PIO. If an exception is not granted prior to the 525-day deadline, the concept or protocol will be terminated. All concepts and protocols that have not submitted an exception request and have not met the absolute deadline will be automatically terminated.

Correlative science studies embedded in NCORP clinical trials/studies at the time of initial concept submission should be appropriately designed as integral and/or integrated studies with robust statistical designs and analysis plans that address specific and important scientific hypotheses. Exploratory studies and those without a specific hypothesis and robust statistical analysis plan will not be approved. Although optional collection of biospecimens without an approved research plan may be approved for a trial, use of the specimen must be approved by DCP and must be based on studies with specific hypotheses and statistical analysis plans (i.e., biospecimens cannot be "reserved" for future unspecified research without a subsequent study proposal being reviewed and approved).

Detailed policies and procedures for developing concepts, protocols and amendments for NCORP cancer prevention, control and screening/post-treatment surveillance clinical trials as well as cancer care delivery research studies are described in Part 3 of these guidelines.

1.3.2 Conduct of Cancer Control, Prevention and Care Delivery Research Studies

These procedures apply to cancer control, prevention, and care delivery clinical research studies except as specifically noted.

Specific regulations regarding conduct of NCORP studies include the following:

1.3.2.1 NCI/DCP Approval Prior to Study Activation and Approval of Protocol Amendments

The Research Base has the responsibility for overseeing conduct of approved studies within its Network regardless of whether the study proposal originates from an investigator within or outside the Research Base.

Since public funds are used to support Research Base studies sponsored under NCORP Cooperative Agreement, no Research Base study using funds supplied under the Cooperative Agreement can be opened without prior approval from the NCI/DCP as communicated in approval letters sent to the Research Base Chair directly from the NCI DCP Protocol Information Office (PIO). The Research Base also is not allowed to expend any NCI funds under this Cooperative Agreement to support any study disapproved by the NCI/DCP. In addition, all protocol amendments must be submitted to DCP's PIO and be approved by NCI/DCP prior to implementation. Depending on the nature of the amendment, the study

may or may not be put on hold to further accrual and/or conduct until the amendment is approved.

1.3.2.2 Use of the NCI Central Institutional Review Board

The NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research (NOT-OD-17-076) became effective on January 25, 2018. In compliance with this policy, the NCI Central IRB (NCI CIRB) is the sole IRB of record for all sites conducting clinical trials through the NCORP and NCTN networks and is responsible for study review (initial review, amendments, continuing reviews, recruitment materials, unanticipated problems and serious or continuing noncompliance) and approval of local context considerations.

To comply with the NIH policy:

- All NCORP sites must be enrolled in the CIRB as of the date of their award.
- All new NCORP protocols will be opened under the CIRB.
- All CIRB-enrolled sites must open all new studies under the CIRB.
- Patients on CIRB-approved protocols who are followed by local IRBs must be transferred to the CIRB within a timeframe to be specified in the new NCTN and NCORP grants (12-18 months). This transfer is initiated by the local site via the filing of a Study Specific Worksheet through the CIRB Local Context Review Process.
- Legacy NCORP protocols (e.g. CCOP studies opened before 2/1/2015 and CCDR studies opened before 6/1/2016) currently conducted under the oversight of local IRBs will complete accrual and follow-up under their existing IRB arrangements. NCI anticipates that most of these trials will be completed before the Common Rule compliance date of January 20, 2020.

All NCORP sites with comply with the conditions of their Federal-Wide Agreement (FWA) and the CIRB Standard Operating Procedures.

1.3.2.3 Clinical Trials Reporting Program (CTRP)/clinicaltrials.gov Registration and Outcomes Reporting

All NCORP trials must also be registered and appropriate information updated in the NCI CTRP as described at: http://www.cancer.gov/clinicaltrials/conducting/ncictrp/main as well as registered in the U.S. National Library of Medicine clinical trials database (i.e., at www.clinicaltrials.gov).

Changes in the trial design and accrual as well as results reporting from NCORP trials are also required to be reported in clinicaltrials.gov as required under the Food and Drug Administration Amendments Act (FDAAA), Section 801. The Research Base should ensure information on its NCORP trials is appropriately updated in these systems.

1.3.2.4 Study Access (not applicable for cancer care delivery research)

Research Bases' member institutions/sites will be able to enroll patients on all adult phase 3 trials (and selected phase 2 trials) conducted by NCORP, irrespective of the specific Research Base which is leading the study.

Research Base phase 3 trials (including phase 2/3 studies) using funds supplied under this Cooperative Agreement cannot be conducted under a company IND; all phase 3 IND trials supported, in whole or in part, under this Cooperative Agreement must be conducted under a Research Base IND or a DCP IND. This also applies to phase 3 trials requiring an IDE. Phase 1 and phase 2 trials may be conducted under Research Base or company INDs or IDEs with appropriate monitoring per the Research Base data and safety monitoring plan or Data and Safety Monitoring Board (Data Monitoring Committee) policy for randomized phase 2 trials.

1.3.2.5 Agents from NCI/DCP Collaborators (not applicable for cancer care delivery research)

All NCORP studies using NCI/DCP-sponsored investigational agents under Collaborative Agreements (such as Cooperative Research and Development Agreements [CRADAs], Clinical Trial Agreements [CTAs], and Clinical Supply Agreements [CSAs]) must be conducted in accordance with the terms of the NCI/CTEP Intellectual Property Option to Collaborators, found on the CTEP website at: http://ctep.cancer.gov/industryCollaborations2/intellectual_property.htm, and the NCI Standard Protocol Language for CRADAs and CTAs. When new avenues of cancer prevention or control involving any investigational agents are pursued, the clinical information obtained in the study should be acceptable to the FDA and other health authorities for inclusion in a possible licensing application. When NCI/DCP and the Research Base contract with the same company (or companies) for support for the same trial (i.e., trials conducted under a NCI/DCP Collaborative Agreement, the Research Base contracts may require review by the appropriate DCP program at the discretion of NCI.

1.3.2.6 NCORP Investigational Agent Development and Regulations (not applicable for cancer care delivery research)

The clinical development of new cancer preventive agents is an important use of Research Base resources. The Research Bases are a vital component of the research apparatus necessary for the clinical development of new investigational agents. NCI/DCP Program Directors (working as needed with other NCI program staff members) will advise investigators of specific requirements and changes in requirements concerning investigational drug management that the FDA may mandate.

NCI/DCP and NCI/DCTD staff will review general policies and procedures periodically, as needed, and provide advice regarding mechanisms established by the Research Bases to meet FDA regulatory requirements for studies involving DCP-sponsored investigational agents.

1.3.2.7 NCORP Required Tools and Services

Research Bases are **required** to use standard NCI tools and services for all NCORP trials including, but not limited to: (a) NCTN information system for tracking biospecimen collection from NCTN trials (e.g., OPEN, RAVE, etc.); (b) the NCI Common Terminology Criteria for Adverse Events (CTCAE); and (c) review of all trials by the NCI Central Institutional Review Board (CIRB). NCORP Cancer Center Research Bases are expected to use all tools and services except for RAVE.

During the approval process for study protocols and amendments, NCI/DCP ensures that standard NCI tools and services are used. In addition, Research Base trial protocols will be periodically audited by NCI/DCP to ensure that the tools related to common data elements in compliance with NCORP approved sections of the data dictionary for common data elements in caDSR are used in the data collection instruments for NCORP trials.

It is required that the Cancer Trials Support Unit (CTSU) be utilized for all NCORP trials. NCORP trials using CTSU must also use the NCTN Oncology Patient Enrollment Network (OPEN) and Regulatory Support Services (RSS) for central registration and randomization of patients onto NCORP trials. It is expected that all cancer prevention, screening/post-treatment surveillance and control trials will be available on the CTSU. NCORP Cancer Center Research Bases are expected to use all the tools and services except for RAVE.

1.3.2.8 Data Management

The Research Base should establish data management policies and procedures for ensuring data accuracy, timeliness, completeness, and consistency for NCORP studies. The general categories that should be addressed by the data management policies are listed below:

- Central storage, security, processing and retrieval of study results that incorporates security features consistent with DHHS guidelines.

- Procedures for backing up the Research Base's clinical and administrative data, including intermittent duplication of the database with storage at a remote facility.

- Protection of participant confidentiality at all steps in the submission and analysis of participant data, including the technical integrity and security of participant information in compliance with federal regulations, such as the Health Insurance Portability and Accountability Act (HIPPA).

1.3.2.9 CDUS/CDS Reporting

In addition, data must be submitted in a timely manner on all NCORP trials, as appropriate, to the NCI/DCTD Clinical Data Update System (CDUS/CDS) at http://ctep.cancer.gov/protocolDevelopment/electronic_applications/cdus.htm. Reporting will generally consist of CDUS abbreviated data (primarily demographic and accrual). The Research Base should coordinate activities to ensure information on its NCORP trials is appropriately updated in all these systems.

1.3.2.10 Collection and Transmission of Data and Biospecimens

All data, as well as any biospecimens collected for an NCORP study must be sent by the institutions/sites participating in the study to the Research Base that is leading the study, unless an exception is approved by the NCI/DCP to accommodate the needs of a specific study. The Research Base is responsible for overseeing the timely collection and transmission of data and biospecimens from all its member institution/sites to NCORP studies for patient accruals that are credited to the Research Base. Collection and banking of tissues and other biological specimens is an increasingly important aspect of the clinical research performed by the Research Bases. For NCORP trials that it leads, the Research Base is responsible for coordinating the acquisition and shipping of protocol-specified tumor specimens and biological fluids (with relevant clinical data) to the appropriate laboratories for testing and to a tumor/specimen repository for storage of specimens for future correlative science laboratory studies. The Research Base is also responsible for ensuring that all its members submit required biospecimens for NCORP studies when the Research Base is credited with the accrual even if the Research Base is not leading the trial.

1.3.2.11 Data Reporting

The Research Base must have policies and procedures in place to ensure that data reporting requirements are fulfilled in a timely manner including the major data reporting requirements outlined below.

- NCI Access to Research Base Website and Data Files Requested by NCI: The Research Base is responsible for ensuring that the NCORP Director, CCDR Scientific Lead and applicable Program Director have access to the Research Base website, including the member side of the website.

  Upon request by the NCI, the Research Base is also responsible for providing true copies of data files and supporting documentation for specific NCI-supported trials and other studies in a timely manner.

- Data for Member Performance Evaluations, Audits, & Data Monitoring Safety Boards (DSMBs): The Research Base is responsible for providing accurate and timely reporting of data on accrual, data timeliness, and accuracy, protocol compliance, long term participant follow-up, and audit results related to the conduct of Research Base clinical trials and other studies by member sites for Performance Evaluations of the sites. The Research Base will also provide all data required for member site auditing as well as data evaluation of trials for the Research Base's Data and Safety and Monitoring Board.

1.3.2.12 DSMB/DMC Recommendations for NCORP Studies

The Research Base is required to send a listing (or an email with internet access link to a listing) of all Data and Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC) recommendations accepted by the Research Base Chair(s) to the NCORP Director after every scheduled DSMB/DMC meeting. DSMB/DMC recommendations accepted by the Research Base Chair(s) after ad hoc DSMB/DMC meetings/calls must also be communicated to the NCORP Director.

1.3.2.13 Adverse Event Reporting and Patient Safety

Research Bases must establish a system for assuring expedited reporting of all serious adverse events to ensure potential patient safety issues can be identified and addressed quickly. Adverse events should be reported using the Common Terminology Criteria for Adverse Events v5.0 (CTCAE) or most recent version, which is NCI standard language for reporting adverse events in oncology clinical trials and is provided on the NCI/DCTD/CTEP website at: https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm .

For agents under DCP-sponsored INDs, this involves reporting to DCP via CTEP-AERS according to the guidelines specified in each protocol. Research Bases must also use CTEP-AERS, or its successor application, for expedited reporting of serious adverse events for all NCORP trials (even those not under a DCP IND or not under any IND/IDE) since CTEP-AERS provides reporting pathways for studies that do not include DCP IND agents, as well as pathways for studies that do not include any agents (e.g. surgical only study, radiation only study). Expedited reporting using CTEP-AERS should be performed as described at: https://ctep.cancer.gov/protocolDevelopment/electronic_applications/adverse_events.htm. Serious adverse event reporting for all NCORP trials should also follow the "NCI Guidelines for Investigators: Adverse Event Reporting Requirements for DCTD (CTEP and CIP) and DCP INDs and IDEs" available at: http://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/aeguidelines.pdf

In addition, for any study using agents under a DCP-sponsored IND, any increase in the incidence of expected toxicities and any plans to change a trial design or close a trial early due to toxicity should immediately be discussed with DCP before any action is taken. For NCORP studies that are not being conducted under a DCP IND, any major patient safety issues (e.g., study closure/suspension for adverse events, inappropriate randomization of patients to treatment arms, etc.) also require immediate notification to DCP before any action is taken.

In general, for studies with these types of immediate safety issues that are under monitoring by a Data and Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC) as defined in Part 1: Section IV.B.1.5.6, immediate notification should be made to the DSMB/DMC Chair and the NCORP Director. Immediate notification for studies not under DSMB/DMC monitoring should be made to the NCORP Director.

1.3.2.14 Early Trial Closure

The Research Base must establish policies and procedures for early closure of studies in conjunction with its associated DSMB based on the NCORP Guidelines below. The Research Base should explicitly describe the policies in place for cancer prevention and control trials and longitudinal clinical studies. Statistical guidelines for early closure should be presented in sufficient detail in the protocol in order to facilitate decisions regarding early closure. Outlined below are NCI/DCP approved early stopping guidelines for slowly-accruing randomized cancer prevention and control trials and longitudinal clinical studies for NCORP. If accrual is behind expectations for a specific study, the Research Base should involve the appropriate NCORP Program Staff in discussions about possible ways to enhance accrual in order to avoid study closure. Screening, over diagnosis and post treatment surveillance trials are excluded.

Procedures regarding notifying NCORP Program Staff about early study closure are outlined below and should be incorporated into the Research Base's policy for study closure of an NCORP study.

Early Stopping Rules for Slowly-Accruing DCP NCORP Studies:

The following early stopping guidelines are stated in terms of the fraction of cumulative (planned) accrual at Quarter 4 **(Q4)** and Quarter 8 **(Q8)** after protocol **activation**.

- If Q4 accrual is < 15% of the total accrual:
  - The Research Base will inform the study team that their study is at risk for early closure.
  - The Research Base study team will need to evaluate the accrual assumptions and address the recruitment of participants in a concrete fashion (develop a plan to increase accrual or close the study).
  - The Research Base will inform the assigned NCORP Program Staff that the study has been identified as potentially slow accruing and submit plans to remediate the accrual efforts to the NCORP Program Staff.

- If Q8 accrual is < 20% of total accrual:
  - The Research Base will inform the study team that their study has a very low likelihood for meeting its accrual goal and therefore the study should be closed.
  - The Research Base will inform the assigned NCORP Program Staff that the study has been selected for early closure.
  - In rare circumstances DCP Program Staff may consider a waiver to early closure.

Implementation: The NCORP Protocol Review Committee will review the accrual plan at the time of initial protocol review with regard to how realistic the estimate is and the relevance of study results at the end of the planned accrual time.

As soon as the Q4 cumulative accrual figures become available, the Research Base will review them and apply the guidelines above to identify any studies that are potentially slow accruing. As soon as the Q8 cumulative accrual figures become available the Research Base will review them and apply the guidelines above and identify studies that should be closed. This procedure generally allows studies identified at Q4 to have a full year to address accrual issues.

Previous experience suggests that failing to reach at least 20% cumulative accrual at Q8 strongly predicts failure to meet accrual target. Thus, if a study has failed to reach > 20% cumulative accrual by Q8, the study should close unless, after discussions with the DCP Program Staff, a special waiver has been issued.

Screening, Over Diagnosis and Post Treatment Surveillance Trials:

The Research Base should also establish policies and procedures for early closure of screening, over diagnosis and post treatment surveillance trials in conjunction with its associated DSMB. Statistical guidelines for early closure should be presented in sufficient detail in each protocol in order to facilitate decisions regarding early closure. If accrual is behind expectations for a specific study, the Research Base should involve the appropriate NCORP Program Staff in discussions about possible ways to enhance accrual in order to avoid study closure.

For studies that are closed or amended, the Research Base will notify the Group Data and Safety Monitoring Board (DSMB) of the closure or amendment at their next regularly scheduled meeting. Research Base chairs may consult with their DSMB regarding the decision for early closure, if desired. In the unusual circumstance that the Research Base Chair believes that the guidelines are inappropriate for a given study, he or she will initiate a discussion with the assigned NCORP Program Staff to reach a joint decision concerning what course to take.

1.3.3 Quality Assurance and Onsite Auditing

The Research Base is responsible for establishing mechanisms to assure the accuracy and reliability of the Research Base's study data. Quality assurance is a complex undertaking spanning the entire range of studies conducted by the Research Base including but not limited to: observational, survey research, registry, administrative, screening/post-treatment surveillance, biomarker, omics, diagnostic, interventional, and imaging. Key items that should be addressed in a Research Base's quality control procedures include the following:

1.3.3.1 Study Monitoring

The Research Base is responsible for overall organization and oversight of study teams that monitor data from specific research studies. All research carries with it an obligation to ensure optimal therapy for participating patients, providers and organizations and optimal conduct of the research such that the participation is meaningful. Accurate and timely knowledge of the progress of each study is a critical Research Base responsibility. The elements described below are considered essential for study monitoring:

- Precise tracking of participant accrual (both eligible and ineligible participants) and adherence to protocol-defined accrual goals. In the event that the Research Base wishes to continue accrual to a study beyond the protocol-specified total accrual goal for eligible and ineligible participants, the Research Base must seek approval from NCORP prior to continuing accrual

- Ongoing assessment of participant eligibility, participant evaluability, and appropriate assignment of participants to study groups (e.g., randomization)

- Adequate measures to ensure timely submission of study data as well as adequate measures to ensure timely medical review and assessment of individual patients' data with rapid reporting of treatment-related morbidity information and measures to ensure communication of this information to all appropriate parties

- Interim evaluation of outcome measures and patient safety analyses

- Tracking of response rates, including those respondents that either decline or could not be found, those that responded, and oversight and monitoring of missing data

Study monitoring reports describing accrual and demographics, data timeliness, toxicity, and other items should be prepared as appropriate for Study Chairs, for Data and Safety Monitoring Boards (DSMBs), and for inclusion in the semi-annual Report of Studies.

1.3.3.2 Member Performance Evaluations

The Research Base is responsible for oversight of all its members (i.e., Community sites, Minority/Underserved Community Sites, and other non-NCORP member institutions) including placing members on probation for inadequate performance and for removing them from the Research Base if performance is not adequate during the probationary period or at any time during which the participating site does not meet established Research Base standards. Performance factors to be considered include the following:

- Accrual of adequate number of eligible patients onto NCORP trials;
- Accrual of adequate number of eligible participants onto cancer care delivery clinical research studies;
- Timely and accurate submission of required data;
- Conscientious observance of protocol requirements;
- Compliance with regulatory requirements for the protection of human subjects and Good Clinical Practice;
- Participation in study development, leadership, and publication; and
- Participation in Research Base leadership and/or other Research Base activities.

1.3.3.3 Training Program

The Research Base should have training activities that address data collection, data management, and overall data quality, including but not limited to the following areas:

- Training of new Clinical Research Professionals (CRPs) in the Research Base's data submission policies and ongoing training of all CRPs concerning changes to Research Base procedures and instructions for data submission in new protocols;

- Instruction of Study Chairs on their responsibilities for study monitoring;

- Instruction of Principal Investigators and other investigators at member participating Sites on their responsibilities for complying with Research Base SOPs, including conflict of interest and all other federal regulations at their institution/site and any additional site(s) for which the member site has oversight responsibility;

- Training/guidance provided to all participants on how to comply with NCI/NIH policies and procedures (e.g., policies regarding human subjects protection, ethics, conflict of interest, and procedures such as those regarding use of the CTSU), in addition to the policies and procedures of other governmental agencies (e.g., OHRP, FDA) that are also important to the conduct of NCORP studies; and

- Training /guidance provided to all participants on the breadth, specificity and the quality of cancer care delivery research data from hospital registries, organizations, medical records, financial and administrative data, and delivery characteristics, as well as the ability to relate these databases and incorporate core data elements.

1.3.3.4 Central Review and Scientific Research Committees

Research Bases should either develop or utilize established Committees for conducting central review of the major elements that affect the outcome of cancer prevention and control studies or provide integral/integrated translational science associated with specific trials, including the following:

- *Integral or Integrated Correlative Science and/or Translational Research Committees:* integral and/or integrated correlative science or translational science studies included in NCORP Research Base studies that address specific and important scientific hypotheses (or are integral to the primary study design) should be appropriately designed. Funding for these studies is not provided directly by NCORP award but may be applied for via BIQSFP funding.

- *Pathology*: Pathology review may be either by a committee within the Research Base Cancer Centers associated NCTN Network Group, or by an external reference panel. Prospective central verification of pathologic diagnosis may be required for specific trials in which it is integral or essential to the study design (i.e., cases in which known variability in the accuracy of histologic (or other) diagnosis is a potentially serious problem and in which pathology data is integral to appropriate study design and analysis). Funding for this central review, whether retrospective or prospective, is not provided by NCORP award; however, it can be provided via BIQSFP funding.

- *Imaging support including diagnostic imaging:* When relevant, central review (either prospective or retrospective) of imaging in NCORP trials may be required for evaluating response, establishing a diagnosis, and/or screening of patients and should be provided via coordination with the Research Base's (or associated NCTN Network Group's) Radiotherapy and Imaging Core Services Centers.

- *Systemic Interventions (Chemotherapy or other Biologic Agents):* Central review may be performed by the Research Base study team for the trial to determine protocol compliance with dose administration and dosage modification.

- *Surgery:* When relevant, adequacy of protocol-specified surgical procedures may be assessed (e.g., through review of operative notes, study-specific surgical forms, and pathology reports) by the Network Group study team for the trial.

- *Legacy Large Cancer Prevention Trials:* In some cases, there may be a separate structure for the review of data and correlative studies in large legacy cancer prevention trials.

Research Bases should develop Committees for conducting central review of cancer care delivery research studies and review infrastructure development of affiliated sites, determine study needs, and allocate resources.

1.3.3.5 Onsite Auditing

The NCORP Research Base has responsibilities with respect to onsite auditing. In particular, the Research Base should ensure that policies and procedures are in place to ensure that auditors participating in the onsite auditing program maintain confidentiality of all participant materials.

Information on the requirements for onsite auditing is provided within the NCI Guidelines for Auditing Clinical Trials prepared by the Clinical Trials Monitoring Branch (CTMB) of NCI/DCTD/CTEP available at:
https://ctep.cancer.gov/branches/ctmb/clinicalTrials/monitoring_coop_ccop_ctsu.htm

In order for the NCI to review the Research Base's compliance with this requirement, each Research Base should provide annually an accounting of audit activities for all its members.

CTMB provides direct oversight of each Research Base's auditing program. The purpose of an audit is to document the accuracy of data submitted to the Research Bases and to verify investigator compliance with protocol and regulatory requirements. In addition, the

monitoring program provides an opportunity for the audit team to share with the staff at the participating site information concerning data quality, data management, and other aspects of quality assurance. The main objective of the audit program used by the Research Bases is to verify study data that could affect the interpretation of primary study endpoints. This is done through independent verification of study data with source documents.

The Research Base is responsible for oversight of all its members enrolling patients on NCORP studies that any member credits to the Research Base regardless of whether the Research Base is leading the study or not. This includes ultimate oversight responsibility for Community and Minority/Underserved Community Site members as well as non-NCORP institutions when accrual for an enrollment in an NCORP trial is credited to the Research Base. The Research Base should be aware of all sites participating in its studies under the aegis of an institutional member, Community site, or Minority/Underserved Community site via its consolidated roster. Any members of a Research Base found not to be in compliance with the NCI Guidelines for Auditing Clinical Trials by the CTMB may be suspended from participating in any NCORP trials until a corrective action plan is submitted by the institution/site to the Research Base and is reviewed and approved by the Research Base and DCP. Research Base decisions to suspend or to place NCORP Community Sites or Minority/Underserved Community Sites on probation are to be reported immediately to CTMB and to the NCORP Director.

Additional information on quality assurance required of Research Bases with respect to trial data and, in particular, procedures a Research Base is required to follow in the event any data irregularities are identified through the audit program or other quality control procedures are explained in the NCI Guidelines for Auditing Clinical Trials document located at https://ctep.cancer.gov/branches/ctmb/clinicalTrials/monitoring_coop_ccop_ctsu.htm

1.3.4 Financial Management

The Research Base is responsible for its own financial management, including appropriate funding for all Research Base activities and provision of funding to member institutions/sites through purchase service agreements or subcontracts as well as funding for other important scientific and administrative services needed for Research Base functions such as support for Study Chairs and Scientific Research Committee Chairs.

Each Research Base's control and prevention protocol approved by NCI for Community or Minority/Underserved Community Site and/or non-NCORP institution use will be assigned a credit value by NCI/DCP. The credit assignment will be detailed within the protocol approval letter. Credits will be based on the complexity of the intervention, the amount of data management required, and the duration of follow-up. The credit is claimed one time by Community or Minority/Underserved Community Site grantee against the grant year in which the participant was enrolled on the protocol.

Non-NCORP institutions will receive per case reimbursements for accruals to cancer prevention and control trials from the Research Bases and will be paid from the Research Base NCORP grant funds.

Cancer care delivery research studies do not receive a credit assignment at the time of protocol review. Instead, CCDR restricted funding is provided to the Research Base and Site grantees at the beginning of each grant year and used to support CCDR work throughout the year. Non-NCORP institutions may not participate in care delivery research studies.

The Research Base should ensure that funding is allocated at the site so that investigators and research staff from different departments and disciplines at the institution that participate in NCORP studies are appropriately represented in the disbursement of funding. For example, the Principal Investigator(s) at an institution/member site, with which a

Research Base has a subcontract or purchase service agreement (PSA) for work related to enrollment of patients and conduct of studies in NCORP, may be a member of the Medical Oncology department at the institution, yet work under the subcontract or PSA which is performed across multiple departments at the institution (e.g., surgery, pathology, radiation oncology). The Research Base should strive to ensure that all member institutions/sites distribute funding to all departments involved in support of NCORP studies in a manner that reflects the work performed by the various members of the research team.

Any separate, non-NCI/DCP funding (i.e., funding not provided under the Cooperative Agreements of NCORP) dispensed by a Research Base to cover costs associated with participant enrollment on NCORP studies that it leads must be provided to all qualified institutions/sites that participate in its NCORP studies regardless of which Research Base the enrolling institution belongs to and/or applicable credits with the patient clinical trial accrual. This principle is considered an essential feature of NCORP and the Terms and Conditions of Award as it is fundamental to ensure fairness for work performed across the Network.

1.3.5 Legacy Studies

Legacy studies supported by the Community Clinical Oncology Program will be conducted under the same Terms and Conditions of Award as NCORP studies. Hence, the awardees of any of the key components of NCORP (i.e., NCORP Research Bases, NCORP Community Sites, and NCORP Minority/Underserved Community Sites) are bound by the Terms and Conditions of their Award under NCORP when working on legacy studies that are supported by NCORP.

1.4 Program for Collaborations and Participation in Collective Management

NCORP Research Bases are responsible for developing collaborations with other Research Bases as well as other NCI-sponsored programs and investigators (e.g., Cancer Centers, R01/P01 investigators) to augment and enhance the cancer control, prevention and care delivery research strategy and research productivity of its portfolio of studies conducted in NCORP. In addition, the Research Base is also responsible for participating in the collective management of the NCORP Network including participation in appropriate NCORP Program activities and initiatives (e.g., NCI Scientific Steering Committees, NCI CIRB, etc.) and through the NCORP Leadership Management Committee by making recommendations to NCI for modifications to the Program as well as to standard NCORP common tools and services. Finally, the NCORP Research Bases are expected to cooperate in any program evaluation processes that are conducted including interacting with NCI representatives in coordinating the evaluation.

Each Research Base is required to have policies to encourage other Research Bases to name co-principal investigators for studies that the Research Base leads (in areas that other Research Bases have scientific research goals and/or scientific research committees) in order to augment accrual and participation in NCORP trials and cancer care delivery research.

1.5 Compliance with Federal Regulations for Clinical Research & Resource Sharing Plans

The Research Base is responsible for assuring that the Research Base and its member sites are in compliance with all applicable federal regulations concerning the conduct of human subjects research. Policies and guidelines to be addressed include the following:

1.5.1 Office for Human Research Protection (OHRP) Assurances

The Research Base must assure that each member (this includes all affiliates or participating sites enrolling participants under any of the membership categories for the Research Base) has a current, approved Federal Wide Assurance (FWA), on file with OHRP. Information on assurances is available on the OHRP website at: http://www.hhs.gov/ohrp/.

In addition, federal regulations (45CFR46) require that applications and proposals involving human subjects must be evaluated with reference to risks to the subjects, the adequacy of protection against these risks, the potential benefits of the research to the subjects and others, and the importance of the knowledge gained or to be gained.

1.5.2 IRB Review of NCORP Studies by Member Institutions/Sites

The Research Base must assure that each NCORP protocol is reviewed and approved by the appropriate Institutional Review Board (IRB) of the Research Base member prior to patient entry via the Regulatory Support Services (RSS) of the CTSU, and assure that each protocol is reviewed annually by the IRB so long as the protocol is active (it is anticipated that the adult or pediatric NCI CIRB will be the IRB of record in most cases).

1.5.3 Assurance of Appropriate Informed Consent by Member Institutions/Sites

The Research Base must have procedures in place to ensure that each member institution/site is trained and understands the policies and procedures relevant to ensuring that participants are enrolled on studies with appropriate informed consent per NCI/NIH policy and federal regulations. The template for the NCI informed consent document must be used for all NCORP trials, with appropriate modifications as approved by NCI/DCP for specific trials during the protocol development and review process. Compliance with the use of the NCI informed consent template will decrease unnecessary tailoring of local consent templates by local site staff. Information on the NCI informed consent templates is available at: https://ctep.cancer.gov/protocolDevelopment/informed_consent.htm .

Translated copies of NCI CIRB-approved documents such as consent forms, patient reported outcome documents (PRO) or recruitment materials, may be submitted by the Study Chair or Principal Investigator to the NCI CIRB. All NCI CIRB approved model consent documents will be translated into Spanish via the CTSU, approved by the CIRB and then posted with the trial documents on the CTSU website with the exception of the following:

1) Trials utilizing PRO documents (e.g., QoL forms)

    a. Non-English-speaking patients are generally not eligible for these trials and therefore translating the consent document is not appropriate. In these circumstances, if the PRO element is mandatory and is only available in English, the eligibility criteria should specifically exclude non-English speaking patients. If the PRO is optional, completion of the PRO must be optional for all study participants.

    b. For validated instruments that are available in languages other than English, the CIRB's approval of the English instrument as part of its review of a study is considered to extend to the validated translated versions. In general, the protocol should indicate the languages in which the instrument is available and provide investigators with information on how to obtain the translated instrument.

2) Recruitment materials

    a. Sites requiring translation of these documents will need to have them translated at the local level and submit them to the NCI CIRB for approval via the Study Specific Worksheet. Documents submitted to the NCI CIRB need to include the protocol version date (PVD) or version number that corresponds to the approved English version and a statement of accuracy referencing the PVD/version number.

Sites may obtain the CIRB-approved Spanish consent form from the CIRB tab on the CTSU website. In order to use the CIRB-approved Spanish consent form, the site must have its CIRB-approved consent form boilerplate language translated into Spanish and approved as part of the Signatory Institution Worksheet about Local context. PI's and their research

staff may develop materials specific to their site such as recruitment materials or additional information sheets. These materials are submitted to the CIRB for review and approval according to the description in 2a above.

1.5.4 Inclusion of Women, Minorities, and Children in Clinical Research

NIH policy requires that women and members of minority groups and ethnic subgroups be included in all NIH-supported research projects involving human subjects at: https://grants.nih.gov/grants/funding/women_min/women_min.htm. Compliance with this policy requires appropriate study designs, targets for total protocol accrual with distribution by ethnic/racial categories and by sex/gender, as well as reporting of accrual by ethnic/racial categories and by sex/gender. Since Research Bases conduct multiple phase 3 clinical trials, the amended NIH Policy on inclusion of women and minorities in research also applies (see NIH Guide Notice on NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research – Amended October 2001 at: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html, with a complete copy of the updated Guidelines available at: https://grants.nih.gov/grants/funding/women_min/guidelines.htm). A description of plans to conduct analyses, as appropriate, by sex/gender and/or ethnic/racial groups must be included in clinical trial protocols. Cumulative subject accrual and progress in conducting subset analyses must be reported to NIH in the annual Progress Reports.

Note: A Research Base should report this data for all patients enrolled on studies it leads regardless of whether it is credited with the patient enrollment or not and this data should be reported in the Research Base annual progress reports. Final analyses of sex/gender and ethnic/racial differences must be reported in the required Final Progress Report or any future competitive renewal applications.

NIH policy requires that children (i.e., individuals under 21 years of age) must be included in all human subjects research, conducted or supported by the NIH, unless there are clear and compelling reasons not to include them as described at: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-010.html. For cancer clinical research, Research Bases conducting research in adult cancers can provide a rationale for not including children because the majority of children with cancer in the United States are already accessed by a NCTN Network Group devoted to pediatric cancer research, so that requiring inclusion of children in the proposed adult study would be both difficult and unnecessary (since the research question is already being addressed in children by the pediatric network) as well as potentially counterproductive since fewer children would be available for the pediatric Network study if other studies were required to recruit and include children. This does not apply to cancer care delivery research. Children may be included in cancer care delivery studies if appropriate to answer the research question(s).

1.5.5 Data and Safety Monitoring Policy and Plans

The Research Base must establish a Data and Safety Monitoring Policy for the cancer control, prevention and care delivery clinical trials conducted by the Group in compliance with NIH and NCI guidelines for data and safety monitoring for clinical trials. Data and Safety Monitoring Boards (DSMBs) or Data Monitoring Committees (DMCs) must comply with the "NCI NCORP Program Data Monitoring Committee Policy" as provided in Part 5 – Appendices. One NCI NCORP Program staff is assigned to each Research Base DSMC. For the purposes of these Guidelines, the terms DSMB and DMC are used interchangeably to refer to committees established under with this policy. The DSMB/DMC must be used to monitor all phase 3 trials and randomized phase 2 trials led by the Research Base. According to NCI policy (https://deainfo.nci.nih.gov/grantspolicies/datasafety.pdf): Proposed DSMB members must be reviewed and approved by the awarding NCI Division Director or designee prior to their appointment.

Monitoring Plans for Trials Not Under DSMB/DMC: Data and Safety Monitoring plans developed for other NCORP Research Base studies (e.g., phase 1 and phase 2 studies, pilot studies, etc.) must comply with the NIH policy for data and safety monitoring, posted on the NIH website at: http://grants.nih.gov/grants/guide/notice-files/not98-084.html, with additional description at: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html.

1.5.6 Resource Sharing Plans

1.5.6.1 Data Sharing Policy

The NCORP Research Base is required to have a plan for sharing research data. Information on the NIH policy regarding sharing research data can be found on the NIH website at: http://grants.nih.gov/grants/policy/data_sharing. The Research Base's policy for data sharing must be submitted to and approved by the NCORP Director. A template to help Research Bases develop their own Data Sharing Policies is provided in Part 5 – Appendices. Per this policy, requests for data will only be considered once the primary study analyses have been published.

Requests for data from clinical trials, conducted under a binding collaborative agreement between NCI/DCP and a pharmaceutical/biotechnology company, that are not under DSMB monitoring but are not yet subject to the Data Sharing Policy (e.g., because the primary study analyses have not yet been published) must be in compliance with the terms of the binding collaborative agreement and must be approved by NCI/DCP (i.e., the NCORP Director and for cancer care delivery research studies, the CCDR Scientific Lead, in conjunction with the NCI/DCTD Regulatory Affairs Branch). Release of data may also be subject to the terms of any contracts the Research Base has with other entities which cover any of the requested data.

1.5.6.2 Biospecimen Sharing Policy

The Research Base is required to follow the NCI/DCP policy regarding review of requests for use of banked biospecimens collected in association with NCORP trials that it leads which requires approval by DCP's Protocol Review Committee or an NCI/DCTD-approved NCTN Correlative Science Committee. Research Bases are also required to have a plan/policy in place to describe how information on its inventory of biospecimens will be made available to the public that is submitted to and approved by the NCORP Director and the Lead NCTN Program Director, Associate Director Cancer Diagnosis Program, and Program Director of the Tumor Banking Program for the Network Groups. This inventory should be consistent with standards established by the Network Tumor Banking Committee for the NCTN Program.

Research Bases having legacy prevention trials must have policies in place for review and approval for requests for use of specimens in research studies.

Research Bases should also have plans in place regarding the following types of resources, as appropriate for the clinical research it conducts: Sharing Model Organisms and Genome Wide Association Studies (GWAS).

1.5.7 Education on the Protection of Human Subjects and Good Clinical Practice

NIH policy requires education on the protection of human subject for all investigators submitting NIH applications for research involving human subjects and individuals designated as key personnel. This policy is available on the NIH website at: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html. DCP will require verification of Human Subjects Protection Training for all Study Chairs.

NIH policy also requires all NIH-funded investigators and staff who are involved in the conduct, oversight, or management of clinical trials to be trained in Good Clinical Practice (GCP), consistent with the principles of the International Conference on Harmonisation (ICH) E6 (R2) (http://www.fda.gov/downloads/Drugs/.../Guidances/ucm073122.pdf). DCP requires verification of GCP training for all Study Chairs.

1.5.8 Other Federal Regulations

The NIH Public Access Policy ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central *upon acceptance for publication*. To help advance science and improve human health, the Policy requires that these papers are accessible to the public on PubMed Central no later than 12 months after publication. More information about this policy or the submission process is available on the NIH Public Access Policy website at: http://publicaccess.nih.gov/.

Information on other federal regulations (and their associated citations/URLs) that may be applicable to the Research Base's research is provided in Part 5: Appendices.

1.6 Conflict of Interest Policy

NCORP Research Bases receiving NIH funding from a grant or cooperative agreement must establish a Conflict of Interest Policy that is in compliance with all of the DHSS regulatory requirements for conflict of interest as outlined by NIH grants policy available at: http://grants.nih.gov/grants/policy/coi. This policy should ensure that there is no reasonable expectation that any investigator or staff member of the Research Base or at any of its member institutions/sites involved in the design, conduct, or reporting of research will be biased by any conflict of interest (using the definition of investigator provided in the NIH grants policy). A management plan is also required for situations in which Conflicts of Interest are identified.

1.7 Special Requests for Use of NCORP Infrastructure Services

The infrastructure of NCORP, including NCI/DCP and NCI/DCCPS supported contract services, can only be used for NCORP studies approved by NCI/DCP under this Cooperative Agreement. In special circumstances, a Research Base may request limited use of certain services (e.g., regulatory support services (RSS), the Oncology Patient Enrollment Network (OPEN) for a related research effort or study such as a banking protocol not associated with a specific NCORP clinical trial that is supported by charitable funds or a related oncology research study funded by another NIH-funded program). These requests must be reviewed and approved by NCI/DCP and NCI/DCCPS via an official written approval by the NCORP Director and NCORP CCDR Scientific Lead. In addition, any special request for use of NCORP infrastructure services for cancer care delivery research studies (e.g. studies sponsored through the Department of Veterans of Affairs) also must be approved by the NCORP Director and CCDR Scientific Lead. It is expected that only requests that are compatible with and are anticipated to benefit the overall research goals of NCORP would be approved, subject to the availability of NCORP resources/funding, since the use of the requested services are funded under NCORP.

2. Specific Awardee Rights & Responsibilities – NCORP Community Sites

These rights and responsibilities apply to cancer control, prevention and care delivery research studies except as specifically noted.

Each NCORP Community Site is under the leadership of the Site PD(s)/PI(s). The Multiple Principal Investigator (PD/PI) option is encouraged given the team science approach of the research effort. Information on the Multiple PDs/PIs option is available at http://grants.nih.gov/grants/multi_pi/index.htm. If the Multiple PI option is used, the Community Site should designate a "Contact PD/PI" among the multiple PIs.

See RFA for the PD/PI (or Contact PD/PI under the Multiple PI option) responsibilities.

2.1 Definition, Eligibility, and Accrual Threshold

See RFA for additional information

2.1.1 Definition of an NCORP Community Site

See RFA for additional information

2.1.2 Annual Accrual Threshold

See RFA for additional information

2.2 Overall Responsibilities for Community Sites

2.2.1 Scientific Leadership & Contribution to NCORP Activities

Investigators at NCORP Community Sites should demonstrate scientific leadership for NCORP studies as well as support of and participation in other NCORP activities in a variety of ways through their membership in the Research Bases, including but not limited to the following:

- Offering eligible participants NCORP studies and enrolling sufficient participants to meet accrual targets;
- Participating in research design and protocol development for NCORP studies, including collaborations between Research Bases and other NCI-supported programs and investigators, particularly at their institution;
- Co-authorship on Research Base publications;
- Participating in the Scientific and Administrative Committees of the Research Bases;
- Participating in major meetings of the Research Bases and in other meetings deemed necessary for performance of the activities of NCORP;
- Participating in NCORP activities and initiatives such as the NCI Scientific Steering Committees and associated Task Forces and Working Groups and their activities such as NCI Clinical Trials Planning Meetings or Cancer Care Delivery Planning Meetings;
- Participating as members on the pediatric or adult NCI Central IRB;
- Providing secondary data on patients, providers or organizations from sources such as registries, electronic medical records, other clinical or administrative databases in NCORP studies and providing sufficient data to meet the sample requirements;

- Providing data on program characteristics, patterns and organizational policies of care to the affiliated Research Base;
- Participate in any program evaluation processes that are conducted including interacting with NCI representatives in coordinating the evaluation.

2.2.2 Young Investigator and Leadership Mentoring/Training

Each NCORP Community Site should provide a mentorship program or activities to involve young investigators from diverse populations and across interdisciplinary backgrounds at their institution in cancer control, prevention, and care delivery research studies to help train them eventually to take on senior leadership responsibilities for components of research at their institution(s).

2.2.3 Operational Management (Governance/Organization, Institutional Support, Components)

Governance & Organizational Structure: Each NCORP Community Site is under the leadership of the Site Principal Investigator(s) or Contact Principal Investigator under the Multiple PI option.

The Community Site is responsible for development and maintenance of a governance and organizational structure to coordinate NCORP activities at the institution. The organizational structure of the Community Site should be established with clear and appropriate staff roles and reporting responsibilities, especially with respect to the role and reporting responsibilities of any multiple PIs.

NCORP Community Sites will be expected to have a minimum of one Affiliate, preferably more, participate in cancer care delivery Landscape Assessments as offered.

Community Sites are to provide documentation of where actual research activities are being conducted across their program sites. Sites that are engaged in research (i.e., consenting, enrolling and treating) must have a CTEP Site ID, be covered under an FWA (confirmed on the OHRP website), are to be rostered as a primary affiliate or sub-affiliate site within NCORP-SYS, and after DCP approves, any associated accrual must be credited to that site. RT facilities or chemotherapy treatment centers/sites providing treatment only (not consenting/enrolling patients) or are located within a hospital campus (e.g., departments, clinics, offices) that are owned and operated by the hospital and are covered under the hospital FWA do not need a separate site code or an FWA and therefore do not need to be rostered. However, RT facilities or chemotherapy treatment centers/sites that are consenting and treating patients and are not owned and managed by another institution (i.e., independent business entities) do require a site code, an FWA, and will need to be rostered. Research sites that are located within a hospital campus (e.g., clinics, offices) that are not owned and operated by the hospital (i.e., independent business entities) and are not covered under the hospital FWA will require a separate site code and FWA and do need to be rostered.

Primary Affiliate & Sub-Affiliate Network: If the Community Site has primary affiliate(s) and sub-affiliate(s), the network must be clearly described (including reference to the distinct CTEP institution code(s) for the primary affiliate(s) and sub-affiliate(s) that are used for patient enrollment). The Community Site is

responsible for complete monitoring and management of the enrollment of patients at the primary affiliate and sub-affiliate site(s) to NCORP and NCTN clinical trials and cancer care delivery research studies if they are included in the award. The primary affiliate site(s) participating in cancer care delivery research must be clearly identified. Any post-award changes to primary affiliate and sub-affiliate sites will need to be approved by NCI per the Organizational Change Guidelines located in Part 4 of these guidelines.

Institution(s)/site(s) with the following NCTN Network Group membership status may not be included as a primary affiliate/sub-affiliate site of a NCORP Community Site unless the membership status is relinquished:

- NCTN Lead academic participating site (LAPS) (academic center and its integrated components)
- Affiliates or sub-affiliates included in a LAP cooperative agreement award
- Other Network Group main member, affiliate sites, or non-affiliated sites
- Primary affiliate/sub-affiliate of another NCORP grant (Community or Minority/Underserved).

2.2.4 Use of the NCI Central Institutional Review Board

The NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research (NOT-OD-17-076) became effective on January 25, 2018. In compliance with this policy, the NCI Central IRB (NCI CIRB) is the sole IRB of record for all sites conducting clinical trials through the NCORP and NCTN networks and is responsible for study review (initial review, amendments, continuing reviews, recruitment materials, unanticipated problems and serious or continuing noncompliance) and approval of local context considerations.

To comply with the NIH policy:

- All NCORP sites must be enrolled in the CIRB as of the date of their award.
- All new NCORP protocols will be opened under the CIRB.
- All CIRB-enrolled sites must open all new studies under the CIRB.
- Patients on CIRB-approved protocols who are followed by local IRBs must be transferred to the CIRB within a timeframe to be specified in the new NCTN and NCORP grants (12-18 months). This transfer is initiated by the local site via the filing of a Study Specific Worksheet through the CIRB Local Context Review Process.
- Legacy NCORP protocols (e.g. CCOP studies opened before 2/1/2015 and CCDR studies opened before 6/1/2016) currently conducted under the oversight of local IRBs will complete accrual and follow-up under their existing IRB arrangements. NCI anticipates that most of these trials will be completed before the Common Rule compliance date of January 20, 2020.

All NCORP sites with comply with the conditions of their Federal-Wide Agreement (FWA) and the CIRB Standard Operating Procedures.

2.2.5 Study Operations – Conduct of Studies and Data Management

The Community Sites should have a clearly articulated process for prioritizing which NCORP protocols to activate at their institutions. Investigators at Community Sites form the cornerstone of the research programs for NCORP and must perform at a high level through submission of accurate and timely clinical data as well as ancillary materials necessary to support NCORP (e.g., tumor specimens, imaging studies, pathology slides). The Principal Investigator(s) at each Community Site is responsible for the performance of their primary affiliate and sub-affiliate sites for which it provides oversight related to research activities and for assuring adherence to NCORP, NCI, OHRP, and FDA policies and procedures.

It is also the responsibility of the Principal Investigator(s) at the site to ensure that the procedures for data submission for each NCORP protocol are understood by all investigators at the Community Site and its primary affiliates as well as at any sub-affiliates, and that protocol-specified data are submitted accurately and in a timely manner to the appropriate NCORP Research Base.

2.2.6 Quality Assurance and Onsite Auditing

Responsibilities for quality assurance of the data (and biospecimens) submitted for NCORP studies as well as auditing include, but are not limited to, the following:

- *Pathology:* Submission of appropriate materials to allow verification of pathologic diagnosis, when relevant.
- *Biospecimens (including integral assays, omics, Pharmacokinetics, Pharmacodynamics):* Submission of appropriate biospecimens to allow for review/analysis of protocol-specified tests and parameters, when relevant.
- *Radiation therapy:* Submission of appropriate materials to allow review (either concurrent or retrospective) of port films and compliance with protocol-specified radiation doses for individual patients, when relevant.
- *Chemotherapy & Other Systemic Therapies:* Submission of appropriate data to allow determination of protocol compliance with chemotherapy or other systemic therapy dose administration and dosage modification.
- *Surgery:* Submission of appropriate information to allow review of protocol-specified surgical procedures.
- *Diagnostic Imaging:* Submission of appropriate imaging data [images and associated meta-data (clinical or technical) as appropriate] to allow central review of staging, reported responses, and adequacy of imaging when required by a particular protocol or for an audit.
- *Cancer Care Delivery*: Submission of appropriate data to allow determination of protocol compliance, including data from clinicians and organizations.
- *Onsite Auditing:* Cooperation with Research Bases' data monitoring and onsite auditing programs with appropriate compliance with the onsite auditing program requirements. For clinical trials, see Quality Assurance and On Site Auditing (Part 1.IV.C.Section 1.8) for information on the procedures that should be followed in the event that any data irregularities are identified through the audit program or other quality control procedures.

2.3 Site Responsibilities

The following NCI/DCP policy applies. Community Sites are responsible for accrual to all clinical trial studies conducted across NCORP and its primary affiliates and sub-affiliates, and for achieving threshold accruals. Investigators at the Community Sites should be involved in the acquisition of protocol-specified tumor specimens and other biospecimens in addition to all relevant protocol required clinical data. Community Site investigators should ensure that biospecimens and/or other data required for ancillary studies are submitted to the appropriate laboratories/tumor banks and Research Base SDMCs.

Community Sites are responsible for assuring that institutional investigators enrolling patients on NCORP studies are NCI registered investigators (i.e., completed NCI Registration and Credentialing Repository (RCR) processes) and that they meet Federal and local regulatory guidelines. For all drug studies, investigators must have prescriptive authority that is in compliance with local or state regulations. Community Sites also must ensure that the main institution, as well as any primary affiliates and sub-affiliates, are in compliance with NCI/DCTD/CTEP requirements for storage and accounting for investigational agents, including complying with NCI/DHHS Drug Accountability Records (DAR) procedures as described in the DCTD Investigators' Handbook at: https://ctep.cancer.gov/investigatorResources/investigators_handbook.htm and the NCI Guidelines for Auditing Clinical Trials at: https://ctep.cancer.gov/branches/ctmb/clinicalTrials/monitoring_coop_ccop_ctsu.htm and are in compliance with FDA requirements for investigational agents.

2.4 Compliance with Federal Regulations for Research

Community Site awardee(s) including the primary affiliates and sub-affiliates should have policies and procedures for ensuring compliance with federal regulations for the protection of human subjects. These include the following:

- Assuring that all primary affiliate(s) and sub-affiliate(s) have current, approved Federal Wide Assurances (FWAs) on file with OHRP and verifiable on the OHRP website: http://ohrp.cit.nih.gov/search/search.aspx?styp=bsc;

- Assuring that each protocol is reviewed by the NCI CIRB prior to participant entry (or, where applicable, by the local site IRB) and that each protocol is reviewed annually by the appropriate IRB as long as the protocol is active;

- Assuring that each participant (or legal representative) gives written informed consent prior to entry on study;

- Where relevant, assuring that all regulatory documents verifying the FWA assurance and initial and annual IRB approval of protocols as well as IRB approval of required amendments are submitted to the Regulatory Support System (RSS) of the NCI Cancer Trials Support Unit (CTSU) for NCORP trials;

- Assuring that all investigators comply with procedures for assuring timely reporting of adverse events, including all expedited reporting of all serious adverse events, per the protocol documents of NCORP studies in which the sites participate.

2.4.1 Inclusion of Women, Minorities, and Children in Clinical Research

NIH policy requires that women and members of minority groups and ethnic subgroups be included in all NIH-supported research projects involving human subjects at:
https://grants.nih.gov/grants/funding/women_min/women_min.htm.

Community Sites should ensure that it will provide the appropriate demographic data to the applicable NCORP Research Base for any NCORP study patient enrollment in which it participates per the protocol so that the Research Base SDMCs can meet this NIH policy.

NIH policy requires that children (i.e., individuals under 21 years of age) must be included in all human subjects research, conducted or supported by the NIH, unless there are clear and compelling reasons not to include them as described at: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-010.html.

2.4.2 Resource Sharing Plans

Generally, Resource Sharing Plans (Data Sharing Plan, Sharing Model Organisms if applicable, and GWAS Sharing Plan) are required for all key components of NCORP. However, since it is expected that all data on patients enrolled on NCORP studies by the Community Site will be transmitted to the appropriate Research Base SDMCs, the Resource Sharing Plans of those Research Bases will be applied to the patient data from the Community Sites.

2.4.3 Education on the Protection of Human Subjects and Good Clinical Practice

NIH policy requires education on the protection of human subject for all investigators submitting NIH applications for research involving human subjects and individuals designated as key personnel. This policy is available on the NIH website at: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html.

NIH policy also requires all NIH-funded investigators and staff who are involved in the conduct, oversight, or management of clinical trials to be trained in Good Clinical Practice (GCP), consistent with the principles of the International Conference on Harmonisation (ICH) E6 (R2) (http://www.fda.gov/downloads/Drugs/.../Guidances/ucm073122.pdf). The NIH policy is available at: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-148.html .

2.4.4 Other Federal Regulations

The NIH Public Access Policy ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central *upon acceptance for publication*. To help advance science and improve human health, the Policy requires that these papers are accessible to

the public on PubMed Central no later than 12 months after publication. More information about this policy or the submission process is available on the NIH Public Access Policy website at: http://publicaccess.nih.gov/.

Information on other federal regulations (and their associated citations/URLs) that may be applicable to the Community Site's activities is provided in Part 5: Appendices.

2.5 Conflict of Interest Policy

Community Sites receiving NIH funding from a grant or cooperative agreement must be in compliance with all of the DHSS regulatory requirements for conflict of interest as outlined by NIH grants policy available at: http://grants.nih.gov/grants/policy/coi. Community Sites must also comply with the Conflict of Interest Policy of the applicable Research Base leading an NCORP study in which the site participates. These policies should ensure that there is no reasonable expectation that any investigator or staff member of the Community Site involved in the design, conduct, or reporting of research will be biased by any conflict of interest (using the definition of investigator provided in the NIH grants policy). A management plan is also required for situations in which Conflicts of Interest are identified.

3. Specific Awardee Rights & Responsibilities – NCORP Minority/Underserved Community Sites

These rights and responsibilities apply to cancer control, prevention, and care delivery research studies except as specifically noted.

Each NCORP Minority/Underserved Community Site is under the leadership of the Site PD(s)/PI(s). The Multiple Principal Investigator (PD/PI) option is encouraged given the team science approach of the research effort. Information on the Multiple PDs/PIs option is available at http://grants.nih.gov/grants/multi_pi/index.htm. If the Multiple PI option is used, the NCORP Minority/Underserved Community Site should designate a "Contact PD/PI" among the multiple PIs.

See RFA for the PD/PI (or Contact PD/PI under the Multiple PI option) responsibilities.

3.1 Definition, Eligibility, and Accrual Threshold

See RFA for additional information

3.1.1 Definition of an NCORP Minority/Underserved Community Site

See RFA for additional information

Definition of racial/ethnic minorities or rural populations
See RFA for additional information

3.1.2 Annual Accrual Threshold

See RFA for additional information

3.2 Overall Responsibilities for Minority/Underserved Community Sites

3.2.1 Scientific Leadership & Contribution to NCORP Activities

Investigators at NCORP Minority/Underserved Community Sites should demonstrate scientific leadership for NCORP studies as well as support of and participation in other NCORP activities in a variety of way through their membership in the Research Bases, including but not limited to the following:

- Offering eligible participants participation in NCORP studies and entering sufficient participants to meet accrual targets;
- Participating in research design and protocol development for NCORP studies, including collaborations between Research Bases and other NCI-supported programs and investigators, particularly at their institution;
- Co-authorship on Research Base publications;
- Participating in the Scientific and Administrative Committees of the Research Bases;
- Participating in major meetings of the Research Bases and in other meetings deemed necessary for performance of the activities of NCORP;
- Participating in NCORP activities and initiatives such as the NCI Scientific Steering Committees and associated Task Forces and Working Groups and their activities such as NCI Clinical Trials or cancer care delivery research planning meetings;
- Participating as members on the pediatric and adult NCI Central IRBs;

- Mentoring non-minority and underserved community sites within NCORP regarding community outreach, accrual of minority/underserved populations to studies;
- Providing secondary data on patients, providers or organizations from sources such as registries, electronic medical records, other clinical or administrative databases in NCORP studies and providing sufficient data to meet the sample requirements;
- Providing data on program characteristics, patterns and organizational policies of care to the affiliated Research Base;
- Participate in any program evaluation processes that are conducted including interacting with NCI representatives in coordinating the evaluation.

3.2.2 Young Investigator and Leadership Mentoring/Training

Each NCORP Minority/Underserved Community Site should provide a mentorship program or activities to involve young investigators from diverse populations and across interdisciplinary backgrounds at their institution in cancer control, prevention and care delivery research studies to help train them eventually take on senior leadership responsibilities for components of research at the institution.

3.2.3 Operational Management (Governance/Organization, Institutional Support, Components)

Governance & Organizational Structure: Each NCORP Minority/Underserved Community Site is under the leadership of the Site Principal Investigator(s) or Contact Principal Investigator under the Multiple PI option.

The Minority/Underserved Community Site is responsible for development and maintenance of a governance and organizational structure to coordinate NCORP activities at the institution. The organizational structure of the Minority/Underserved Community Site should be established with clear and appropriate staff roles and reporting responsibilities, especially with respect to the role and reporting responsibilities of any multiple PIs.

NCORP Minority/Underserved Community Sites will be expected to have at least one Affiliate, preferably more, participate in cancer care delivery Landscape Assessments as offered.

NCORP Minority/Underserved Community Sites are to provide documentation of where actual research activities are being conducted across their program sites. Sites that are engaged in research (i.e., consenting, enrolling and treating) must have a CTEP Site ID, be covered under an FWA (confirmed on the OHRP website), are to be rostered as a primary affiliate or sub-affiliate site within NCORP-SYS, and after DCP approves, any associated accrual must be credited to that site. RT facilities or chemotherapy treatment centers/sites providing treatment only (not consenting/enrolling patients) or are located within a hospital campus (e.g., departments, clinics, offices) that are owned and operated by the hospital and are covered under the hospital FWA do not need a separate site code or an FWA and therefore do not need to be rostered. However, RT facilities or chemotherapy treatment centers/sites that are consenting and treating patients and are not owned and managed by another institution (i.e., independent business entities) do require a site code, an FWA, and will need to be rostered. Research sites that are located

within a hospital campus (e.g., clinics, offices) that are not owned and operated by the hospital (i.e., independent business entities) and are not covered under the hospital FWA will require a separate site code and FWA and do need to be rostered.

Primary Affiliate & Sub-Affiliate Network: If the Minority/Underserved Community Site has primary affiliate(s) and sub-affiliate(s), the network must be clearly described (including reference to the distinct CTEP institution code(s) for the primary affiliate(s) and sub-affiliate(s) that are used for patient enrollment). The Minority/Underserved Community Site is responsible for complete monitoring and management of the enrollment of patients at the primary affiliate and sub-affiliate site(s) to NCORP and NCTN clinical trials and cancer care delivery research studies if they are included in the award. The primary affiliate site(s) participating in cancer care delivery research must be clearly identified. Any post-award changes to primary affiliate or sub-affiliate sites will need to be approved by NCI per the Organizational Change Guidelines located in Part 4 of these guidelines.

Institution(s)/site(s) with the following NCTN Network Group membership status may not be included as a primary affiliate /sub-affiliate site of a NCORP Minority/Underserved Community Site unless the membership status is relinquished:

- NCTN Lead academic participating site (LAP) (academic center and its integrated components)
- Affiliates or sub-affiliates included in a LAP cooperative agreement award
- Other Network Group main member, affiliate sites, or non-affiliated sites
- Primary affiliate/sub-affiliate of another NCORP grant (Community or Minority/Underserved).

3.2.4 Use of the NCI Central Institutional Review Board

The NIH Policy on the Use of a Single Institutional Review Board for Multi-Site Research (NOT-OD-17-076) became effective on January 25, 2018. In compliance with this policy, the NCI Central IRB (NCI CIRB) is the sole IRB of record for all sites conducting clinical trials through the NCORP and NCTN networks and is responsible for study review (initial review, amendments, continuing reviews, recruitment materials, unanticipated problems and serious or continuing noncompliance) and approval of local context considerations.

To comply with the NIH policy:

- All NCORP sites must be enrolled in the CIRB as of the date of their award.
- All new NCORP protocols will be opened under the CIRB.
- All CIRB-enrolled sites must open all new studies under the CIRB.
- Patients on CIRB-approved protocols who are followed by local IRBs must be transferred to the CIRB within a timeframe to be specified in the new NCTN and NCORP grants (12-18 months). This transfer is initiated by the local site via the filing of a Study Specific Worksheet through the CIRB Local Context Review Process.
- Legacy NCORP protocols (e.g. CCOP studies opened before 2/1/2015 and CCDR studies opened before 6/1/2016) currently conducted under the oversight of local IRBs will complete accrual and follow-up under their existing IRB arrangements. NCI anticipates that most of these

trials will be completed before the Common Rule compliance date of January 20, 2020.

All NCORP sites with comply with the conditions of their Federal-Wide Agreement (FWA) and the CIRB Standard Operating Procedures.

3.2.5 Study Operations and Data Management

The Minority/Underserved Community Sites should have a clearly articulated process for prioritizing which NCORP protocols to activate at their institutions. Investigators at Minority/Underserved Community Sites form the cornerstone of the research programs for NCORP and must perform at a high level through submission of accurate and timely clinical data as well as ancillary materials necessary to support NCORP (e.g., tumor specimens, imaging studies, pathology slides). The Principal Investigator(s) at each Minority/Underserved Community Site is responsible for the performance of the academic center and its primary affiliates as well as of any sub-affiliates for which it provides oversight related to research activities and for assuring adherence to NCORP, NCI, OHRP, and FDA policies and procedures.

It is the responsibility of the Principal Investigator(s) at the site to ensure that the procedures for data submission for each NCORP protocol are understood by all investigators at the academic center and its primary affiliates as well as at any sub-affiliates, and that protocol-specified data are submitted accurately and in a timely manner to the appropriate NCORP Research Base.

3.2.6 Quality Assurance and Onsite Auditing

Responsibilities for quality assurance of the data submitted for NCORP studies as well as auditing include, but are not limited to, the following:

- *Pathology:* Submission of appropriate materials to allow verification of pathologic diagnosis, when relevant.
- *Biospecimens (including integral assays, -omics, Pharmacokinetics, Pharmacodynamics):* Submission of appropriate biospecimens to allow for review/analysis of protocol-specified tests and parameters, when relevant.
- *Radiation therapy:* Submission of appropriate materials to allow review (either concurrent or retrospective) of port films and compliance with protocol-specified radiation doses for individual patients.
- *Chemotherapy & Other Systemic Therapies:* Submission of appropriate data to allow determination of protocol compliance with chemotherapy or other systemic therapy dose administration and dosage modification.
- *Surgery:* Submission of appropriate information to allow review of protocol-specified surgical procedures.
- *Diagnostic Imaging:* Submission of appropriate imaging data [images and associated meta-data (clinical or technical) as appropriate] to allow central review of staging, reported responses, and adequacy of imaging when required by a particular protocol or for an audit.
- *Cancer Care Delivery*: Submission of appropriate data to allow determination of protocol compliance, including data from clinicians and organizations.
- *Onsite Auditing:* Cooperation with Research Bases' data monitoring and onsite auditing programs with appropriate compliance with the onsite auditing program requirements. See Quality Assurance and On Site Auditing (Part1.IV.C.Section 1.8) for information on the procedures that should be

followed in the event that any data irregularities are identified through the audit program or other quality control procedures.

3.3 Site Responsibilities

Minority/Underserved Community Sites are responsible for accrual to clinical trials conducted across NCORP from its primary affiliates and its sub-affiliates, and for achieving threshold accruals. Investigators at the Minority/Underserved Community Sites should be involved in the acquisition of protocol-specified tumor specimens and other biospecimens in addition to all relevant protocol required clinical data. Minority/Underserved Community Site investigators should ensure that biospecimens and/or other data required for ancillary studies are submitted to the appropriate laboratories/tumor banks and Research Base SDMCs.

Minority/Underserved Community Sites are responsible for assuring that institutional investigators enrolling patients on NCORP clinical trials are NCI registered investigators (i.e., completed NCI Registration and Credentialing Repository (RCR) processes) and that they meet Federal and local regulatory guidelines. For all drug studies, investigators must have prescriptive authority that is in compliance with local or state regulations. Minority/Underserved Community Sites also must ensure that the main institution, as well as any primary affiliates and sub-affiliates, are in compliance with NCI/DCTD/CTEP requirements for storage and accounting for investigational agents, including complying with NCI/DHHS Drug Accountability Records (DAR) procedures as described in the DCTD Investigators' Handbook at: https://ctep.cancer.gov/investigatorResources/investigators_handbook.htm and the NCI Guidelines for Auditing Clinical Trials at: https://ctep.cancer.gov/branches/ctmb/clinicalTrials/monitoring_coop_ccop_ctsu.htm and are in compliance with FDA requirements for investigational agents.

3.4 Compliance with Federal Regulations for Research

Minority/Underserved Community Site awardee(s) should have policies and procedures for ensuring compliance by the main academic center and its primary affiliates (and any sub-affiliates completely managed by the main academic institution/site) for meeting federal regulations for the protection of human subjects. These include the following:

- Assuring that all primary affiliate(s) and sub-affiliates(s) have current, approved Federal Wide Assurances (FWAs) on file with OHRP and verifiable on the OHRP website: http://ohrp.cit.nih.gov/search/search.aspx?styp=bsc;

- Assuring that each protocol is reviewed by the NCI CIRB prior to participant entry (or, where applicable, by the local site IRB) and that each protocol is reviewed annually by the appropriate IRB as long as the protocol is active;

- Assuring that each participant (or legal representative) gives written informed consent prior to entry on study;

- Where relevant, assuring that all regulatory documents verifying the FWA assurance and initial and annual IRB approval of protocols as well as IRB approval of required amendments are submitted to the Regulatory Support System (RSS) of the NCI Cancer Trials Support Unit (CTSU) for NCORP trials;

- Assuring that all investigators comply with procedures for assuring timely reporting of adverse events, including all expedited reporting of all serious adverse events, per the protocol documents of NCORP studies in which the sites participate.

3.4.1 Inclusion of Women, Minorities, and Children in Clinical Research

NIH policy requires that women and members of minority groups and ethnic subgroups be included in all NIH-supported research projects involving human subjects at: https://grants.nih.gov/grants/funding/women_min/women_min.htm.

Minority/Underserved Community Sites should ensure that it will provide the appropriate demographic data to the applicable NCORP Research Base for any NCORP study patient enrollment in which it participates per the protocol so that the Research Base SDMCs can meet this NIH policy.

NIH policy requires that children (i.e., individuals under 21 years of age) must be included in all human subjects research, conducted or supported by the NIH, unless there are clear and compelling reasons not to include them as described at: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-010.html.

3.4.2 Resource Sharing Plans

Generally, Resource Sharing Plans (Data Sharing Plan, Sharing Model Organisms if applicable, and GWAS Sharing Plan) are required for all key components of NCORP. However, since it is expected that all data on patients enrolled on NCORP studies by the Minority/Underserved Community Site will be transmitted to the appropriate Research Base SDMCs, the Resource Sharing Plans of those Research Bases will be applied to the patient data from the Minority/Underserved Community Sites.

3.4.3 Education on the Protection of Human Subjects and Good Clinical Practice

NIH policy requires education on the protection of human subject for all investigators submitting NIH applications for research involving human subjects and individuals designated as key personnel. This policy is available on the NIH website at: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html.

NIH policy also requires all NIH-funded investigators and staff who are involved in the conduct, oversight, or management of clinical trials to be trained in Good Clinical Practice (GCP), consistent with the principles of the International Conference on Harmonisation (ICH) E6 (R2) (http://www.fda.gov/downloads/Drugs/.../Guidances/ucm073122.pdf). The NIH policy is available at: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-148.html .

3.4.4 Other Federal Regulations

The NIH Public Access Policy ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central *upon acceptance for publication*. To help advance science and improve human health, the Policy requires that these papers are accessible to the public on PubMed Central no later than 12 months after publication. More information about this policy

or the submission process is available on the NIH Public Access Policy website at: http://publicaccess.nih.gov/.

Information on other federal regulations (and their associated citations/URLs) that may be applicable to the Minority/Underserved Community Site's activities is provided in Part 5: Appendices.

3.5 Conflict of Interest Policy

Minority/Underserved Community Sites receiving NIH funding from a grant or cooperative agreement must be in compliance with all of the DHSS regulatory requirements for conflict of interest as outlined by NIH grants policy available at: http://grants.nih.gov/grants/policy/coi. Minority/Underserved Community Sites must also comply with the Conflict of Interest Policy of the applicable Research Base leading an NCORP study in which the site participates. These policies should ensure that there is no reasonable expectation that any investigator or staff member of the Minority/Underserved Community Site involved in the design, conduct, or reporting of research will be biased by any conflict of interest (using the definition of investigator provided in the NIH grants policy). A management plan is also required for situations in which Conflicts of Interest are identified.

C. NCI/DCP and DCCPS Staff Responsibilities

1. NCI responsibilities related to research efforts of NCORP Research Bases

See RFA for additional information

1.1 Coordination of National Priorities

NCI/DCP staff is responsible for maintaining a clear set of national priorities for cancer prevention, control and screening/post-treatment surveillance research, based upon substantial consultation with experts in the field. In selected topic areas DCP and DCCPS staff (with support from the Coordinating Center for Clinical Trials [CCCT]) will help in coordinating the organization of Study Planning Meetings under the auspices of the NCI Scientific Steering Committees (SCCs). In addition, DCP and DCCPS staff may support ad hoc scientific meetings to help achieve consensus on critical research problems. These Study Planning meetings and ad hoc meetings will be composed of investigators with established expertise in the particular field of interest and will consist primarily of extramural scientists and members of the SSCs. Priorities will be based upon the state of the science, NCORP Research Base resources, and availability of funds. NCI staff will be responsible for prompt dissemination of the recommendations from these meetings, particularly regarding statements of research priorities from Study Planning meetings, and the Research Bases will be encouraged to address these priorities.

1.2 Scientific Resource for NCORP Research

The NCORP Director and Chief, COPTRG, DCP, the NCORP CCDR Scientific Lead; and DCP and DCCPS Program Directors all serve as resources available to NCORP Research Bases for specific scientific information with respect to cancer control, prevention, and care delivery studies and their design. The NCI/DCP staff also work closely with the NCI/DCTD staff to ensure there is a high level of integration of complementary research efforts on specific trials across the larger NCTN.

The DCP and DCCPS staff listed above will assist NCORP Research Bases as appropriate, in developing information concerning the scientific basis for specific trials or alternative study designs, operational and regulatory issues, and will also be responsible for advising the Research Bases of the nature and results of relevant trials and other studies being carried out nationally or internationally. Where applicable, DCP/COPTRG staff will also provide updated information to the Research Bases on the efficacy, toxicity, and availability of all Investigational New Drugs (IND) supplied by NCI to the Research Bases. In addition, DCP staff advises the Research Bases of potential agents/interventions that will be relevant to new avenues of cancer prevention, control and screening/post-treatment surveillance. In addition, DCCPS/HDRP will provide updated information to compliment research initiatives and projects as part of other NCI research cancer care delivery projects that may be relevant to NCORP research priorities and concept development.

1.3 Scientific and Administrative Program Directors Activities

The NCORP Director is the NIH/NCI Program Official responsible for the routine scientific and programmatic stewardship of all the awards for NCORP and will be named in the award notice. The NCORP CCDR Scientific Lead will be responsible for the routine scientific and programmatic stewardship of the cancer care delivery research components.

Each NCORP Research Base will also have a staff physician, nurse, and/or other professional staff member from DCP/COPTRG assigned to them who acts as liaison for scientific and administrative matters related to clinical trials and clinical research studies. The DCP/COPTRG Program Director serves as the primary contact for scientific inquiries, including information concerning the content of specific protocols or concept reviews, and feedback on general scientific direction of NCORP Research Base. On occasion, the NCORP Director may also serve as Program Director.

Each NCORP Research Base also will have a medical officer, nurse and/or program staff member from DCCPS to act as liaisons for scientific and administrative matters related to cancer care delivery research studies. The DCCPS/HDRP Program Director serves as the primary contact for scientific inquiries, including information concerning the content of specific protocols or concept reviews, and feedback on general scientific direction of NCORP Research Base. On occasion, the CCDR Scientific Lead may also serve as Program Director.

The Program Director monitors the Research Base's progress, attends their meetings, and is responsible for understanding the Research Base's repertoire of studies and scientific activities, including areas of special interest, expertise, and unique resources.

1.4 Attendance at Meetings of NCORP Research Base

NCI/DCP and NCI/DCCPS Program Directors and other NCI staff, as designated by the NCORP Director and/or CCDR Scientific Lead, will attend the regular Research Base meetings and core scientific Research Base meetings, as appropriate. As part of their responsibilities, Program Directors, when available, will attend other Research Base scientific meetings and may also attend Research Base Executive Committee meetings, in addition to the applicable committee meetings.

NCI/DCP and DCCPS staff will be closely involved in the development of NCORP studies. NCI/DCP and DCCPS staff will communicate with NCORP Research Bases during all stages of study development. All concepts for cancer prevention, control, and care delivery studies must be submitted to the NCI DCP Protocol Information Office (PIO) at: **NCI_DCP_PIO@mail.nih.gov**. A detailed description of the NCI responsibilities and roles during concept, protocol and amendment development, review and approval of cancer prevention and control and cancer care delivery research studies is contained within Part 3 of these guidelines.

1.5 Data and Safety Monitoring Boards (Data Monitoring Committees)

The NCORP Director will designate Program Directors to serve as cancer prevention and control liaisons on Data and Safety Monitoring Boards (DSMBs), also known as Data Monitoring Committees (DMCs), for NCORP phase 3 trials as well as phase 2/3 and any other phase 2 trials monitored by the DSMB/DMC. One or more DCP/COPTRG staff will serve as non-voting members at each Research Base DSMB/DMC meeting. The CCDR Medical Officer/Program Director will serve as the cancer care delivery research liaison on Data and Safety Monitoring Boards (DSMBs) for care delivery studies. The Program Directors will review Research Base mechanisms for interim monitoring of results, will monitor clinical trial progress, and will assess Research Base compliance with NCI-established policies on Data and Safety Monitoring Plans for Phase I and II trials and Data and Safety Monitoring

Committees for Phase III trials. NCORP Research Base DSMBs/DMCs must comply with all NCI membership and operational policies as established through the NCTN guidelines (available at: http://ctep.cancer.gov/initiativesPrograms/docs/NCTN_Program_Guidelines.pdf)

Because NCI/DCP and DCCPS staff serve as non-voting members of the Research Base DSMBs/DMCs, to ensure compliance with NIH/NCI policies and protocol requirements, NCI/DCP staff members recuse themselves from NCI NCORP review of substantive protocol amendments (e.g., amendments for increases in sample size or significant changes in trial design) for any study that is also under review by a DSMB/DMC of which they are members, if confidential outcome data on that study have been previously presented to the DSMB/DMC. When this situation arises, the amendment is reviewed by NCI NCORP staff members who are not members of that DSMB/DMC.

1.6 Coordination of Resources to Enhance Accrual/Completion of NCORP Studies

DCP/COPTRG and DCCPS/HDRP staff will take an active role in promoting the timely completion of studies, for example, by encouraging and facilitating collaboration among the Research Bases and collaborations with other NCI-supported programs and investigators when appropriate or by assisting in the mobilization of other available and required resources to enhance accrual to and/or completion of NCORP trials and other studies.

1.7 Study/Trial Closure

NCI/DCP may request that a phase 1 or phase 2 study be closed to accrual for reasons including the following: (1) insufficient accrual rate; (2) poor protocol performance; (3) protection of patient safety; (4) study results are already conclusive; (5) emergence of new information that diminishes the scientific importance of the study question; and (6) unavailability of study agent. NCI will not provide investigational agents or permit expenditures of NCI funds for a phase 1 or phase 2 study after requesting closure (except for patients on treatment and follow-up).

NCI/DCCPS may request that a cancer care delivery research study be closed to accrual for reasons including but not limited to the following: (1) insufficient accrual of study participants; (2) poor protocol performance; (3) protection of participants; (4) study results are already conclusive; (5) emergence of new information that diminishes the scientific importance of the study question; and (6) poor quality of critical data necessary to complete the study.

1.7.1 Early Stopping Rules for Slowly-Accruing Studies

Implementation (not applicable to screening, over diagnosis and post treatment surveillance trials): Protocols submitted to DCP/PIO for review must include an estimate of planned accrual rate. Statistical guidelines for early closure should be presented in sufficient detail in the protocol in order to facilitate decisions regarding early closure. The NCORP Protocol Review Committee will review this estimate with regard to how realistic the estimate is and the relevance of study results at the end of the planned accrual time.

For studies that are closed or amended, the Research Base will notify the Group Data and Safety Monitoring Board (DSMB) of the closure or amendment at their next regularly scheduled meeting. Research Base chairs may consult with their DSMB regarding the decision for early closure, if desired. In the unusual circumstance that the Research Base Chair believes that the study closure for a given study is inappropriate, he or she will initiate a discussion with the responsible NCI Program Director to reach a joint decision concerning what course to take.

1.8 Quality Assurance and Onsite Auditing

1.8.1 Control, Prevention, Treatment and Care Delivery Clinical Research Studies

NCI/NCORP Program Directors will review quality control and monitoring procedures of the Research Bases including the on-site auditing program, and may attend on-site audits conducted by the Research Base or its NCI designee.

The Clinical Trials Monitoring Branch (CTMB) is responsible for establishing guidance for the conduct of quality assurance audits. CTMB provides oversight and monitors compliance of the Network Groups, NCORP Research Bases, and CTSU with the NCI's monitoring guidelines. Compliance with applicable federal regulations is also monitored by CTMB.

In addition, CTMB staff serves as an educational resource to the cancer research community on issues related to monitoring and regulatory requirements for the conduct of clinical trials. CTMB staff review audit reports and findings and assess the adequacy and acceptability of any corrective actions. To assure consistency in the conduct of onsite audits, CTMB staff or its designee(s) may attend certain onsite audits.

The CTMB has developed the CTMB Audit Information System (AIS) which permits the on-line submission by the Research Bases of all data related to quality assurance onsite audits. This includes the submission of audit schedules, acknowledgment of receipt of preliminary reports, transmission of final audit reports, and tracking of follow-up responses to audit findings. The system allows restricted access to the stored data and keeps a record of any data changes. The CTMB AIS can be accessed only after providing a username and password. A major component of the CTMB AIS is a module that maintains a roster of all its member sites in each Research Base. This roster information is used for determining compliance with monitoring requirements.

Each NCORP Research Base is responsible for ensuring that all member sites have routine audits in accordance with the NCI-CTMB Guidelines for Monitoring of Clinical Trials for Cooperative Groups, NCORP Research Bases, and the Cancer Trials Support Unit (CTSU) at: http://ctep.cancer.gov/branches/ctmb/clinicalTrials/monitoring_coop_ccop_ctsu.htm and that the results of audits are reported to the NCI in accordance with the guidelines. In the event that the NCI/CTMB determines that a Research Base member fails to comply with these guidelines, the CTMB may, in consultation with the Research Base, the NCORP Director, applicable NCORP Program staff and Office of Grants Administration, suspend the member institution/site immediately from participating in any NCORP trials led by the Research Base or all NCORP trials

regardless of the Research Base leading the study. The suspension will remain in effect until the Research Base conducts the required audit and the audit report or remedial action is accepted by the Research Base and the NCI.

Each NCORP Research Base will be responsible for notifying any affected member site of the suspension. During the suspension period, no funds from this award may be provided to the member site for new accruals, and no charges to the award for new accruals will be permitted.

The CTMB staff will review and provide advice regarding mechanisms established by the Research Base and its associated Research Base SDMC for quality control of therapeutic and diagnostic modalities employed in its trials. The CTMB staff reviews and approves the mechanisms established by the Research Base and its associated Research Base SDMC for study monitoring including its onsite auditing program. NCI/DCP and NCI/CTEP and/or its contractor staff may attend, as observers, the onsite audits conducted by NCORP Research Base. The frequency of participation by an NCI representative as observer will be determined by the NCI.

Any data irregularities identified through quality control procedures or through the audit program that raise any suspicion of intentional misrepresentation of data must be immediately reported to NCI CTMB, the NCORP Director, applicable NCORP Program staff and Office of Grants Administration. The CTMB must be notified immediately by telephone [240-276-6545] of any findings suspicious and/or suggestive of intentional misrepresentation of data and or disregard for regulatory safeguards for any of the three (regulatory, pharmacy, and patient care) components of an audit. Similarly, any data irregularities identified through other quality control procedures suspicious and/or suggestive of intentional misrepresentation of data must be immediately reported to CTMB. It is the responsibility of NCORP Research Base, or CTSU to immediately notify CTMB when they learn of any significant irregularities or allegations related to scientific misconduct by a staff member or institution participating in NCORP clinical trials. It should be emphasized that the irregularity/misrepresentation does not need to be proven, a reasonable level of suspicion suffices for CTEP CTMB notification. It is also essential that involved individual(s) and/or institutions follow their own institutional misconduct procedures in these matters.

1.9 Data Management and Analysis Review & Use of Standard NCORP Tools and Services

At the request of DCP/COPTRG, DCCPS/HDRP or CTEP, the Biometric Research Branch (BRB) staff, in consultation with other NCI/DCTD staff, will review mechanisms established by the Research Base for data management and analysis. When deemed appropriate, COPTRG or HDRP staff will make recommendations to ensure that data collection and management procedures are adequate for quality control and analysis, yet sufficiently simple to encourage maximum participation on NCORP studies and to avoid unnecessary expense. In addition, the NCI will have access to all Research Base data although the data remain the property of the awardee institution under the Cooperative Agreement. Data must also be available for external monitoring as required by NCI's agreement with the FDA relative to the NCI's responsibility as agent sponsor.

During the approval process for clinical trials and cancer care delivery research study protocols and amendments, NCI/DCCPS ensures that standard NCTN tools and services are used when applicable. To the extent that common data elements and tools are developed and adopted for cancer care delivery, efforts will be made to ensure compliance using standard tools. In addition, NCORP Research Base trial protocols will be periodically audited by NCI/DCP, DCCPS and DCTD to ensure that the tools related to common data elements are in compliance with the NCTN Program data dictionary for common data elements in caDSR. If issues with compliance are identified, the NCI/DCP and NCI/DCCPS will work with the Research Base to develop a corrective action plan.

1.10 Program Review, Strategy Sessions, and Federally Mandated Requirements

The NCORP Research Base will provide an annual progress report and other reports as needed. DCP/COPTRG and/or DCCPS/HDRP Program Directors may perform annual visits as well as periodic site visits as part of the program assessment process. Quarterly accrual reports by clinical trial or other study type will also be assessed. DCP/COPTRG and/or DCCPS/HDRP Program Directors, and DCTD staff, will also review mechanisms established by each Research Base to meet the Department of Health and Human Services (DHHS)/Public Health Service (PHS) regulations for the protection of human subjects and FDA requirements for the conduct of research using investigational agents. Each NCORP Research Base will be evaluated on its progress in designing, developing, implementing, and completing cancer prevention, control and care delivery studies.

Funding for each NCORP Research Base will be adjusted annually based upon the planned scope of work and availability of funds.

NCI Program Directors will sponsor strategy sessions when indicated.

2. NCI Responsibilities Related to NCORP Community Sites and Minority/Underserved Community Sites

See RFA for additional information

2.1 Scientific and Administrative Program Directors & Activities

The NCORP Director is the NIH/NCI Program Official responsible for the routine scientific and programmatic stewardship of all the awards for NCORP and will be named in the award notice. The NCORP CCDR Scientific Lead will be responsible for the cancer care delivery research components of NCORP.

Each NCORP Community Site will have a staff physician, nurse, and/or other professional staff member from DCP/COPTRG or DCCPS/HDRP assigned to them as Program Director for scientific and administrative matters. The Program Director monitors the Community Site's progress, and is responsible for understanding the Community Site's repertoire of selected studies and scientific activities, including areas of special interest, expertise, and unique resources.

The Program Director is also responsible for providing the NCORP Director and CCDR Scientific Lead with ongoing assessments of the key component's activity from a scientific and administrative perspective, including general information on its budget. Primary responsibility for the budgets of NCORP Community Sites, however, resides with the NCORP Director who is assisted by the DCP/COPTRG Senior Program Specialist.

The DCP/COPTRG Senior Program Specialist may be delegated by the NCORP Director to request and receive budgetary and administrative materials from the Community Sites on either an ad hoc or routine basis. The DCP/COPTRG Senior Program Specialist will frequently perform liaison activities concerning budgetary and administrative matters on behalf of the responsible NCI Program Director, interfacing primarily with the primary Administrators for the Community Sites.

2.2 Review of Clinical Trials and Other Studies in NCORP Network for Crediting

All clinical trials and other study designs originating at NCORP Research Bases must be reviewed and approved by the Protocol Review Committee of the Division of Cancer Prevention (DCP) or Division of Cancer Treatment and Diagnosis (DCTD), as appropriate, in order for an NCORP Community Site to receive credit for participant accruals to such studies.

2.3 On-Site Auditing

The NCI/DCP and NCI/DCCPS Program Directors or other NCI-designated entity may conduct periodic on-site audits of NCORP Community Sites. NCI/DCP, NCI/DCCPS and/or NCI/CTEP/CTMB will review and advise on mechanisms for the on-site auditing program. DCP/CTEP representatives (or a designee) may attend on-site audits of NCORP Community Sites conducted by NCORP Research Bases.

2.4 Data Management and Access

The NCI/DCP and NCI/DCCPS Program Director(s) will have access to all data generated under this award. The Program Director will periodically review the data management procedures of NCORP Community Site.

2.5 Investigational Drug Management

RAB/PMB/CTEP/DCTD and DCP/COPTRG/CADRG will advise investigators of specific requirements and updates in requirements about investigational drug management that the FDA and NCI may mandate.

2.6 NCORP Community or Minority/Underserved Community Site Organizational Changes

In addition to standard NIH procedures for approval of organizational changes, such as changes of the PD(s)/PI(s), the NCI Program staff members will review other organizational change requests and provide a written response. Organizational changes requiring NCI approval are outlined in "Guidelines for Approval of NCORP Organizational Changes," available in Part 4 of these guidelines.

2.7 Program Review and Federally Mandated Requirements

NCI Program Director(s) will conduct the following: 1) An analysis of each NCORP Community Site and Minority/Underserved Community awardee's annual report, with follow-up of noted problems and recommendations for improvement; 2) site visits when required; 3) review of NCORP Research Base evaluations of the affiliated NCORP Community or Minority/Underserved Community Site.

NCI DCP and DCCPS staff members will review mechanisms established by each NCORP Community and Minority/Underserved Community Site awardee to meet the Department of Health and Human Services (DHHS)/Public Health Service (PHS) regulations for the protection of human subjects and FDA requirements for the conduct of research using investigational agents.

NCI/DCP may adjust funding annually based on the planned scope and availability of funding. The NCI may also adjust funding, withhold support, suspend or terminate the award, if NCORP Community or Minority/Underserved Community Site awardee fails to meet the performance requirements set forth in the Terms and Conditions of Award in the FOA, and/or the level of performance changes dramatically.

D. Joint Responsibilities (Key Components NCORP, NCI/DCP and NCI DCCPS)

See RFA for additional information

1. General Study Development and Conduct

Because of the significant resource, regulatory, and general administrative issues involved in NCORP key component activities and to ensure required compliance with other federal regulations and federal agencies, NCORP Research Bases should collaborate closely with NCI/DCP and DCCPS staff. This collaboration should occur early on in the development of studies as well as in the development of general research strategies and new initiatives. In particular, when new avenues of cancer prevention or symptom management involving investigational drugs are pursued, the trial should be designed such that the clinical information obtained should be acceptable to the FDA for inclusion in a potential licensing application. Therefore, the NCI/DCP staff and the Research Base should work collaboratively to develop protocols meeting that standard. When intervention studies have indications for Medicare participation, the Research Base should work collaboratively with the NCI to develop protocols meeting these requirements or pursuing the option to obtain waivers for these requirements. All parties (Research Bases, NCI/DCP staff, and company collaborators) should be involved in any conference calls and/or meeting involving the FDA during the development and conduct of any approved NCORP trial with licensing potential, regardless of whether the study is being conducted under DCP IND or a Research Base IND in order to ensure that all sponsors are involved in discussion regarding the trial.

Both the Research Bases and NCI/DCP and DCCPS share the responsibility to ensure that study proposals are reviewed/evaluated, protocols developed, and trials activated in a timely manner.

Both the Research Bases and NCI/DCP and DCCPS also share the responsibility to collaborate on initiatives to promote accrual to NCORP trials and cancer care delivery research intervention studies.

1.1 Data and Safety Monitoring Boards (Data Monitoring Committees)

The appropriate conduct of NCORP Research Base Data Safety and Monitoring Boards (DSMBs), sometimes called Data Monitoring Committees (DMCs), is a collaborative responsibility of the Research Base (Operations Center and associated Statistics and Data Management Center) and NCI/DCP staff. NCORP Research Bases that are funded NCTN Network Groups may augment the NCTN Network Group DSMBs/DMCs and Data Safety and Monitoring Policy to address the types of clinical trials/studies conducted by the Research Base. The Research Base's Data and Safety Monitoring Policy must be submitted to and approved by the NCORP Director. All relevant DSMB members must be approved by the NCORP Director prior to their inclusion in DSMB meetings. Any changes to the Research Base DMSB policy and/or membership must be reviewed and approved by the NCORP Director prior to implementation. The NCORP Director also names the NCI/DCP staff that represents NCI/DCP as non-voting members on the Research Base's DSMB. If the Research Base DSMB includes oversight of studies funded by the Division of Cancer

Treatment and Diagnosis all changes in membership and policy are also reviewed by the appropriate staff in DCTD as applicable and DCTD also names the non-voting NCI/DCTD staff person to represent the Division on the DSMB.

1.2 Development of Collaborative Trials and International Trials

The following information applies only to NCTN Network Groups that are also funded as NCORP Research Bases. Cancer care delivery research will not be conducted at international sites.

The Clinical Investigations Branch staff at CTEP work with the NCTN Network Groups to facilitate international participation in trials when appropriate. When institutions outside the U.S. are members of a U.S. Network Group and wish to participate in a U.S Group Trial, the institution and its investigators must meet ALL the same Network Group membership requirements as U.S. institutional members and their associated investigators, including being audited by the Network Group per CTMB guidelines for international Participating Sites, filing FDA 1572 Forms, etc. However, when trials call for collaboration with a separate international clinical trial organization for its participation in a U.S. Network Group trial, there are varying degrees of logistical and regulatory complexity involved, depending on a number of factors. In these cases, it is critical that proposals for large-scale international trials be discussed with DCP/COPTRG and CTEP/CIB staff in advance for general advice and guidance regarding whether the advantages of international collaboration will outweigh the expected resource costs.

Network Group Operations Centers are required to have a binding collaborative agreement in place with the international clinical trial organization that addresses the major components of clinical trial conduct by the international organization to ensure that the conduct is consistent with all appropriate federal and other appropriate regulations for the clinical research trial. This agreement must be reviewed and approved by the Lead NCTN Program Director in consultation with the Associate Director of CTEP and the Chief, CTEP Regulatory Affairs Branch, and all appropriate U.S. State Department approvals must be in place for countries that will be participating in the research as well as other appropriate approvals (e.g., company partner approvals for trials being conducted under an NCI/DCTD binding collaborative agreement or CRADA).

With respect to participation of U.S. Network Groups and NCORP Research Bases led by a non-U.S. organization (other than the Canadian Collaborating Clinical Trials Network of the NCTN), there are also numerous logistical, regulatory, and company-sponsor issues that must be addressed in addition to approval of the non-U.S. trial by the NCI via the appropriate NCI Scientific Steering Committee (if applicable).

In addition, the lead U.S. Network Group Operations Center that is the primary or lead sponsor for the trial in the U.S. must have U.S. State Department approvals in place for countries that will be participating in the research even though federal funds will only be used to support the participants from the NCTN/NCORP Program enrolling patients on study. The research agreement between the U.S. Network Group Operations Center that

is the primary or lead sponsor for the trial in the U.S. and the international organization leading the trial that governs the conduct of the study must be reviewed and approved by the Lead NCTN/NCORP Program Director in consultation with NCTN/NCORP senior leadership.

A guidance document from NCI/DCTD/CTEP entitled, *Cooperative Group Guidelines for the Development, Conduct and Analysis of Clinical Trials with International Collaborating Institutions,* is available on the CTEP website at: http://ctep.cancer.gov/branches/ctmb/clinicalTrials/docs/nci_clin_intl_guidelines.pdf#search="international". This document addresses the various regulatory issues involved in the conduct of international trials that involve participation/leadership of Network Groups under the NCTN Program.

2. Network-Wide Common Services, Tools, and Resources

Research Bases are **required** to use standard NCI tools and services for all NCORP studies including, but not limited to: (a) NCTN information system for tracking biospecimen collection from NCTN trials (e.g., OPEN, RAVE, etc.); (b) the NCI Common Terminology Criteria for Adverse Events (CTCAE); and (c) review of all trials by the NCI Central Institutional Review Board (CIRB). NCORP Cancer Center Research Bases are expected to use all the tools and services except for RAVE.

During the approval process for study protocols and amendments, NCI/NCORP staff ensures that standard NCORP tools and services are used. Clinical trial Research Base trial protocols will be periodically audited by NCI/NCORP staff to ensure that the tools related to common data elements in compliance with NCORP approved sections of the data dictionary for common data elements in caDSR are used in the data collection instruments for NCORP trials. If issues with compliance are identified, the NCI/NCORP will work with the Network Research Base to develop a corrective action plan.

It is required that the Cancer Trials Support Unit (CTSU) be utilized for all NCORP trials. NCORP trials using CTSU must also use the NCTN Oncology Patient Enrollment Network (OPEN) and Regulatory Support Services (RSS) for central registration and randomization of patients onto NCORP trials. It is expected that all cancer prevention, screening/post-treatment surveillance and control trials will be available on the CTSU. NCORP Cancer Center Research Bases are expected to use all the tools and services except for RAVE.

V. Budget Levels for Per Case Management Funding & Budget Adjustments for NCORP

The final decision regarding funding for the all NCORP awards, administrative supplements, and amounts selected for all "per case management" funding, including "special per case management" funding and" biospecimen per case management" funding for specific trials, rests with the NCI/DCP and/or DCCPS. NCI/DCP also sets the threshold levels for accrual for "high-performance" sites for NCORP (i.e., Community and Minority/Underserved Community Sites, depending on the availability of funding).

VI. Changes in Principal Investigator(s) for Any Key Component of NCORP

The change of PI must go through the NCI Office of Grants Administration. The final approval of a change of PI comes through a revised Notice of Grant Award. The change becomes official only after the NCI Program Director indicates approval of the new Principal Investigator to the Grants Management Specialist and the Grants Administration Branch prepares a revised Notice of Award indicating the new Principal Investigator. Once approved by OGA NCORP SYS will be updated to reflect the change. An email with updated information should also be sent to ncorp@mail.nih.gov so that the respective NCORP Listservs can be updated. The process for requesting a change of PI is outlined in "Guidelines for Approval of NCORP Organizational Changes," available in Part 4 of these guidelines.

VII. Changes in Awardee Institution for Any Key Component of NCORP

Only under exceptional circumstances will NCI permit transfer of a Cooperative Agreement from one institution to another for any key component of NCORP as the recipient institution would not have undergone peer review. Any such request should be approved in accordance with the Research Base's Constitution and By-laws (e.g., approval required by an oversight committee such as its Board of Governors or Executive Committee) or in the case of Community Sites must be agreed upon in writing from the grant signatory institution official (if different from the transferring or receiving institution), as well as the transferring and receiving institutions. The NCORP Director, Program Director and the NCI/DCP Senior Program Specialist should be consulted for further advice if the Research Base or Community Site contemplates such a transfer request. For institutional changes affecting cancer care delivery research, responsible NCI/DCCPS Program Director also should be consulted. Any such request, if accepted, will require a full PHS 398 application or electronic SF424 Research & Related (R&R) application, a detailed plan regarding policies and procedures related to personnel issues, resources, etc., and approval and oversight by the responsible NCORP Director. NCI Program staff will review organizational change requests and provide a written response.

Organizational changes requiring NCI approval are outlined in "Guidelines for Approval of NCORP Organizational Changes," available in Part 4 of these Guidelines.

VIII. Appeals Process for Decisions Regarding Study Proposals & Types of Studies Performed by NCORP

This appeal process is only for disagreements related to scientific merit decisions made on study proposals for NCORP or the programmatic definition of study types supported under NCORP.

A. Decisions on Study Proposals

The appeals process for decisions related to study proposals supported under NCORP (including both intervention and non-intervention studies) is described below.

For NCORP concepts evaluated by NCI Scientific Steering Committees or the DCP Concept Review Committee, or the DCCPS Concept Review Committee that are not approved for development based on scientific merit, the Research Base may "appeal" the decision to the Director, Division of Cancer Prevention, if the Research Base believes that there were factual errors in the evaluation that led to the disapproval. If the Director agrees with the appeal request by the Research Base, the Director will direct the appropriate NCI Steering Committee, DCP or DCCPS Concept Review Committee to re-evaluate the study proposal. The result of the re-evaluation will be considered final.

Any approval of a concept, even after appeal, is subject to feasibility/resource considerations as determined by NCI/DCP.

IX. Other NCI Administrative Considerations

A. Program Staff Administration of NCORP

Within NCI/DCP, major scientific policy and programmatic decisions concerning NCORP are made only after appropriate consultation with and involvement by the NCORP Director, the NCORP CCDR Scientific Lead, the Program Directors, and NCI/DCP Branch Chiefs and Program Chiefs that are involved in the Program and the Deputy Director, DCP, and DCCPS leadership as necessary and appropriate. Routine programmatic administration is the responsibility of NCORP Director, who assures uniformity of implementation across the various key components in conjunction with the CCDR Scientific Lead and Program Director.

The NCORP Director or his/her designee has responsibility for addressing and approving non-competitive award (Type 5) budget requests, any supplemental budget requests, and new/competitive award (Type 1) budgets, as well as future Type 2 applications. NCORP Director will administer these tasks in conjunction with the Grants Management Specialist in the Office of Grants Administration (OGA) and will be assisted by the NCORP CCDR Scientific Lead and Program Directors of NCORP as well as the NCI/DCP Senior Program Specialist for the Program.

B. Senior Program Specialist for NCORP

The NCI/DCP Senior Program Specialist for NCORP works closely with the NCORP Director and NCORP CCDR Scientific Lead in reviewing administrative materials supporting Research Base requests, performing budget analyses, and facilitating the completion of action items involving coordination between NCI/DCP and NCI/DCCPS, the NCI Office of Grants Administration (OGA), and the awardees under the Program. The NCI/DCP Senior Program Specialist exchanges information with the Research Base Directors of Operations for the key components of NCORP and OGA staff on administrative changes and priorities.

C. NCI Office of Grants Administration (OGA)

The Grants Management Specialist for the NCI Office of Grants Administration (OGA) is responsible for the fiscal and administrative aspects of each application and award. The Grants Management Specialist for OGA works closely with the NCORP Director, NCORP CCDR Scientific Lead and NCI/DCP Senior Program Specialist to assure that appropriate science is funded in accordance with applicable laws, regulations, policies, and peer review recommendations to the extent that the budget allows and NCI priorities dictate.

D. Miscellaneous Budgetary Considerations

1. Carryover Requests

Carryover of unobligated (i.e. unspent) funds from one budget period to the next is not automatic for NCORP grantees. If there is a bona fide need for use for some or all of the unobligated (i.e., unspent) funds from a prior year in addition to the current year funding, a carryover request may be submitted.

The request should be submitted once the FFR has been accepted by the NIH for the year associated with the available unobligated balance but **no later than March 31**, of the current grant year (i.e., budget period). This deadline gives adequate time for NCI review of the request and a reasonable timeframe over which to spend the funds, should the request receive approval.

Grantees are encouraged to discuss the need for additional funding in the form of carryover with their NCI Program Director prior to submitting a formal request. The formal carryover request must be submitted by the appropriate business official to the NCI grants specialist with a copy to their NCI Program Director.

The request must, at a minimum address the following items which will assist in the determination of bona fide need:

- Status of expenditures in the current grant cycle (for CCDR and Clinical Trials)
- Projected balance by the end of the grant cycle (for CCDR and Clinical Trials)
- Amount of carryforward requested, spending plan, and justification (e.g. what additional activities will the carryover funds be used to support)

The request will be reviewed by the relevant NCI Program Director(s)as well as staff from the NCI Office of Grants Administration. Providing the information as outlined above, and additional information deemed relevant by the grantee will help to expedite the review process. The grantee will be notified of an approved (either full or partial) carryover via a revised Notice of Grant award. Notification of a disapproval will be made by the grants specialist to the business official who submitted the formal request.

If a request is not made for use of the funds and/or a carryover request is denied, NCI may utilize those funds as an offset/partial payment to the next type 5 award.

Additional guidance can be found in the NIH Grants Policy Statement Section 8.1.2.4 Carryover of Unobligated Balances
https://grants.nih.gov/grants/policy/nihgps/html5/section_8/8.1_changes_in_project_and_budget.htm#Carryover.

2. Requests for Non-competing Supplemental Funding

Informal discussions about the possibility of receiving non-competing supplemental funding for special needs and/or additional funding to cover data collection and management and biospecimen collection on a per case basis may be initiated by the awardee for the key component of NCORP. However, formal requests must be made for funding to be received and must always be countersigned by the business official responsible for the Cooperative Agreement/grant and the Principal Investigator(s). Electronic facsimile signatures on documents transmitted via email are acceptable.

The request should be sent to the NCORP Director and the NCORP CCDR Scientific Lead when involving cancer care delivery research, in care of the NCI/DCP Senior Program Specialist.

X. Appendix

I. NCI/DCTD/DCP Policies for the NCTN/NCORP Programs (URLs to Websites)

A. NCI National Clinical Trials Network Program (NCTN) Guidelines
http://ctep.cancer.gov/initiativesPrograms/docs/NCTN_Program_Guidelines.pdf

B. Investigator's Handbook (A Handbook for Clinical Investigators Conducting Therapeutic Clinical Trials Supported by CTEP, DCTD, NCI)
https://ctep.cancer.gov/investigatorresources/docs/InvestigatorHandbook.pdf

C. NCI-CTMB Guidelines for Auditing Clinical Trials for the NCI National Clinical Trials Network (NCTN) Including NCI Community Oncology Research Program (NCORP) and NCORP Research Bases
https://ctep.cancer.gov/branches/ctmb/clinicalTrials/monitoring_coop_ccop_ctsu.htm

D. NCI Guidelines for Collaborations with Industry
http://ctep.cancer.gov/industryCollaborations2/default.htm

E. NCI Guidelines for Investigators: Adverse Event Reporting Requirements for DCTD (CTEP and CIP) and DCP INDs and IDEs – (AdEERS -2013)
https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/aeguidelines.pdf

F. Operational Efficiency Working Group (OEWG) Policy and Timelines:
http://ctep.cancer.gov/SpotlightOn/OEWG.htm

G. NCI – Cooperative Group – Industry Relationship Guidelines
http://ctep.cancer.gov/industryCollaborations2/guidelines.htm

H. NCI CTEP Protocol Development
http://ctep.cancer.gov/protocolDevelopment/default.htm#cde_data_pol_cdus

I. CTEP Adverse Event Expedited Reporting System (CTEP-AERS)
https://ctep.cancer.gov/protocolDevelopment/electronic_applications/adverse_events.htm

J. Information on Common Data Elements (CDE) Approved for Use in CTEP-sponsored Clinical Trials
https://ctep.cancer.gov/protocolDevelopment/cde_data_policies.htm

K. NCI's Common Terminology Criteria for Adverse Events (CTCAE)
https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm
http://ctep.cancer.gov/reporting/ctc.html

L. NCI Clinical Trials Cooperative Group Program Guidelines for the Development, Conduct and Analysis of Clinical Trials with International Collaborating Institutions (Under Guidelines & Policies)
https://ctep.cancer.gov/initiativesPrograms/docs/NCTN_Program_Guidelines.pdf#search=%22international%20%22

M. CTEP Conflict of Interest Policy for Cooperative Group Phase 3 Clinical Trials (Under Guidelines and Policies)
https://ctep.cancer.gov/initiativesPrograms/docs/NCTN_Program_Guidelines.pdf#search=%22conflict%20of%20interest%22

N. NCI Templates for Simplified Model Informed Consent Documents for NCTN Trials
https://ctep.cancer.gov/protocolDevelopment/informed_consent.htm

II. Other Important NIH/NCI URLs, Federal Citations, List of Abbreviations and Key Definitions

A. Website URLs referenced in these Guidelines

NCI Website
http://www.cancer.gov/

NCI Biomarker, Imaging, and Quality of Life Studies Funding Program (BIQSFP)
http://biqsfp.cancer.gov/

NCI Cancer Trials Support Unit (CTSU) Website
http://www.ctsu.org

NCI Request for Application (RFA) Limited Competition: Biospecimen Banks to Support NCI-Clinical Trials Network (NCTN) (U24)
https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-14-501.html

NCI Cancer Diagnosis Program's Website
http://cdp.cancer.gov/

NCI Center to Reduce Cancer Health Disparities (CRCHD)
https://www.cancer.gov/about-nci/organization/crchd

NCI Central IRB Website
https://www.ncicirb.org

NCI Central IRB Standard Operating Procedures
https://www.ncicirb.org/system/files/CIRB_SOPs_101817.pdf

NCI Clinical Trials and Translational Research Advisory Committee (CTAC)
https://deainfo.nci.nih.gov/advisory/ctac/ctac.htm

NCI Clinical and Translational Research Operations Committee
http://ccct.cancer.gov/committees/ctroc

NCI Coordinating Center for Clinical Trials (CCCT)
https://www.cancer.gov/about-nci/organization/ccct

NCI CTWG Steering Committee System (Information on NCI Scientific Steering Committees)
http://transformingtrials.cancer.gov/steering/overview

NCI Clinical Trials Reporting Program (CTRP)
https://www.cancer.gov/about-nci/organization/ccct/ctrp

NCI Division of Cancer Control and Population Sciences (DCCPS)
http://cancercontrol.cancer.gov/

NCI Division of Cancer Prevention (DCP)
https://prevention.cancer.gov/

NCI Cancer Therapy Evaluation Program (CTEP)
http://ctep.cancer.gov/

NCI CTEP Policy on the Issuance of Waivers for Protocol Deviation(s)
https://ctep.cancer.gov/protocolDevelopment/policies_deviations.htm

NCI Division of Cancer Treatment and Diagnosis (DCTD)
http://dctd.cancer.gov/

NCI DCTD Clinical Data Update System (CDUS/CDS)
https://ctep.cancer.gov/protocolDevelopment/electronic_applications/cdus.htm

NCI Guide to Readers to Information on Other NCI Divisions/Branches
http://www.cancer.gov/aboutnci

Code of Federal Regulations – Dispute Resolution (42CFR Part 50 Subpart D)
http://www.ecfr.gov/cgi-bin/text-idx?rgn=div5&node=42:1.0.1.4.23

Diagnostics Evaluation Branch (DRB) of the Cancer Diagnosis Program (CDP) Program for the Assessment of Clinical Cancer Tests (PACCT) – Clinical Tumor Marker Study Guidelines
http://www.cancerdiagnosis.nci.nih.gov/diagnostics/advice/guidelines.htm

Good Clinical Practice in FDA-Regulated Clinical Trials
http://www.fda.gov/oc/gcp/default.htm

Guidance for Industry: E6 Good Clinical Practice Consolidated Guidance
https://ctep.cancer.gov/branches/ctmb/clinicalTrials/docs/good_clinical_practices.pdf

Guidance Document on Inclusion of Manuscripts/Publications in Appendix Material with NIH/NCI Grant Applications
March 16, 2006: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-06-051.html

Appendix Material for NIH/AHRQ/NIOSH Applications Submitted for Due Dates on or After January 25, 2017
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-129.html

NIH & AHRQ Announcement New Form for PHS Awarding Component and Peer Review Requests
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-008.html

NIH National Library of Medicine – ClinicalTrials.gov
https://clinicaltrials.gov/

NIH Data Sharing Policy
https://grants.nih.gov/grants/policy/data_sharing

NIH Freedom of Information Act Office
http://www.nih.gov/icd/od/foia/index.htm

NIH Grants Policy Statement
https://grants.nih.gov/policy/nihgps/index.htm

NIH Grant Policy for Program Income
http://grants.nih.gov/grants/policy/nihgps_2011/nihgps_ch8.htm#_Program_Income

NIH Notice of Extension of Effective Date for Final NIH Policy on the Use of Single Institution Review Board for Multi-Site Research
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-076.html

NIH Policy for Multiple Principal Investigators
https://grants.nih.gov/grants/multi_pi/index.htm

NIH Public Access Policy (and Manuscript Submission System)
http://publicaccess.nih.gov/policy.htm

NCBI Pub Med Central
https://www.ncbi.nlm.nih.gov/pmc/

NIH Guide Notice on NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research (Amendment October 2001).
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html

NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research – Amended, October 2001 (COMPLETE COPY OF UPDATED GUIDELINES)
https://grants.nih.gov/grants/funding/women_min/guidelines.htm

NIH Policies on Inclusion of Women and Minorities as Participants in Research Involving Human Subjects – Policy Implementation
http://grants.nih.gov/grants/funding/women_min/women_min.htm

NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects – Policy Implementation
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-010.html

NIH Policy and Guidelines on the Inclusion of Individuals Across the Lifespan as Participants in Research Involving Human Subjects (Revision)
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-116.html

NCI Policy for Data and Safety Monitoring of Clinical Trials
https://deainfo.nci.nih.gov/grantspolicies/datasafety.pdf

NIH Policy for Data and Safety Monitoring
http://grants.nih.gov/grants/guide/notice-files/not98-084.html

(Further) NIH Guidance on Data and Safety Monitoring for Phase 1 and Phase 2 trials
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html

NIH Policy on Financial Conflict of Interest
https://grants.nih.gov/grants/policy/coi/index.htm

NIH Genomic Data Sharing Policy
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-124.html

NIH Policy on Sharing Model Organisms
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html

PHS 398 Grant Application
http://grants.nih.gov/grants/funding/phs398/phs398.html

SF424 (R&R) Application and Electronic Submission Information
http://grants.nih.gov/grants/funding/424/index.htm

Office for Human Research Protections (OHRP) Database for Registered IORGs & IRBs, Approved FWAs, and Documents Received in Last 60 Days
http://ohrp.cit.nih.gov/search/search.aspx?styp=bsc

Office for Human Research Protections Website
http://www.hhs.gov/ohrp/

Required Education on the Protection of Human Subject Participants
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html

Office and Management Budget (OMB) Definition of Race/Ethnicity
https://obamawhitehouse.archives.gov/omb/fedreg_1997standards

Health Resources & Services Administration Defining Rural Population
https://www.hrsa.gov/rural-health/about-us/definition/index.html

Hudson KL, Lauer MS, Collins FS. Toward a New Era of Trust and Transparency in Clinical Trials. *JAMA*. 2016;316(13):1353–1354. doi:10.1001/jama.2016.14668
https://jamanetwork.com/journals/jama/fullarticle/2553888?guestAccessKey=554e0981-9434-45f2-b122-d0e673cd1182

Hart LG, Larson EH, Lishner DM. Rural Definitions for Health Policy and Research. *American Journal of Public Health*. 2005;95(7):1149-1155. doi:10.2105/AJPH.2004.042432.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1449333/

B. **Other Federal Citations for NIH Grants Involved in Human Subjects Research & Websites**

Sharing of Model Organisms
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html
NIH is committed to support efforts that encourage sharing of important research resources including the sharing of model organisms for biomedical research (see http://grants.nih.gov/grants/policy/model_organism/index.htm). At the same time, the NIH recognizes the rights of grantees and contractors to elect and retain title to subject inventions developed with Federal funding pursuant to the Bayh-Dole Act (see the NIH Grants Policy Statement at http://grants.nih.gov/grants/policy/nihgps_2011/nihgps_ch8.htm#_Program_Income.

All investigators submitting an NIH application or contract proposal, beginning with the October 1, 2004, receipt date, are expected to include in the application/proposal a description of a specific plan for sharing and distributing unique model organism research resources generated using NIH funding or state why such sharing is restricted or not possible. This will permit other researchers to benefit from the resources developed with public funding. The inclusion of a model organism sharing plan is not subject to a cost threshold in any year and is expected to be included in all applications where the development of model organisms is anticipated.

Standards for Privacy of Individually Identifiable Health Information
This Department of Health and Human Services (DHHS) issued final modification to the "Standards for Privacy of Individually Identifiable Health Information," the "Privacy Rule," on August 14, 2002. The Privacy Rule is a federal regulation under the Health Insurance Portability and Accountability Act (HIPAA) of 1996 that governs the protection of individually identifiable health information, and is administered and enforced by the DHHS Office for Civil Rights (OCR). Decisions about applicability and implementation of the Privacy Rule reside with the researcher and his/her institution. The OCR website (http://www.hhs.gov/ocr/) provides information on the Privacy Rule, including a complete Regulation Text and a set of decision tools on "Am I a covered entity?" Information on the impact of the HIPAA Privacy Rule on NIH processes involving the review, funding, and progress monitoring of grants, cooperative agreements, and research contracts can be found at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-025.html.

Healthy People 2020
The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2020," a PHS-led national activity for setting priority areas. The funding opportunity announcement (FOA) for this cooperative agreement is related to one or more of the priority areas. Potential applicants can obtain a copy of "Healthy People 2020" at http://www.health.gov/healthypeople.

Authority and Regulations

This program is described in the Catalogue of Federal Domestic Assistance at https://www.cfda.gov/ and is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency Review. Awards are made under the authorization of Sections 301 and 405 of the Public Health Service (PHS) Act as amended (42 USC 241 and 284) and under Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. All awards are subject to the terms and conditions, cost principles, and other considerations described in the NIH Grants Policy Statement. The NIH Grants Policy Statement can be found at http://grants.nih.gov/grants/policy/policy.htm.

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American People.

Loan Repayment Program

NIH encourages applications for educational loan repayment from qualified health professionals who have made a commitment to pursue a research career involving clinical, pediatric, contraception, infertility, and health disparities related areas. The Loan Repayment Program (LRP) is an important component of NIH's efforts to recruit and retain the next generation of researchers by providing the means for developing a research career unfettered by the burden of student loan debt. Note that an NIH grant is not required for eligibility and concurrent career award and LRP applications are encouraged. The periods of career award and LRP award may overlap providing the LRP recipient with the required commitment of time and effort, as LRP awardees must commit at least 50% of their time (at least 20 hours per week based on a 40-hour week) for 2 years to the research. For further information, please see http://www.lrp.nih.gov/.

C. Important Abbreviations

ABBREVIATION	FULL TERM
AD	Associate Director
AHRQ	Agency for Healthcare Research and Quality
ARA	Awaiting Receipt of Application
BIQSFP	Biomarker, Imaging, and Quality of Life Studies Funding Program
BRB	Biometric Research Branch (in DCTD)
CBO	Common Budget Outline
CCCT	Coordinating Center for Clinical Trials (in NCI OD)
CDE	Common Data Elements
CDP	Cancer Diagnosis Program (in DCTD)
CDUS	Clinical Data Update System
CFR	Code of Federal Regulations
CIB	Clinical Investigations Branch (in CTEP)
CIP	Cancer Imaging Program (in DCTD)
CIRB	Central Institutional Review Board at NCI
CoC	Certificate of Confidentiality
CRA	Clinical Research Associate
CRADA	Cooperative Research and Development Agreement
CSA	Clinical Supply Agreement
CSR	Center for Scientific Research (at NIH)
CTA	Clinical Trial Agreement
CTAC	Clinical Trials and Translational Research Advisory Committee
CTCAE	Common Toxicity Criteria for Adverse Events

ABBREVIATION	FULL TERM
CTEP	Cancer Therapy Evaluation Program (in DCTD)
CTEP AERS	Cancer Therapy Evaluation Program Adverse Event Reporting System
CTMB	Clinical Trials Monitoring Branch (in CTEP)
CTSU	Cancer Trials Support Unit
CTRP	Clinical Trials Reporting Program
CTWG	Clinical Trials Working Group
CTROC	Clinical and Translational Research Operations Committee
DAR	Drug Accountability Record
DCP	Division of Cancer Prevention
DCTD	Division of Cancer Treatment and Diagnosis
DEA	Division of Extramural Activities
DHHS	Department of Health and Human Services
DMC	Data Monitoring Committee (also known as Data and Safety Monitoring Board)
DRB	Diagnostics Evaluation Branch (in CDP)
DSMB	Data and Safety Monitoring Board (also known as Data Monitoring Committee)
eFSR/FFR	Electronic Financial Status Report/Federal Financial Report
F&A	Facilities and Administrative (costs)
FOA	Funding Opportunity Announcement
FDA	Food and Drug Administration
FSR	Financial Status Report (SF 269 or 269A)
FWA	Federal Wide Assurance (for OHRP)
GCP	Good Clinical Practice
GMO	Grants Management Officer

ABBREVIATION	FULL TERM
GMS	Grants Management Specialist
GWAS	Genome-Wide Association Studies
HDRP	Healthcare Delivery Research Program (in DCCPS)
HIPAA	Health Insurance Portability and Accountability Act
HSP	Human Subjects Protection
IDB	Investigational Drug Branch (in CTEP)
IDE	Investigational Device Exception
IND	Investigational New Drug Application
IRB	Institutional Review Board
LOI	Letter of Intent
NCAB	National Cancer Advisory Board
NCI	National Cancer Institute
NCI SSC	NCI Scientific Steering Committees
NCT	National Clinical Trial
NIH	National Institutes of Health
NCTN	National Clinical Trials Network
NoA	Notice of Award
OD	Office of the Director at the NCI
OER	Office of Extramural Research, NIH
OEWG	Operational Efficiency Working Group
OGA	Office of Grants Administration
OHRP	Office for Human Research Protections
OMG	Office of Management and Budget
OPEN	Oncology Patient Enrollment Network

ABBREVIATION	FULL TERM
ORI	Office of Research Integrity
PA	Program Announcement
PD	Program Director
PHS	Public Health Service
PI	Principal Investigator
PIO	Protocol and Information Office (in CTEP)
PMB	Pharmaceutical Management Branch (in CTEP)
PRC	Protocol Review Committee
RAB	Regulatory Affairs Branch (in CTEP)
RFA	Request for Applications
RFP	Request for Proposals
RPPR	Research Performance Progress Report
RRP	Radiation Research Program (in DCTD)
RSS	Regulatory Support System (in CTSU)
SDMC	Statistics and Data Management Center
SO	Signing Official
SOP	Standard Operating Procedure
SPORE	Specialized Programs of Research Excellence
SRG	Scientific Review Group
SRO	Scientific Review Officer
URL	Uniform Resource Locator (internet address of resource)
VA	Department of Veterans Affairs

D. Key Definitions

- **Clinical Research** - follow the NIH definition - https://grants.nih.gov/policy/clinical-trials/glossary-ct.htm#ClinicalResearch
- **Clinical Trials** - follow the NIH definition - https://grants.nih.gov/policy/clinical-trials/glossary-ct.htm#ClinicalResearch
- **Cancer Control Research** – Applied research aimed at reducing the morbidities associated with cancer and its treatment, as well as improving quality of life of individuals undergoing cancer treatment or with a history of cancer. Areas of research include but are not limited to symptom management, supportive care, palliative care, and end of life care.
- **Cancer Prevention Research** – Research aimed at reducing cancer risk, incidence and mortality. Research areas include but are not limited to testing new agents, modifying lifestyle behaviors, testing new screening technologies, and examining optimal time periods for detecting tumor response (surveillance) during and following cancer treatment and overdiagnosis.
- **Cancer Care Delivery Research** - A multidisciplinary science that seeks to improve clinical outcomes and patient well-being by intervening on patient, clinician, and organizational factors that influence care delivery.
- **Cancer Disparities Research** - Research in which cancer outcomes and treatment-related toxicities are studied considering the impact of race, ethnicity, age (e.g. AYA, elderly), biological factors, and other social determinants. Cancer Disparities Research also includes examining healthcare disparities, e.g., access to care, availability and utilization of services, provider, and/or organizational factors affecting care provided to underserved populations. Further, a focus includes addressing barriers to enrollment of underrepresented populations in clinical research.
- **Underrepresented Populations in Community-based Research**: Refers to NIH-designated health disparity populations, defined by race/ethnicity, socioeconomic disadvantage, geographic region (e.g. rural, frontier), sexual/gender minority, and other participants traversing the lifespan that are underrepresented in clinical research (AYA – ages 15-39; elderly – ≥ age 65).
- **Community Site Primary Affiliate**: In the context of NCORP Community Site structure, a "primary affiliate" refers to a hospital, cancer center, physician practice, or other institution where patients/participants are enrolled on a regular and ongoing basis to the menu of NCI-approved clinical trials available to the NCORP Community Site or Minority/Underserved Site. In addition, one or more of the NCORP Site primary affiliates are expected to participate in cancer care delivery research.
- **Community Site Sub-Affiliate**: In the context of NCORP Community Site structure, a "sub-affiliate" refers to a practice or organization that contributes to the overall accrual of a primary affiliate site but is located in a separate geographic location(s), is part of the primary affiliate's business entity, and is managed by the primary affiliate and is under the primary affiliate site's Federal Wide Assurance (FWA).