\*\*Required for Protocols Granted Approval on Hold After October 24, 2025\*\*

Optional for Other Studies

DCP CP-CTNET CHEMOPREVENTION PROTOCOL TEMPLATE

INSTRUCTIONS

The protocol template is a tool to facilitate rapid protocol development. It is not intended to supersede the role of the Protocol Principal Investigator in the authoring and scientific development of the protocol. It contains the language required in protocols submitted to the NCI, Division of Cancer Prevention (DCP). Please modify all sections as necessary to meet the scientific aims of the study and development of the protocol.

Specific documents mentioned in this protocol template are available at:

<https://prevention.cancer.gov/clinical-trials/clinical-trials-management/protocol-information-office/pio-instructions-and-tools/cp-ctnet-instructions-forms>

1. Each protocol submission consists of four parts:
   1. DCP CP-CTNet Protocol Submission Worksheet (PSW): Must complete all relevant sections of the PSW via the DCP PIO Document Submission System website. The PSW is built into the website. The PSW is required for all protocol submissions including the original protocol, revisions, and amendments.
   2. Main Body and Appendices of the protocol: This document provides standard language plus instructions and prompts for information required in each DCP protocol. Please ensure the current version of the template always is used for protocol development.

Please note that the Informed Consent Template is provided as a separate document file. Also, please note that the protocol and Informed Consent Document Version dates must match.

* 1. Additional Study-Related Documents: These documents include the Recruitment, Retention and Adherence Plan, the Pharmacokinetic and Biomarker Methods Development Report, the electronic Case Report Forms (eCRFs)\* and the Data and Safety Monitoring Plan (DSMP)**. \*Note: The System Variable and Attribute Report (SVAR) template will be used to create the eCRFs.**

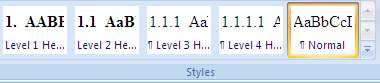
1. The Pharmacokinetic and Biomarker Methods Development Report and protocol-specific addenda to the DSMP are submitted with the initial protocol. These documents are not considered a part of the protocol document. Unless required by local practices, these documents do not need to be submitted to the local Institutional Review Board (IRB) and should not be referenced in the protocol.
2. The Recruitment, Retention and Adherence Plan and the SVAR workbook are not submitted with the initial protocol. The Recruitment, Retention and Adherence Plan is to be submitted with the second iteration of the protocol.
3. DMASC will contact the Lead Academic Organization (LAO) to determine if a meeting is needed to discuss the trial and eCRFs before the DMASC creates the draft SVAR
4. A standardized DSMP will be approved for each LAO’s network. Submit supplemental information or addenda to these plans (*e.g*., a protocol-specific addendum to the DSMP) only as required.

* 1. Protocol budget

1. An “administratively complete” protocol submission must include the following components:
   1. First submission
      1. DCP CP-CTNet PSW which is integrated into the DCP PIO Document Submission System website. For those protocols that were authored from DCP approved concepts, the relevant data fields from the previous concept submission will be shown for review and updates.
      2. Protocol including the informed consent document
         1. A protocol document version number and date must be on the cover page.
         2. All pages of the protocol must include a header that identifies the protocol by DCP protocol number, protocol document version number and version date. Pagination must be complete.
         3. The Table of Contents (TOC) sections and page numbers must match the protocol.
      3. All appendices (correct header and pagination)
      4. Additional Study-Related Documents (Pharmacokinetic and Biomarker Methods Development Report, supplemental information or addenda to the standardized DCP-approved documents (DSMP), if applicable). Note: The completed Recruitment, Retention and Adherence Plan Outline Form is to be submitted with the second submission of the protocol.
      5. Protocol budget
   2. All subsequent submissions (protocol revisions and amendments) must include:
      1. Cover letter with a point-by-point response to DCP reviewer required and recommended changes with references to the changed document section.
      2. An updated PSW. The information from the previous submission will be displayed for review and modification.
      3. “Tracked changes” or highlighted version of the protocol with informed consent and study-related documents, as appropriate, indicating changes from previous version.
      4. Clean copy of all documents with “Track Changes” and highlights removed.
      5. Any changes to the eCRFs or other Additional Study-Related Documents resulting from a protocol revision or amendment must be included with the submission for review and approval. (See section 1.c.ii)
      6. The completed Recruitment Retention and Adherence Plan Outline Form (is to be submitted with the second submission of the protocol).
      7. Amended protocol budget, if applicable, or a statement indicating that the proposed revision or amendment will not result in a change to the budget.
      8. Standard font indicates suggested language that should be retained in the document.
      9. **Bold font** indicates language that must be retained in the document.
      10. Blank space or \_\_\_\_\_\_\_\_ indicates that you should fill in the appropriate information.

“Administratively Incomplete” submissions will be returned to the LAO lead PI for completion. The review process will begin following receipt of an administratively complete submission.

1. All sections in the Protocol Template should be retained within the body of the document. If not appropriate for a given study, please insert “Not Applicable” after the section number and delete the corresponding text.
2. *All Protocol Template instructions and prompts are in italics*. *Italicized information should be deleted prior to submitting the protocol to DCP.*
3. Please note that the Protocol Template has built-in styles for headings levels 1–4 (Level 1 Heading – Level 4 Heading; see image below).

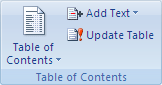


These heading styles will automatically update the Table of Contents (TOC) and convert to Bookmarks in a final PDF protocol document. **Please retain the heading styles.**

1. To update the TOC in your protocol document:

2007 or later MS Word:

a. On the **References** tab, in the **Table of Contents** group, click **Update Table**.



b. Click **Update entire table**.

2003 MS Word:

a. Click the table of contents.

b. Press F9.

**Please do not edit the TOC manually**.

1. DCP terminology for changes to protocol:
   1. Changes made prior to the initial DCP study approval are “Revisions”
   2. Changes made after DCP approval are “Amendments”
2. Indicate changes using the ‘tracked changes’ function, highlighting, or underlining new or modified text in protocol revisions or amendments to facilitate the review process.
3. All document submissions must be sent electronically to the DCP Protocol Information Office via the DCP PIO Document Submission System website. Please contact the NCI DCP Protocol Information Office at [NCI\_DCP\_PIO@mail.nih.gov](mailto:NCI_DCP_PIO@mail.nih.gov) for more information. Documents submitted elsewhere will not be accepted for review.

**Questions:**

**Contact the DCP Protocol Information Office at (240) 276-7130 or e-mail** [**NCI\_DCP\_PIO@mail.nih.gov**](mailto:NCI_DCP_PIO@mail.nih.gov)

# PROTOCOL TRACKING SHEET

***Note:*** *Please leave protocol tracking sheet before the Cover Page.*

*A Protocol Tracking Sheet will be submitted with each protocol change starting with the first amendment. The first entry on the initial tracking sheet will always be the same – The submitting LAO must note the date of DCP Final Approval to open the study in the “Reason for Change” column. After this initial entry, the “Reason for Change” is to be a brief high-level summary of the amendment. If administrative changes are the only reason for the amendment, please state that as the reason. The details for any protocol change will continue to be captured in the change memo submitted with each version change. Please see the table below as an example:*

|  |  |  |
| --- | --- | --- |
| **VERSION NUMBER** | **VERSION DATE** | **REASON FOR CHANGE (high-level)** |
| *V7* | *September 20, 2020* | *Date of DCP Final Approval to open study: October 5, 2020* |
| *V7.1* | *November 19, 2020* | *Changed Eligibility: menopausal status* |
| *V7.2* | *December 1, 2020* | *Central (CIRB) stipulations added* |
| *V7.3* | *March 10, 2021* | *New biomarker for altered coagulation added. Amendment withdrawn March 18, 2021* |
| *V7.4* | *April 20, 2021* | *New biomarkers added for altered coagulation and LFT assessment.* |

*Standard versioning of protocols, accompanying informed consent(s) and recruitment and other participant facing materials will consist of a new whole version number and date change with each revision until DCP Final Approval is granted. In the example above, DCP Final Approval occurred on V7, 9/20/2020. Each subsequent amendment after this final approval will use .1, .2, .3 etc. as noted in the table above.*

***Note:*** *If a protocol receives CIRB approval and then undergoes a CIRB amendment change prior to Final DCP Approval this too is considered a revision and remains a whole number version change until DCP Final Approval is granted.*

# COVER PAGE

**DCP Protocol #:** *This number will be assigned by DCP and may be the same as or different from the local protocol number. The DCP protocol number must appear on all protocol document versions and all communication to DCP.*

**Local Protocol #:** *Insert your local protocol # for this study. If a local protocol number has not been assigned, indicate ‘pending’. DEFINITION: The local protocol number is assigned per LAO local institutional conventions or per the LAO network guidelines*

**PROTOCOL TITLE**

**Lead Academic Organization (LAO) Name:**

*Insert name of LAO*

**Name of LAO Principal** *Name & Title of the Principal Investigator of LAO*

**Investigator:** *Address (Enter Research Site Address)*

*Address*

*Telephone*

*E-mail address*

**Organization Name:** *Organization Name (Enter CTEP ID)*

**Protocol Principal Investigator:** *Protocol Principal Investigator*

*Investigator’s Specialty*

*Address (Enter Research Site Address)*

*Address*

*Telephone*

*E-mail address*

**Organization:** *Organization Name (Enter CTEP ID)*

**Investigator:** *Investigator’s Name*

*Investigator’s Specialty*

*Address (Enter Research Site Address)*

*Address*

*Telephone*

*E-mail address*

**Organization:** *Organization Name (Enter CTEP ID)*

**Investigator:** *Investigator’s Name*

*Investigator’s Specialty*

*Address (Enter Research Site Address)*

*Address*

*Telephone*

*E-mail address*

**Organization:** *Organization* *Name (Enter CTEP ID)*

**Statistician:** *Statistician Name*

*Address (Enter Research Site Address)*

*Address*

*Telephone*

*E-mail address*

**Organization Name:** *NCI/Division of Cancer Prevention*

**Medical Monitor:** *Medical Monitor Name*

*Address*

*Telephone*

*E-mail address*

**Scientific Lead:** *Scientific Lead Name*

*Address*

*Telephone*

*E-mail address*

**Nurse Consultant:** *Nurse Consultant Name*

*Address*

*Telephone*

*E-mail address*

***NOTE: If this is a multi-institution study:***

1. ***The protocol title page(s) must include the name and address of each participating institution and any affiliated organizations participating in the study.***
2. ***The protocol title page(s) must include the names of all investigators at each institution; his/her telephone, and e-mail address.***
3. ***Indicate the protocol principal investigator responsible for the study at each institution; his/her telephone number, and e-mail address.***
4. ***Indicate administrative (non-accruing) sites with an asterisk and an associated footnote (e.g., “No participant accrual occurs at this site”).***

**IND Sponsor:** *NCI/Division of Cancer Prevention (or other Sponsor)*

*If other sponsor, please add contact information.*

**IND#** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Agent(s)/Supplier**: *Study Agent(s)/Supplier Name*

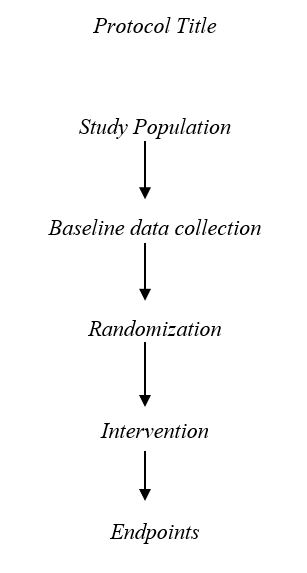
**Protocol Version Date:** \_\_\_\_\_ *(Date)* \_\_\_\_\_

**Protocol Revision or**

**Amendment #** *Revision or Amendment #*

# SCHEMA

*Please provide a schema for the study.*

****TABLE OF CONTENTS**

*NOTE: The page numbers in the TOC should update as you incorporate text into the protocol. If the numbers do not automatically update, follow these steps:*

*1. Select the TOC by highlighting it.*

*2. Right-click on the highlighted TOC. You will see a dialogue box asking if you want to update the whole table or just the page numbers.*

*3. Choose update page numbers.*

[DCP CP-CTNET CHEMOPREVENTION PROTOCOL TEMPLATE i](#_Toc202793938)

[INSTRUCTIONS i](#_Toc202793939)

[PROTOCOL TRACKING SHEET iv](#_Toc202793940)

[COVER PAGE 5](#_Toc202793941)

[SCHEMA 7](#_Toc202793942)

[1. OBJECTIVES 13](#_Toc202793943)

[1.1 Primary Objectives 13](#_Toc202793944)

[1.2 Secondary Objectives 13](#_Toc202793945)

[2. BACKGROUND 13](#_Toc202793946)

[2.1 *Study Disease* 13](#_Toc202793947)

[2.2 *Study Agent* 13](#_Toc202793948)

[2.3 Rationale 13](#_Toc202793949)

[3. SUMMARY OF STUDY PLAN 14](#_Toc202793950)

[4. Participant SELECTION 14](#_Toc202793951)

[4.1 Inclusion Criteria 14](#_Toc202793952)

[4.2 Exclusion Criteria 16](#_Toc202793953)

[4.3 Inclusion of Women and Minorities 16](#_Toc202793954)

[4.4 Recruitment 16](#_Toc202793955)

[4.5 Planned Accrual 17](#_Toc202793956)

[5. REGISTRATION PROCEDURES 18](#_Toc202793957)

[5.1 Investigator and Research Associate Registration with CTEP 18](#_Toc202793958)

[6. NCI CENTRAL INSTITUTIONAL REVIEW BOARD 19](#_Toc202793959)

[7. AGENT ADMINISTRATION 20](#_Toc202793960)

[7.1 Dose Regimen and Dose Groups 20](#_Toc202793961)

[7.2 (*Study Agent*)Administration 20](#_Toc202793962)

[7.3 Run-in Procedures 20](#_Toc202793963)

[7.4 Contraindications 20](#_Toc202793964)

[7.5 Concomitant Medications 20](#_Toc202793965)

[7.6 Dose Modification 20](#_Toc202793966)

[7.7 Adherence/Compliance 21](#_Toc202793967)

[8. PHARMACEUTICAL INFORMATION 21](#_Toc202793968)

[8.1 *Study Agent* (*IND #, IND Sponsor*) 21](#_Toc202793969)

[8.2 Reported Adverse Events and Potential Risks 21](#_Toc202793970)

[8.3 Availability 21](#_Toc202793971)

[8.4 Agent Distribution 22](#_Toc202793972)

[8.5 Agent Accountability 22](#_Toc202793973)

[8.6 Packaging and Labeling 22](#_Toc202793974)

[8.7 Storage 23](#_Toc202793975)

[8.8 Registration/Randomization 23](#_Toc202793976)

[8.9 Blinding and Unblinding Methods 23](#_Toc202793977)

[8.10 Agent Destruction/Disposal 24](#_Toc202793978)

[9. CLINICAL EVALUATIONS AND PROCEDURES 24](#_Toc202793979)

[9.1 Schedule of Events 24](#_Toc202793980)

[9.2 Baseline Testing/Pre-Study Evaluation 24](#_Toc202793981)

[9.3 Evaluation During Study Intervention 25](#_Toc202793982)

[9.4 Evaluation at Completion of Study Intervention 25](#_Toc202793983)

[9.5 Post-intervention Follow-up Period 25](#_Toc202793984)

[9.6 Methods for Clinical Procedures 25](#_Toc202793985)

[\* If utilized in this study 26](#_Toc202793986)

[10. CRITERIA FOR EVALUATION AND ENDPOINT DEFINITION 26](#_Toc202793987)

[10.1 Primary Endpoint 26](#_Toc202793988)

[10.2 Secondary Endpoints 26](#_Toc202793989)

[10.3 Off-Agent Criteria 26](#_Toc202793990)

[10.4 Off-Study Criteria 27](#_Toc202793991)

[10.5 Study Termination 27](#_Toc202793992)

[11. CORRELATIVE/SPECIAL STUDIES 27](#_Toc202793993)

[11.1 Rationale for Methodology Selection 27](#_Toc202793994)

[11.2 Comparable Methods 27](#_Toc202793995)

[12. SPECIMEN MANAGEMENT 27](#_Toc202793996)

[12.1 Laboratories 27](#_Toc202793997)

[12.2 Collection and Handling Procedures 27](#_Toc202793998)

[12.3 Shipping Instructions 28](#_Toc202793999)

[12.4 Tissue Banking 28](#_Toc202794000)

[13. REPORTING ADVERSE EVENTS 28](#_Toc202794001)

[13.1 Adverse Events 28](#_Toc202794002)

[13.2 Serious Adverse Events 30](#_Toc202794003)

[14. STUDY MONITORING 32](#_Toc202794004)

[14.1 Data Management 32](#_Toc202794005)

[14.2 Electronic Case Report Forms 32](#_Toc202794006)

[14.3 Source Documents 32](#_Toc202794007)

[14.4 Data and Safety Monitoring Plan 32](#_Toc202794008)

[14.5 Sponsor or FDA Monitoring 33](#_Toc202794009)

[14.6 Record Retention 33](#_Toc202794010)

[14.7 Cooperative Research and Development Agreement (CRADA)/Clinical Trials Agreement (CTA) 33](#_Toc202794011)

[14.8 Genomic Data Sharing Plan 35](#_Toc202794012)

[15. STATISTICAL CONSIDERATIONS 35](#_Toc202794013)

[15.1 Study Design/Description 35](#_Toc202794014)

[15.2 Randomization/Stratification 35](#_Toc202794015)

[15.3 Sample Size 35](#_Toc202794016)

[15.4 Primary Objective, Endpoint(s), Analysis Plan 35](#_Toc202794017)

[15.5 Secondary Objectives, Endpoints, Analysis Plans 36](#_Toc202794018)

[15.6 Reporting and Exclusions 36](#_Toc202794019)

[15.7 Evaluation of Toxicity 36](#_Toc202794020)

[15.8 Evaluation of Response 36](#_Toc202794021)

[15.9 Interim Analysis 36](#_Toc202794022)

[15.10 Ancillary Studies 36](#_Toc202794023)

[16. REGULATORY And ETHICAL CONSIDERATIONS 37](#_Toc202794024)

[16.1 Required Documents 37](#_Toc202794025)

[16.2 Informed Consent 37](#_Toc202794026)

[16.3 Collection of Regulatory Documents 37](#_Toc202794027)

[16.4 Other 37](#_Toc202794028)

[17. ROSTER MANAGEMENT 38](#_Toc202794029)

[18. FINANCING, EXPENSES, AND/OR INSURANCE 38](#_Toc202794030)

[REFERENCES 38](#_Toc202794031)

[APPENDIX A PERFORMANCE STATUS CRITERIA 39](#_Toc202794032)

[APPENDIX B **(OPTIONAL)** 40](#_Toc202794033)

[ALCOHOL AND TOBACCO QUESTIONNAIRE INSTRUCTIONS 40](#_Toc202794034)

[ALCOHOL ASSESSMENT-- BASELINE 41](#_Toc202794035)

[ALCOHOL ASSESSMENT - FOLLOW-UP 44](#_Toc202794036)

[TOBACCO ASSESSMENT – BASELINE 46](#_Toc202794037)

[TOBACCO ASSESSMENT - FOLLOW-UP 50](#_Toc202794038)

[NATIONAL AND LOCAL RESOURCES TO HELP WITH ALCOHOL ABUSE AND ALCOHOLISM 53](#_Toc202794039)

[NATIONAL AND LOCAL RESOURCES TO HELP WITH QUITTING SMOKING 54](#_Toc202794040)

[APPENDIX C 55](#_Toc202794041)

[PARTICIPANT DRUG INTERACTIONS HANDOUT AND WALLET CARD 55](#_Toc202794042)

## 1. OBJECTIVES

*Study objectives are concise statements of the primary and secondary clinical and statistical questions that the study is designed to answer. Each objective should be stated as specifically and succinctly as possible. Both primary and secondary hypotheses must relate to the hypotheses presented in the rationale (section 2.3) and should be consistent with the objectives described in the statistical section (section 13.0). Clearly differentiate between primary and secondary objectives. Number the objectives in order of priority.*

1.1 Primary Objectives – *Insert primary protocol objective.*

1.2 Secondary Objectives – *Insert secondary protocol objectives, if pertinent.*

# 2. BACKGROUND

## 2.1 *Study Disease*

*Please provide background information on the study disease. (May not be applicable in phase 1 trials).*

## 2.2 *Study Agent*

*Please provide background information on the study agent, including information to support safety issues and the rationale for the study dose and duration of exposure.*

## 2.3 Rationale

*Please provide the background rationale for evaluating this agent in this cohort/target organ. Present possible mechanisms and/or theoretical framework for conducting the study. Include relevant literature review and pertinent preclinical, pilot, and preliminary and/or unpublished data to support conduct of the trial. Clearly state the hypotheses for the primary and secondary objectives. Justify selection of target population including rationale for each eligibility criterion, agent, endpoints and choice of techniques for endpoint assessment, measurement of drugs, metabolites and drug effects. Describe the contributions that the proposed study will make to the current knowledge base.*

*Include the following text as rationale for tobacco and alcohol use questionnaires if appropriate for cohort/agent and utilized in this study:*

Increasing evidence suggests that tobacco and alcohol use are risk factors in the development of intraepithelial neoplasia and cancer. In addition, tobacco and alcohol use may adversely affect agent intervention, for example by altering the safety profile or metabolism of a drug. Standardized assessments of tobacco and alcohol use during clinical trials will aid in understanding the potential relationship between the use of these products and clinical endpoints or cancer prevention biomarkers. Therefore, NCI, DCP is including assessment of tobacco and alcohol use at baseline and *(include follow-up timepoint*), to determine the potential impact of tobacco and alcohol use on 1) treatment toxicity and symptom burden, and 2) the efficacy of treatment intervention.

# 3. SUMMARY OF STUDY PLAN

*For the convenience of the reader, this section should provide a brief synopsis of the following points:*

* *Study design*
* *Number of participants to be enrolled (total number and number per arm)*

*Example: A maximum of 25 participants will be accrued into each of four intervention arms. Three additional participants are anticipated to accrue per arm to account for an anticipated dropout rate of 10%. Assuming a screening rate of approximately 25 participants per month and an accrual rate of approximately 8–10 participants per month, we expect the study to be complete within 18–24 months.*

* *Brief description of the study population*
* *Intervention plan, including doses, dose groups, and duration of exposure to the study agent.*

*Example: Participants will be given two 30 gram tubes of study agent at the baseline visit and at months 3, 6, 9, and 12. Participants will take study agent for 54 ± 2 weeks (minimum) to 102 ± 2 weeks (maximum). Duration of administration will depend on when a participant is randomized in relationship to when the final participant is randomized. The study will be terminated when all participants have…*

* *Description of run-in period, if applicable.*
* *Time points for performing study assessments*
* *Description of measurements taken to meet study objectives*
* *Description of clinical procedures, lab tests or other measurements taken to monitor effects of study agent on human safety and to minimize risks*
* *Duration of study*

# 4. Participant SELECTION

The Protocol Risk for Auditing for this study is (*please insert assigned risk low, intermediate or high*)

High Risk studies require 100% review and confirmation of eligibility of **all participants** by the LAO **prior to enrollment**

Low and Intermediate risk studies require confirmation of eligibility of the first two participants enrolled at each accruing LAO or AO. This review should take place as soon as possible but not more than two weeks following enrollment/randomization. Continuing eligibility review can be determined based on the LAO assessment of AO performance and protocol complexity.

For those international sites where data sharing is prohibited, this policy does not apply.

## 4.1 Inclusion Criteria

4.1.1 *Please insert specific health risk or disease requirements. State acceptable methods for assessing risk or disease requirements, e.g., risk assessment tools, clinical evaluation, pathology review criteria, etc. For populations with cancer or precancer, include requirements for histological confirmation of diagnosis, time from diagnosis, and disease status at entry.*

4.1.2 *Please state allowable type and amount of prior therapy, if applicable. Include separate definitions for duration as needed. Include site/total dose for prior radiation exposure as needed.*

4.1.3 *Specify age range. Please state reason for age restriction.* ***For example:***

Because no dosing or adverse event (AE) data are currently available on the use of *Study Agent*  in participants <18 years of age, children and adolescents are excluded from this study but will be eligible for future pediatric trials, if applicable.

4.1.4 *ECOG performance status ≤2 (Karnofsky ≥60%; see Appendix A) ) Please state reason for more restrictive performance status requirement*

4.1.5 Participants must have adequate organ and marrow function as defined below

*Insert baseline lab parameters appropriate to agent and cohort,* ***for example****:*

*Absolute neutrophil count ≥1,000/microliter*

*Platelets ≥100,000/microliter*

*Total bilirubin ≤ 1.5 x institutional upper limit of normal (ULN) Note: Higher total bilirubin levels (≤ 3 mg/dL) can be allowed if due to known benign liver condition, i.e. Gilbert’s*

*AST (SGOT)/ALT (SGPT) ≤3.0 × institutional upper limit of normal*

*Creatinine ≤1.5 × institutional upper limit of normal*

1. *These are guidelines that may or should be modified based on protocol-specific or drug development-specific needs.*
2. *Laboratory test results should only be used as exclusion criteria when scientifically justified and when abnormal test results confer safety concerns.*
3. *Laboratory reference values should account for potential normal variations due to race, ethnicity, age and sex.*

4.1.6 Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial

4.1.7 For individuals with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated

4.1.8 Individuals with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load

4.1.9 Individuals on chronic suppressive antiviral therapy for herpes simplex virus (HSV) are eligible

4.1.10 *Insert other appropriate inclusion criteria relevant to the methodology of the study.*

4.1.11 *Please use or modify the following paragraph as appropriate (if an agent has restrictions on pregnancy or sperm donation after stopping the agent, please include that language as well):*

The effects of  *Study Agent*  on the developing human fetus at the recommended therapeutic dose are unknown. For this reason and because  *Agent Class*  are known to be teratogenic, women of child-bearing potential and men must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) prior to study entry and for the duration of study participation or for *x* number of days after stopping the study agent. Additionally, men must not donate sperm for the purpose of reproduction during the study and for a minimum of *x* days after receiving the last dose of the study agent. Should a woman become pregnant or suspect she is pregnant while participating in this study, she should inform her study physician immediately.

4.1.8 Ability to understand and the willingness to sign a written informed consent document.

## 4.2 Exclusion Criteria

4.2.1 *List contraindications to participation based on agent pharmacology and metabolism, toxicology, clinical and methodology considerations.*

4.2.2 *Healthy volunteers may be required to demonstrate absence of chronic medical conditions or regular use of certain medications.*

4.2.3 Participants may not be receiving any other Investigational Agents.

4.2.4 History of allergic reactions attributed to compounds of similar chemical or biologic composition to  *Study Agent.*

4.2.5 Uncontrolled intercurrent illness., or psychiatric illness/social situations that would limit compliance with study requirements.

4.2.6 *The investigator(s) must state a medical or scientific reason if pregnant or nursing participants or participants who are cancer survivors or those who are HIV-positive will be excluded from the study. Detailed information regarding these special populations is available in the DCP Clinical Trials Reference Material located at* <https://prevention.cancer.gov/clinical-trials/clinical-trials-management/protocol-information-office/clinical-trials-reference>. *Suggested text is provided below:*

Pregnant women are excluded from this study because  *Study Agent is a/an Agent Class*  agent with the potential for teratogenic or abortifacient effects. Because there is an unknown but potential risk for AEs in nursing infants secondary to treatment of the mother with  *Study Agent,* Breastfeeding should be discontinued if the mother is treated with  *Study Agent.*

## 4.3 Inclusion of Women and Minorities

Both men and women (as applicable) and members of all races and ethnic groups are eligible for this trial.

*Women and members of minority groups and their subpopulations must be included in the study population of research involving human participants, unless a clear and compelling rationale and justification are provided indicating that inclusion is inappropriate with respect to the health of the participants or the purpose of the research. NIH requires accrual estimates by sex/race/ethnicity. This information should be recorded on the DCP PSW. Additional information regarding the NIH policy is available in the DCP Clinical Trials Reference Materials located at*  <https://prevention.cancer.gov/clinical-trials/clinical-trials-management/protocol-information-office/clinical-trials-reference>

## 4.4 Recruitment

*Complete the CP-CTNet Recruitment, Retention and Adherence Plan Outline Form which is one of the required Additional Study-Related Documents. This will include the specific strategies planned for pre-screening, screening, recruiting, consenting and protocol adherence of participants. Recruitment, Retention and Adherence Plans will include sex and minority-directed strategies and will be tailored to the characteristics of the individual protocol, sample size, target population, enrolling site(s) and resources. Since the Recruitment, Retention and Adherence Plan document is not part of the protocol document itself, please do not reference it in the protocol. In addition, any revisions to the initial plan reviewed and approved by the DCP Protocol and Safety Review Committee (PSRC), should be electronically submitted to the DCP Protocol Information Office for review by the PSRC.*

*In this section, in order to assure regulatory approval of the activities proposed for obtaining information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective participants without the informed consent of the prospective participant or the participant's legally authorized representative, please provide a description of the planned process, including explanation of how one of the following required conditions are met:*

*(1) The investigator will obtain information through oral or written communication with the prospective participant or legally authorized representative, or*

*(2) The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.*

## 4.5 Planned Accrual

*The targeted number of participants from ethnic and racial subpopulations should be proportionate to the prevalence distribution of the study cohort in the U.S. population. If the targets do not reflect the US population prevalence distribution, please provide justification.*

*The study population should be representative demographically (race, ethnicity, sex, age) of those affected by the disease or condition of interest, with the goal of study findings that are applicable to all populations affected and to provide the opportunity to participate to all affected or potentially affected populations. Please provide a breakdown of the prevalence of the disease being studied by race and ethnicity, to better justify the planned accrual numbers. As much as possible seek planned accrual numbers that correspond to disease prevalence among racial and ethnic categories. Provide racial and ethnic distribution of the study population being studied at each participating site.*

***Enter actual estimates, whole numbers only (percentages, fractions, or decimals are not acceptable). The total provided for Ethnicity must match the total given for Race.***

**Domestic (including Puerto Rico participants) Planned Enrollment Report**

|  | **Ethnic Categories** | | | | |
| --- | --- | --- | --- | --- | --- |
| **Racial Categories** | Not Hispanic or Latino:  Female | Not Hispanic or Latino:  Male | Hispanic or Latino:  Female | Hispanic or Latino:  Male | Total |
| American Indian/Alaska Native |  |  |  |  |  |
| Asian |  |  |  |  |  |
| Native Hawaiian or Other Pacific Islander |  |  |  |  |  |
| Black or African American |  |  |  |  |  |
| White |  |  |  |  |  |
| More Than One Race |  |  |  |  |  |
| Total |  |  |  |  |  |

**INTERNATIONAL (including Canadian participants) PLANNED ENROLLMENT REPORT**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Ethnic Categories** | | | | |
| **Racial Categories** | Not Hispanic or Latino:  Female | Not Hispanic or Latino:  Male | Hispanic or Latino:  Female | Hispanic or Latino:  Male | Total |
| American Indian/Alaska Native |  |  |  |  |  |
| Asian |  |  |  |  |  |
| Native Hawaiian or Other Pacific Islander |  |  |  |  |  |
| Black or African American |  |  |  |  |  |
| White |  |  |  |  |  |
| More Than One Race |  |  |  |  |  |
| Total |  |  |  |  |  |

# REGISTRATION PROCEDURES

## 5.1 Investigator and Research Associate Registration with CTEP

Food and Drug Administration (FDA) regulations require IND sponsors to select qualified investigators. NCI policy requires all persons participating in any NCI-sponsored clinical trial to register and renew their registration annually which is done via the Registration and Credential Repository (RCR).

To register, all individuals must obtain a [Cancer Therapy Evaluation Program (CTEP) Identity and Access Management (IAM) account](https://ctepcore.nci.nih.gov/iam). In addition, persons with a registration type of Investigator (IVR), Non-Physician Investigator (NPIVR), or Associate Plus (AP) (*i.e.*, clinical site staff requiring write access to Rave or acting as a primary site contact) must complete their annual registration using [CTEP’s web-based Registration and Credential Repository (RCR)](https://ctepcore.nci.nih.gov/rcr). Documentation requirements per registration type are outlined in the table below.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Documentation Required** | **IVR**  **(Investigator)** | **NPIVR**  **(Non-physician Investigator)** | **AP**  **(Associate Plus)** | **A**  **(Associate)** | **AB**  **(Associate Basic)** |
| FDA Form 1572 | ✔ | ✔ |  |  |  |
| Financial Disclosure Form | ✔ | ✔ | ✔ |  |  |
| NCI Biosketch (education, training, employment, license, and certification) | ✔ | ✔ | ✔ |  |  |
| GCP training | ✔ | ✔ | ✔ |  |  |
| CV (optional) | ✔ | ✔ | ✔ |  |  |

An active CTEP-IAM user account and appropriate RCR registration is required to participate in all CP-CTNet clinical trials.

All personnel directly involved in the performance of procedures required by the protocol and the collection of data should be registered in the RCR.

Personnel associated with the five registration types include, but is not limited to, the following:

* **Investigator (IVR)** — MD, DO, or international equivalent
* **Non-Physician Investigator (NPIVR)** — advanced practice providers (e.g., NP or PA) or graduate level researchers (e.g., PhD)
* **Associate Plus (AP)** — clinical site staff (e.g., RN or CRA) with data entry access to RAVE. Also includes site administrator, data administrator, and consenting person. Individuals with an auditing role should register as an AP.
* **Associate (A)** — other clinical site staff involved in the conduct of NCI-sponsored trials.
* **Associate Basic (AB)** — individuals (e.g., pharmaceutical company employees) with limited access to NCI-supported systems

In addition, the site protocol Principal Investigator (PI) must meet the following criterion:

* Active registration status
* The IRB number of the CIRB (IRB of record) listed on their Form FDA 1572

Additional information can be found on the CTEP website. For questions, please contact the RCR ***Help Desk*** by email at [RCRHelpDesk@nih.gov](mailto:RCRHelpDesk@nih.gov).

# NCI CENTRAL INSTITUTIONAL REVIEW BOARD

The NIH policy on the Use of a Single Institutional Review Board for Multi-Site Research <https://grants.nih.gov/grants/guide/notice-files/not-od-16-094.html>became effective on January 25, 2018. In compliance with this policy, [NCI Central IRB](https://www.ncicirb.org/) (NCI CIRB) is the sole IRB of record for all accruing sites conducting clinical trials through the CP-CTNet, all CP-CTNet U.S.-based sites must be members of the NCI CIRB, and utilize the Cancer Prevention and Control CIRB as their IRB of record. International sites should submit Research Ethics Board (REB) approval to the DCP Regulatory contractor following country-specific regulations.

Signatory Institutions must submit a Study Specific Worksheet (SSW) to the CIRB via the IRB Manager @ https://nci.my.irbmanager.com/Login.aspxto indicate their intent to open the study locally. The CIRB’s approval of the SSW is then communicated to the PIs at the Signatory Institution and the Regulatory Contractor. In order for the SSW approval to be processed, the Signatory Institution must inform which CIRB-approved institutions aligned with the Signatory Institution are participating in the study.

Should changes to the study become necessary, protocol amendments will be submitted to the DCP PIO according to DCP Amendment Guidelines. The DCP-approved amended protocol must be approved by the CIRB prior to implementation.

# 7. AGENT ADMINISTRATION

Intervention will be administered on an *inpatient/outpatient* basis. Reported AEs and potential risks are described in Section 6.2.

## 7.1 Dose Regimen and Dose Groups

*Please describe the regimen and dose groups. State any special precautions or warnings relevant for study agent administration. Each dose group should specify:*

* *Agent(s)*
* *Daily dose(s) and regimen(s) for each agent (e.g., two capsules bid)*
* *Duration (days/weeks/months) for each agent.*

## 7.2 (*Study Agent*)Administration

* *Indicate who will administer the agent,*
* *How much agent (*e.g.*, number of pills) should be administered at how many times/day (be specific; for example: 20 mg capsules, 100 capsules/bottle, 2 bottles distributed at the baseline visit and at months 3, 6, 9,* etc*.),*
* *Time of day dose is to be taken,*
* *Special instructions for taking the agent (*e.g.*, with morning meal).*

## 7.3 Run-in Procedures

*If the study includes a placebo run-in phase prior to randomization to assess compliance, please describe the procedure, including method of administering placebo, dose, duration, and methods for assessing compliance. Compliance should be clearly defined.*

## 7.4 Contraindications

*Indicate any restrictions that participants should follow when using the agent (e.g., limit sun exposure, dietary restrictions, etc.).*

## 7.5 Concomitant Medications

*Indicate any limitations on medications, herbs, and vitamin and mineral supplements (other than study agents) while participating in the study. Include time period for the limitation, if applicable.*

All medications (prescription and over-the-counter), vitamin and mineral supplements, and/or herbs taken by the participant will be documented and will include: 1) start and stop date, dose and route of administration, and indication. Medications taken for a procedure (*e.g*., biopsy) should also be included.

All vaccines received within the past 6 months should also be included.

## 7.6 Dose Modification

*Explicitly identify when dose modifications are appropriate. Modifications and the factors predicating dose modification should be explicit and clear. If dose modifications are anticipated, please provide a dose de-escalation schema with modifications expressed as a specific dose or amount rather than as a percentage of the starting or previous dose. Also indicate if the agent supply may be used for dose modifications or will an additional supply (smaller doses) be needed to achieve dose modification. If applicable, describe procedures for increasing dose following a toxicity-required dose reduction.*

## 7.7 Adherence/Compliance

7.7.1 *Provide* *a definition of compliance that will be used to describe when participants are considered evaluable for statistical analysis.*

7.7.2 *Describe* *the method(s) used to monitor each* *participant’s agent compliance. Methods may include diaries, pill counts, drug/metabolite plasma levels, and/or drug effect biomarkers.*

# 8. PHARMACEUTICAL INFORMATION

## 8.1 *Study Agent* (*IND #, IND Sponsor*)

*Confidential pharmaceutical information for investigational study agents supplied by NCI, DCP will be provided as an attachment to the Concept Submission form approval letter and should be inserted here.*

*Non-DCP supplied agents: insert appropriate agent information here. Specify:*

* *Formulation to be used in this study*
* *Justification for this formulation if other formulations are available,*
* *Physical description of agent*
* *List of excipients*

## 8.2 Reported Adverse Events and Potential Risks

*Describe the toxicity profile and related data for the agent at the selected doses and schedule. For vaccine/immunologic studies, include solicited local and systemic reactogenicity events for which causality can be reasonably attributed to vaccination.*

## 8.3 Availability

*Study Agent* is an Investigational Agent supplied to investigators by the Division of Cancer Prevention (DCP), NCI*.*

*Example: Agent A and Agent B are Investigational Agents for chemoprevention studies provided by NCI/DCP. Agent C will be supplied to NCI/DCP by XXX (20 mg capsules, 30 capsules/bottle). Agent D and matching placebo D will be supplied to NCI/DCP by XXX (50 mg capsules, 30 capsules/bottle).*

*Non-DCP supplied agents: delete the above statement and specify source and availability of supply.*

*Example: Agent XXX and matching placebo will be manufactured and supplied by XXX. Agent XXX and matching placebo will be packaged by (name the co. responsible for packaging the study supply) and supplied in bottles containing 100 capsules.*

*If the study agent is provided by NCI under a Clinical Trials Agreement (CTA) with the manufacturer, the appropriate text below must be included in the protocol and the* ***irrelevant text deleted****. Information on the study agent’s CTA status will be provided in Concept Submission form approval letter.*

*Study Agent* is provided to the NCI under a Clinical Trials Agreement (CTA) between *Agent Manufacturer*  and the DCP, NCI (see §14.7)*.*

## 8.4 Agent Distribution

Agents will only be released by NCI, DCP after documentation of CIRB approval of the DCP-approved protocol and consent is provided to DCP and the collection of all Essential Documents is complete (see DCP website for description of Essential Documents).

NCI, DCP-supplied agents may be requested by the Investigator (or his/her authorized designees) at each Organization. DCP guidelines require that the agent be shipped directly to the institution or site where the agent will be prepared and administered. DCP does not permit the transfer of agents between institutions (unless prior approval from DCP is obtained). DCP does not automatically ship agents; the site must make a request. Agents are requested by completing the DCP Clinical Drug Request form: <https://prevention.cancer.gov/clinical-trials/clinical-trials-management/cp-ctnet-instructions-forms-and-templates> (to include complete shipping contact information) and e-mailing the form to the DCP agent repository contractor:

MRIGlobal

DCP Repository

1222 Ozark Street

North Kansas City, MO 64116

Phone: (816) 753-7600

E-mail: NCI.DCP@mriglobal.org

*For non-DCP supplied agents indicate the manufacturer, supplier and mechanism for distribution. DCP procedures for agent distribution and the required forms are available on the DCP website.*

## 8.5 Agent Accountability

The Investigator, or a responsible party designated by the Investigator, must maintain a careful record of the inventory and disposition of all agents received from DCP. The Investigator is required to maintain adequate records of receipt, dispensing and final disposition of study agent. This responsibility has been delegated to \_\_\_\_ [*insert responsible party] \_\_\_.* Include on receipt record from whom the agent was received and to whom study agent was shipped, date, quantity and batch or lot number. On dispensing record, note quantities and dates study agent was dispensed to and returned by each participant.

## 8.6 Packaging and Labeling

\_\_\_[Agent]\_\_ will be packaged by \_\_[manufacturer or NCI, DCP]\_\_\_.

*The DCP agent repository contractor will package, label, and distribute agent for all DCP-supplied agents. Occasionally, a pharmaceutical collaborator or the site may perform one or more of these activities. The DCP agent repository contractor will send a draft label to the Protocol PI, the DCP Medical Monitor, DCP Scientific Lead, DCP Nurse Consultant, and the DCP regulatory support contractor for review and approval. Final labels are printed and attached to the bottle prior to shipping to the site. DCP will provide information regarding packaging (container, amount of agent per container) and labeling The information provided by DCP should be inserted into this section of the protocol.*

*Example: Each bottle will be labeled with a one-part label identifying study specific information, such as Study title, DCP protocol number, dosing instructions, recommended storage conditions, the name and address of the distributor, randomization number, and a caution statement indicating that the agent is limited by United States law to investigational use only and the agent should be kept out of reach of children.*

*Protocols using non-DCP supplied agents: describe in detail how the agent will be packaged and distributed, including container, amount of agent per container, container label information, and if blinded, how the label will be constructed to maintain the blind. Label information should include dose, number of doses per day, time of day for dosing, with or without food, and any other specific instructions.*

## 8.7 Storage

*Provide instructions regarding proper storage of the agent at the study site(s). Storage temperatures should be expressed as a range, not a specific number. For example, room temperature should be specified (e.g., between 59°F and 86°F). Refer to the Pharmacy Manual for the Temperature Excursion policy and procedure(s). The Pharmaceutical partner (if required), CP-CTNet LAO, the DCP agent repository contractor, DCP Medical Monitor and Nurse Consultant should be notified in the event of a Temperature Excursion.*

## 8.8 Registration/Randomization

This trial will use a web-based Registration/Randomization System, developed and maintained by the CP-CTNet Data Management, Auditing, and Statistical Center (DMASC). The Help Desk includes technical personnel and administrators of the registration programs at the Data Management Center in Amherst, NY, USA. The Help Desk is available round the clock 7 days per week, except for New Year's Eve, Memorial Day, Independence Day, Thanksgiving Day, and Christmas Day.

Frontier Science Randomization Help Desk

4033 Maple Rd, Amherst, NY 14226 USA

Phone: +1 716 834 0900 Extension 7301

Email: [UserSupport\_CP-CTNet@frontierscience.org](mailto:UserSupport_CP-CTNet@frontierscience.org)

*Give specific details on how a participant will be registered in a trial. Registration and randomization, if applicable, will be performed through the DMASC portal. Describe the procedure for randomizing a participant to a dose group.*

Note: The Registration and Randomization process is documented in the "Stars User Guide".

## 8.9 Blinding and Unblinding Methods

*For blinded studies, describe blinding and unblinding methods and procedures. Address the following points:*

* *Procedure for retaining the blind (including specific procedures for protecting the blind should data collected in the study offer evidence of a participant’s assignment to a particular study arm)*
* *If the study allows for some investigators to remain unblinded (e.g., to allow them to adjust medication), the means of shielding other investigators should be explained*
* *Describe efforts to ensure that the study intervention and control/placebo are as indistinguishable as possible*
* *Measures to prevent unblinding by laboratory measurements, if used, should be described*
* *Individual authorized to break the blind (the local PI and the Protocol PI must be notified)*
* *Circumstances for breaking the blind (including breaking the blind for an individual or for all participants (e.g. for serious adverse events (SAEs)).*
* *Procedure for breaking the blind*
* *A description of plans to manage and report inadvertent unblinding*

*The NCI Medical Monitor must be notified anytime that the blind has been broken.*

*Provide DCP Medical Monitor Name and title (see Concept Submission* *Decision Letter)*

NCI/Division of Cancer Prevention

*Insert the full contact information including address, telephone number, , and email of the DCP Medical Monitor*

## 8.10 Agent Destruction/Disposal

*DCP supplied commercial agents: at the completion of investigation, unused study agent may be destroyed on site via local institutional procedures and provide documentation of destruction to NCI, DCP Repository or unused agent may be returned to NCI, DCP Repository according to the DCP “Guidelines for AGENT RETURNS” and using the DCP form “DCP Returned Agents List”.*

*Non-DCP agents, please provide the procedure for handling the unused drug: method of disposal, documentation of disposal, and any other relevant standard operating procedures.*

# 9. CLINICAL EVALUATIONS AND PROCEDURES

## 9.1 Schedule of Events

*A table that lists baseline testing/pre-study evaluation, agent administration, study assessments, procedures and case report forms should be included. Tobacco and alcohol use assessments should be included at baseline and end of treatment or follow-up if utilized in this study. A sample schedule of events is provided on the following page. The protocol should state the expected duration of participation in the study and the sequence and duration of all study periods, including follow-up, if any.*

## 9.2 Baseline Testing/Pre-Study Evaluation

*Describe all procedures (including registration and randomization) that must be completed for a participant before the study intervention may begin. Note any time restrictions for testing (e.g., pre-study labs must be done <14 days prior to registration). Include tobacco and alcohol use assessment, using the Baseline questionnaires if utilized in this study.*

*Specify the amount of study agent that will be distributed to the participant at each visit. Also describe how the participant will return study agent, for example: Day 0, participants will be randomized to receive either study agent or placebo and will be given a supply of study agent (3 bottles for a total of 90 capsules); day 60, participants will return any unused study agent and will be given a supply of study agent (3 bottles for a total of 90 capsules).*

*Refer to §7.3, Run-In Procedures, if applicable.*

## 9.3 Evaluation During Study Intervention

*Indicate the procedures to be performed during the study intervention phase. Include language regarding PI review of safety labs or other diagnostic testing prior to intervention administration if appropriate.* *For vaccine/immunologic studies, include use of a participant-completed Vaccine Report Card* (*Appendix <#>)* *to solicit local and systemic/vital sign reactogenicity events during a specified time period as described in §13.1.3.2.*

## 9.4 Evaluation at Completion of Study Intervention

*Specify the evaluations that must be performed upon discontinuation of study agent. Ensure that these evaluations are consistent with the endpoints described in the objectives and statistical analysis sections of the protocol. Include tobacco and alcohol use assessments, using the Follow-up questionnaires if utilized in this study..*

## 9.5 Post-intervention Follow-up Period

*If a defined post-intervention follow-up period is required, specify observations or tests to be performed. Define the length and purpose of the follow-up period.*

## 9.6 Methods for Clinical Procedures

*If applicable, document any special processes, instructions or methodology for clinical procedures required by the protocol, such as invasive procedures and imaging. Include special instructions for procedure prep (*e.g.*, NPO after midnight) and scheduling instructions for tests that may be available only at certain locations or times. . Include language regarding PI review of safety labs or other diagnostic testing prior to intervention administration if appropriate.*

**SCHEDULE OF EVENTS**

| **Evaluation/ Procedure** | **Registration** | **Baseline** | **Randomization** | **Months 1–3** | **Months 4–5** | **Month 6 or Early Termination** | **Follow-Up Visit** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Informed Consent | X |  |  |  |  |  |  |
| Assess Eligibility | X | X |  |  |  |  |  |
| Medical History |  | X |  |  |  |  |  |
| Physical Exam |  | X |  |  |  |  |  |
| Vital Signs/ Height and Weight |  | X |  | X |  | X |  |
| Laboratory Tests |  | X |  | X |  | X |  |
| X-Rays |  | X |  |  |  | X |  |
| EKG |  | X |  |  |  | X |  |
| Biopsies |  | X |  |  |  | X |  |
| Biomarkers |  | X |  |  |  | X |  |
| Study Evaluations/ Assessments |  | X |  | X |  | X |  |
| Tobacco and Alcohol Use Assessment \* |  |  |  |  |  |  |  |
| Concomitant Medications |  | X |  | X | X | X | X |
| Dispense Study Agent |  |  | X | X |  |  |  |
| Collect Study Agent |  |  |  |  |  | X |  |
| Review Agent Diary/Record |  |  | X | X |  | X |  |
| *Vaccine Report Card (if applicable)* |  |  |  |  |  |  |  |
| Adverse Events |  |  |  | X | X | X | X |
| Telephone Contact |  |  |  |  | X |  |  |

# \* If utilized in this study

# 10. CRITERIA FOR EVALUATION AND ENDPOINT DEFINITION

*Delineation of study endpoints, methods for measuring or evaluating, and timing of endpoint ascertainment should be described here.*

## 10.1 Primary Endpoint

*Depending on the study hypotheses and design, the primary endpoint may be an incidence of invasive or preinvasive disease (*e.g*., polyp incidence), clinical response (*e.g*., change in number and severity of leukoplakia by physical exam), histologic or cytologic response (*e.g*., change in severity of dysplasia in biopsy materials), and/or modulation of surrogate endpoint biomarkers (SEBs). Define endpoints clearly and briefly describe methods and intervals for assessment. A detailed description of methods should be included in the Pharmacokinetic and Biomarker Method Development Report document (part of the Additional Study-Related Documents that are submitted with the protocol) as appropriate. Do not reference the Pharmacokinetic and Biomarker Method Development Report here since it is not an actual part of the protocol.*

## 10.2 Secondary Endpoints

*As appropriate, secondary endpoints (serum/plasma/tissue agent/metabolite levels, other agent effect biomarkers) should be defined clearly and prioritized. Methods for assessment should be referenced in this section with detailed descriptions of laboratory and computer modeling procedures provided in the required “Pharmacokinetic and Biomarker Method Development Report” document (part of the additional Study-Related Documents).*

## 10.3 Off-Agent Criteria

Participants may stop taking study agent for the following reasons: completed the protocol-prescribed intervention, AE or serious adverse event (SAE), inadequate agent supply, noncompliance, concomitant medications, medical contraindication, or *specify other reasons, if applicable*. Participants will continue to be followed, if possible, for safety reasons and in order to collect endpoint data according to the schedule of events. *The protocol should state whether and how participants are to be replaced, if applicable.* *The approach to handling withdrawals and protocol non-compliance, i.e., whether participants will be included in the “intent-to-treat” population, replaced, etc. should be described in Section 15.6.**Reporting and Exclusions. For vaccine/immunologic studies, state that local and systemic/vital sign reactogenicity events ≤grade 3 are generally not included as part of AE-related off-agent criteria because they are usually anticipated, self-limiting, have little or no impact on daily activities, and infrequently require treatment.*

## 10.4 Off-Study Criteria

Participants may go ‘off-study’ for the following reasons: the protocol intervention and any protocol-required follow-up period is completed, AE/SAE, lost to follow-up, non-compliance, concomitant medication, medical contraindication, withdraw consent, disease progression, refuse to follow up, physician decision, death, protocol violation, study complete, determination of ineligibility (including screen failure), pregnancy, or *specify other reasons, if applicable.* *For vaccine/immunologic studies, state that local and systemic/vital sign reactogenicity events ≤grade 3 are generally not included as part of AE-related off-study criteria because they are usually anticipated, self-limiting, have little or no impact on daily activities, and infrequently require treatment.*

## 10.5 Study Termination

NCI, DCP as the study sponsor has the right to discontinue the study at any time.

# 11. CORRELATIVE/SPECIAL STUDIES

## 11.1 Rationale for Methodology Selection

*Provide the rationale for selecting the assay methodology, particularly in cases where various assays are available that may assess different qualities of the marker (example: mutation analysis* vs*. IHC for p53; gene expression vs. protein expression). Methodology should be included, as appropriate, in the Pharmacokinetic and Biomarker Methods Development Report.*

## 11.2 Comparable Methods

*Discuss the comparability of the methods proposed to those previously used and the likelihood that the resulting data will be able to be compared to existing data.*

# 12. SPECIMEN MANAGEMENT

## 12.1 Laboratories

*Identify the laboratory(ies) that will perform each analysis for each specimen. Where appropriate, list individuals who will perform analysis and/or procedures for conducting consensus reviews of specimens.*

## 12.2 Collection and Handling Procedures

*For each type of specimen obtained, please describe the following*

* *Amount to be collected*
* *When specimen should be obtained (*e.g*., fasting, prior to a.m. dose)*
* *Processing of specimen (*e.g*., details of tissue fixation, embedding, processing and sectioning)*
* *Labeling of specimen*
* *Tracking of specimens (*e.g.*, logs or tracking sheets for participants)*
* *Temperature storage requirements*
* *Storage duration*

*Note: If this section is too lengthy, please place this information in an appendix to the protocol.*

## 12.3 Shipping Instructions

*Include this section only if specimens will be shipped to an off-site laboratory for analysis. For each specimen, describe the following: packaging, carrier requirements, when specimens may be shipped, and name, address, and telephone number of the person to whom the specimens are being sent.*

All samples will be shipped in compliance with the International Air Transport Association (IATA) Dangerous Goods Regulations.

## 12.4 Tissue Banking

*Indicate methods and procedures for tissue banking here.*

The NCI reserves the right to require the transfer of biologic specimens and data, or true copies of such data, acquired from research supported under this award to an eligible third party. This transfer can occur in order to preserve the specimens and data and/or to continue the research. Third parties supported under this award must be informed of this right.

# 13. REPORTING ADVERSE EVENTS

DEFINITION: An adverse event (AE) means any untoward medical occurrence associated with the use of a drug in humans, whether or not the untoward occurrence is considered drug related. Thus, an AE can include any unfavorable and unintended sign (e.g., an abnormal laboratory finding), symptom, or clinical outcome temporally associated with the use of a test drug, active control, or placebo, regardless of whether the event is thought to be related to the drug. An AE can arise with the use of a drug or biologic (e.g., use for a purpose other than FDA-approved indication or in combination with another drug) and with any route of administration, formulation, or dose, including an overdose.

Please note that, after baseline assessment, all abnormal clinical laboratory values determined to be of clinical significance based on a physician’s assessment are to be reported as AEs. A clinically significant lab value is one that indicates a new disease process, an exacerbation or worsening of an existing condition, or requires further action(s) to be taken**.** Those labs determined to be of no clinical significance or of unknown clinical significance (per the physician’s assessment) should not be reported as AEs. Any lab value of unknown clinical significance should continue to be investigated/followed-up further for a final determination, if possible. (See the [*DCP Baseline and Adverse Event Reporting Guidelines*](https://prevention.cancer.gov/clinical-trials/clinical-trials-management/cp-ctnet-instructions-forms-and-templates)for more detail on reporting abnormal clinical laboratory values.)

A list of AEs that have occurred or might occur can be found in §8.2 Reported Adverse Events and Potential Risks, as well as the Investigator’s Brochure or package insert.

## 13.1 Adverse Events

13.1.1 Reportable AEs

All AEs that occur after the informed consent is signed and baseline assessments are collected must be recorded on the AE CRF whether or not related to study agent.

13.1.2 AE Data Elements:

The following data elements are required for AE reporting.

* AE verbatim term
* NCI Common Terminology Criteria for Adverse Events version 6.0 (CTCAE v6.0) AE term (MedDRA lowest level term)
* CTCAE (MedDRA) System Organ Class (SOC)
* Event onset date and event end date
* Treatment assignment code (TAC) at time of AE onset
* Severity grade
* Attribution to study agent (relatedness)
* Whether or not the event was reported as a SAE
* Whether or not the participant dropped due to the event
* Outcome of the event

*For vaccine/immunologic agents, add “AESI term and severity grading (see 13.1.3.2)” to the list of AE data elements for local and systemic reactogenicity events.*

13.1.3 Severity of AEs

13.1.3.1 Identify the AE using CTCAE v6.0\*\*. The CTCAE provides descriptive terminology (MedDRA lowest level term) and a severity grading scale for each AE listed. A copy of the CTCAE can be found at https://dctd.cancer.gov/research/ctep-trials/for-sites/adverse-events

AE severity will be assessed according to the grade associated with the CTCAE term. AEs that do not have a corresponding CTCAE term will be assessed according to the general guidelines for grading used in the CTCAE v6.0. as stated below.

**(\*\* studies currently accruing using CTCAE 5.0 will continue using CTCAE 5.0**)

*For vaccine/immunologic studies, add a reference to the additional severity grading scale and instructions for local/systemic post-immunization reactions in 13.1.3.1.*

**CTCAE v6.0 general severity guidelines:**

| Grade | Severity | Description |
| --- | --- | --- |
| 1 | Mild | Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated. |
| 2 | Moderate | Moderate; minimal, local or noninvasive intervention indicated;  limiting age-appropriate instrumental activities of daily living (ADL)\*. |
| 3 | Severe | Severe or medically significant but not immediately life-threatening;  hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL\*\*. |
| 4 | Life-threatening | Life-threatening consequences; urgent intervention indicated. |
| 5 | Fatal | Death related to AE. |

\*Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, *etc*.

\*\*Self-care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

*Include the section below for all vaccine/immunologic studies.*

13.1.3.2 Vaccine/Immunologic-related Adverse Events

Reactogenicity refers to the subset of systemic/vital sign and local events that occur soon after administration of a vaccine/immunologic and are anticipated as a manifestation of the immune response. The reactions listed in the table below, considered Adverse Events of Special Interest (AESIs), will be solicited from the time of each vaccination/immunization up to 7 days post-vaccination/immunization through use of a participant-completed Vaccine Report Card (Appendix <#>). If any of the listed reactions occur outside the time period for solicitation, they will be considered non-reactogenic AEs, and recorded and graded as described in §13.1.3.1. If any of the listed reactions has one of the serious outcomes in §13.2.1, the event will be recorded and graded as described below and reported as described in §13.2.2.

*In the table below, list the anticipated local and systemic (including vital signs) reactogenicity events for which causality can be reasonably attributed to the specific vaccine/immunologic.*

| **Local Reactions** | **Systemic Reactions** |
| --- | --- |
| Pain | *Chills* |
| Tenderness | *Fever* |
| Erythema | *Myalgia* |
| Induration/swelling | *Joint pain* |
| *Itching* | *Headache* |
| *Bruising* | *Arthralgi* |
| *Rash (at injection site)* |  |
|  |  |

All AESIs related to reactogenicity (as listed above) should be captured in Rave as they occur and reported expeditiously. These systemic and local AESIs will be reported and graded for severity separately from non-reactogenic AEs since they are not currently part of CTCAE v6. Systemic and local AESIs will be reported using the respective terms “Post-immunization reaction (systemic)” and “Post-immunization reaction (local)” in the SOC “Injury, poisoning and procedural complications” and graded according to the severity guidelines in the tables below. The relationship of AESIs to treatment will also be assessed as described in 13.1.3. These terms, severity grades, and relationship assessments will be used in regulatory and other reporting.

**Post-Vaccination/Immunization Systemic Reactions**

|  |  |  |
| --- | --- | --- |
| **CTCAE SOC/AESI Term** | **Grade** | **Grading Description** |
| Injury, poisoning and procedural complications – Other, specify – Post-immunization reaction (systemic) | 1 | Mild pain; fever |
| Injury, poisoning and procedural complications – Other, specify – Post-immunization reaction (systemic) | 2 | Moderate pain; antipyretics indicated; limiting instrumental ADL or mild/moderate impact on age-appropriate normal daily activity (pediatric) |
| Injury, poisoning and procedural complications – Other, specify – Post-immunization reaction (systemic) | 3 | Severe pain; hospitalization; limiting self-care ADL or severe impact on age-appropriate normal daily activity (pediatric) |
| Injury, poisoning and procedural complications – Other, specify – Post-immunization reaction (systemic) | 4 | Life-threatening consequences; urgent intervention indicated |
| Injury, poisoning and procedural complications – Other, specify – Post-immunization reaction (systemic) | 5 | Death |

 Abbreviations: ADL = activities of daily living; AESI = Adverse Event of Special Interest; SOC = System Organ Class.

**Post-Vaccination/Immunization Local Reactions**

| **CTCAE SOC/AESI Term** | **Grade** | **Grading Description** |
| --- | --- | --- |
| Injury, poisoning and procedural complications – Other, specify – Post-immunization reaction (local) | 1 | Pain; tenderness, mild discomfort to touch; erythema/redness 2.5–5 cm; induration/swelling 2.5–5 cm |
| Injury, poisoning and procedural complications – Other, specify – Post-immunization reaction (local) | 2 | Pain with repeated use of non-narcotic pain reliever >24 hours; tenderness, discomfort with movement; erythema/redness 5.1–10 cm; induration/swelling 5.1–10 cm or limiting instrumental ADL or mild/moderate impact on age-appropriate normal daily activity (pediatric); lipodystrophy; edema; phlebitis |
| Injury, poisoning and procedural complications – Other, specify – Post-immunization reaction (local) | 3 | Pain with any use of narcotic pain reliever; tenderness with significant discomfort at rest; erythema/redness >10 cm; induration/swelling >10 cm; limiting self-care ADL or severe impact on age-appropriate normal daily activity (pediatric) |
| Injury, poisoning and procedural complications – Other, specify – Post-immunization reaction (local) | 4 | Life-threatening consequences; necrosis or exfoliative dermatitis |
| Injury, poisoning and procedural complications – Other, specify – Post-immunization reaction (local) | 5 | Death |

 Abbreviations: ADL = activities of daily living; AESI = Adverse Event of Special Interest; SOC = System Organ Class.

13.1.3 Assessment of relationship of AE to treatment

The possibility that the AE is related to study agent will be classified as one of the following: unrelated, unlikely, possible, probable, definite. Criteria for these classifications are provided in DCP’s *Serious Adverse Event Report Form: Instructions for Completion and Submission* **(**[**https://prevention.cancer.gov/clinical-trials/clinical-trials-management/cp-ctnet-instructions-forms**](https://prevention.cancer.gov/clinical-trials/clinical-trials-management/cp-ctnet-instructions-forms)**).**

13.1.4 Follow-up of AEs

All AEs, including lab abnormalities that in the opinion of the investigator are clinically significant, will be followed according to good medical practices and documented as such. *The protocol should state the maximum length of time for follow-up of clinically significant AEs appropriate for the study (e.g., through 30 days after the end of intervention).*

13.1.5 Collection of AEs

*The protocol should state the maximum length of time during which AEs will be collected for each participant (e.g., through 30 days after the end of intervention).*

## 13.2 Serious Adverse Events

13.2.1 DEFINITION: Regulations at 21 CFR §312.32 define an SAE as any untoward medical occurrence that at any dose has one or more of the following outcomes:

• Death

• A life-threatening AE

(According to FDA safety guidance, an AE is considered life-threatening if, in the view of either the investigator or sponsor, its occurrence places the subject at immediate risk of death. It does not include an event that, had it occurred in a more severe form, might have caused death. Example: An allergic reaction resulting in angioedema of the larynx, allergic bronchospasm or anaphylaxis is considered life-threatening; however, an allergic reaction resulting only in a localized rash is not life-threatening.)

• In patient hospitalization or prolongation of existing hospitalization

(NCI, DCP uses admission or stay (including emergency room) equal to or greater than 24 hours as the definition of hospitalization. Exceptions are hospitalization for treatment of a pre-existing condition [unless the condition increased in severity on study], outpatient surgery, planned/elective procedures, and procedures described in the protocol [e.g., pharmacokinetic sampling, surgery] even if the hospital stay is of the described length; however, it does include events resulting from any of these that fulfill other serious outcome criteria, e.g., prolongation of hospitalization or life-threatening.)

• A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions

• A congenital anomaly or birth defect

• Important medical events that may not be immediately life-threatening or result in death or hospitalization should also be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and may require intervention to prevent one of the other outcomes listed above.

* + 1. Reporting SAEs to DCP
       1. An AE fulfilling one or more of the above criteria should be reported as an SAE to DCP regardless of attribution or grade as described below.

*The regulations at 21 CFR §312.64(b) provide an exception for reporting study endpoints used as outcomes to assess efficacy. For trials designed to evaluate the effect of an agent on disease-related mortality or major morbidity, those study endpoints that fulfill any of the serious criteria above (e.g., new cancer diagnosis, death) should only be reported to DCP as SAEs if there is evidence suggesting a causal relationship between the agent and the event. If applicable, state what study endpoints may not be immediately reported to DCP as SAEs (as described in 13.2.2.2‒13.2.2.4) and describe an alternate reporting process. Also, trials may evaluate the effect of an agent on pre-specified adverse events (safety endpoints).*

* + - 1. The accruing LAO and all Affiliated Organizations (AOs) will report SAEs on the DCP SAE Report Form as described in [DMASC’s CP-CTNet SOP 02-01](https://www.cp-ctnet-dmacc.org/static/resources/CP-CTNet_Manual_of_Standard_Operating_Procedures.pdf) and [DCP’s *Serious Adverse Event Report Form: Instructions for Completion and Submission*](https://prevention.cancer.gov/clinical-trials/clinical-trials-management/cp-ctnet-instructions-forms-and-templates).

13.2.2.3 Contact the DCP Medical Monitor, Protocol PI, and DCP Regulatory Contractor’s Safety Department within 24 hours of knowledge of the event. Contact via email is preferred, but phone contact is acceptable.

*Provide DCP Medical Monitor Name and title (see Concept Approval Letter)*

NCI/Division of Cancer Prevention

*Insert the full contact information including address, telephone number, and email of the DCP Medical Monitor.*

The contact information for the DCP Regulatory Contractor’s Safety Department is: phone: 650-691-4400 x133; email: [safety@ccsainc.com](mailto:safety@ccsainc.com)).

Include the following information when contacting the DCP Medical Monitor, Protocol PI, and DCP Regulatory Contractor’s Safety Department:

* + - * Participant ID
      * Date and time of SAE onset
* Date and time the accruing LAO or AO was notified about the SAE by the study participant or other person(s)
  + - * Name of person reporting the SAE
      * Call back phone number and email address
      * Accruing LAO or AO at which the subject is enrolled
      * DCP protocol number
      * Title of protocol
      * Suspected drugs (if any)
      * Description of the SAE, including attribution to the Investigational Agent

13.2.2.3 The accruing LAO and AOs will email written SAE reports to the DCP Medical Monitor, Protocol PI, LAO Coordinator, and DCP Regulatory Contractor’s Safety Department within 48 hours of learning of the event using the Word SAE Report Form.

*For Cross-Network Trials, in addition to the above, state that the accruing LAO or AO where the SAE occurred must also send the SAE Report Form to the Lead LAO Coordinator and Collaborating LAO Coordinator within 48 hours of knowledge (see REFGD06 Cross-Network Trials Guidelines for more information).*

13.2.2.4 The DCP Medical Monitor and the DCP Regulatory Contractor will determine which SAEs require submission to FDA or the manufacturer as expedited safety reports.

13.2.2.5 The accruing LAO and AOs will comply with applicable regulatory requirements related to reporting SAEs to the CIRB and local IRB/IEC as applicable. Specifically, if an SAE meets the definition of an unanticipated problem (UP; i.e., requires expedited reporting to FDA or the manufacturer as a safety report [serious, unexpected, and related to a study agent]), then it needs to be reported to the CIRB by the Signatory Institution PI at the accruing LAO or AO where the SAE occurred (see SOP 02-02 *Reporting Protocol Deviations* for more information). In addition to CIRB requirements, UPs must be reported to the accruing LAO’s or AO’s local IRB per local requirements.

13.2.3 Follow-up of SAE

Accruing LAO or AO staff should send follow-up reports as requested when additional information is available. Additional information should be entered on the DCP SAE Report Form in the appropriate format. Follow-up information should be sent to the DCP Medical Monitor, Protocol PI, LAO Coordinator, and DCP Regulatory Contractor’s Safety Department as soon as available. *For Cross-Network Trials, state that the Lead LAO Coordinator and Collaborating LAO Coordinator should also be copied.*

*The protocol should state the length of time for follow-up of an SAE.*

# 14. STUDY MONITORING

## 14.1 Data Management

This study will report clinical data using Medidata RAVE, a cloud–based clinical trials data management system managed by the DMASC. RAVE will be the database of record for the protocol and subject to NCI and FDA audit. All RAVE users will be trained to use the system and will comply with the instructions in the guidelines provided to the LAO by the DMASC as well as applicable regulatory requirements such as 21 CFR; Part 11.

*An approved Master Data Management Plan that is applicable to all studies within the CP-CTNet will be available. Study-specific data management plans will be developed by the DMASC and the LAO as required.*

## 14.2 Electronic Case Report Forms

The System Variable and Attribute Report (SVAR) template will be used to create the study-specific eCRFs or SVAR workbook. DMASC will contact the LAO to determine if a meeting is needed to discuss the trial and eCRFs before the DMASC creates the draft SVAR. *The SVAR template contains NCI Common Data Elements (CDEs) to facilitate data collection and analysis across studies. The SVAR template may require modification to capture the unique data elements (*i.e*., biomarkers) of each protocol and prepare a protocol-specific SVAR workbook. NCI CDEs, where available, shall be used for the initial SVAR workbooks and all subsequent workbook modifications.*

*DCP will sign-off on the final SVAR workbook prior to study initiation. The SVAR workbook may require changes throughout the conduct of the clinical trial. The need for change may result from protocol amendments or other reasons. Amended SVAR workbooks and attachments must be submitted to the DCP Protocol Information Office.*

More detailed information about the SVAR development process is available at: [Program Resources | CP-CTNet DMASC website (cp-ctnet-dmacc.or](https://www.cp-ctnet-dmacc.org/public/program-resources/)[[cp-ctnet-dmasc.org](https://www.cp-ctnet-dmacc.org/public/program-resources/)](https://gcc02.safelinks.protection.outlook.com/?url=http%3A%2F%2Fcp-ctnet-dmasc.org%2F&data=05%7C02%7Clisa.bengtson%40nih.gov%7C295cbdfbadec424ef76f08ddf6c099b7%7C14b77578977342d58507251ca2dc2b06%7C0%7C0%7C638938029254936200%7CUnknown%7CTWFpbGZsb3d8eyJFbXB0eU1hcGkiOnRydWUsIlYiOiIwLjAuMDAwMCIsIlAiOiJXaW4zMiIsIkFOIjoiTWFpbCIsIldUIjoyfQ%3D%3D%7C0%7C%7C%7C&sdata=CC3871%2F5GL6vy8Mj7RPiQgtexTgTavr73kkI2HHPiUA%3D&reserved=0)[)](https://www.cp-ctnet-dmacc.org/public/program-resources/)

## 14.3 Source Documents

*The protocol should state what constitutes a source document. Data recorded directly on the eCRFs (*i.e*., no prior written or electronic record of data), which will be considered as source data should be identified.*

## 14.4 Data and Safety Monitoring Plan

*NIH and NCI policy requires a Data and Safety Monitoring Plan (DSMP) to document the institution’s procedures to ensure safety of participants, validity of data, and the appropriate termination of studies for which significant benefits or risks have been uncovered or when it appears that the trials cannot be concluded successfully. Risks associated with participation in research must be minimized to the extent practical and the method and degree of monitoring should be commensurate with risk. The guidelines, essential elements and sample plans are available at:* <http://cancercenters.cancer.gov/GrantsFunding/DSMPRevCriteria>. *Please note that the requirements differ depending on whether a trial is conducted under an IND.*

*An approved Master DSMP applicable to all studies within an LAO Network will be on file at DCP. If there are any changes required to the Master DSMP that are specific to this protocol only, then DSMP Attachment #1 should be submitted with the protocol as part of the set of “Additional Study-Related Documents”.*

*Please provide a brief summary of the Master DSMP in this section.*

## 14.5 Sponsor or FDA Monitoring

The NCI, DCP (or their designee), pharmaceutical collaborator (or their designee), or FDA may monitor/audit various aspects of the study. These monitors will be given access to facilities, databases, supplies and records to review and verify data pertinent to the study.

## 14.6 Record Retention

Clinical records for all participants, including eCRFs, all source documentation (containing evidence of study eligibility, history and physical findings, laboratory data, results of consultations, etc.), as well as NCI CIRB records and other regulatory documentation will be retained by the Investigator in a secure storage facility in compliance with Health Insurance Portability and Accountability Act (HIPAA), Office of Human Research Protections (OHRP), Food and Drug Administration (FDA) regulations and guidances, and NCI/DCP requirements, unless the standard at the site is more stringent. The records for all studies performed under an IND will be maintained, at a minimum, for two years after the approval of a New Drug Application (NDA). For NCI/DCP, records will be retained for at least three years after the completion of the research. NCI must be notified prior to the planned destruction of any materials. The records should be accessible for inspection and copying by authorized persons of the Food and Drug Administration. If the study is done outside of the United States, applicable regulatory requirements for the specific country participating in the study also apply.

## 14.7 Clinical Trials Agreement (CTA)

*If the study agent is provided by DCP under a CTA with the manufacturer, this section must be included in the protocol, but the inappropriate text (CTA)* *should be deleted. Information on the study agent’s CTA status will be provided in the approved Concept Submission form response. If a CTA does not apply to the study agent, this section should be marked “N/A” and the text below deleted.*

The agent(s) supplied by DCP, NCI used in this protocol, is/are provided to the NCI under a CTA) between the Pharmaceutical Company(ies) (hereinafter referred to as Collaborator(s)) and the NCI DCP. Therefore, the following obligations/guidelines, in addition to the provisions in the “Intellectual Property Option to Collaborator” contained within the terms of award, apply to the use of Agent(s) in this study:

14.7.1 Agent(s) may not be used for any purpose outside the scope of this protocol, nor can Agent(s) be transferred or licensed to any party not participating in the clinical study. Collaborator(s) data for Agent(s) are confidential and proprietary to Collaborator(s) and shall be maintained as such by the investigators. The protocol documents for studies utilizing Investigational Agents contain confidential information and should not be shared or distributed without the permission of the NCI. If a Participant participating on the study or participant’s family member requests a copy of this protocol, the individual should sign a confidentiality agreement. A suitable model agreement can be downloaded from the DCP website.

14.7.2 For a clinical protocol where there is an Investigational Agent used in combination with (an) other Investigational Agent(s), each the subject of different collaborative agreements, the access to and use of data by each Collaborator shall be as follows (data pertaining to such combination use shall hereinafter be referred to as "Multi-party Data”).

14.7.3 NCI must provide all Collaborators with prior written notice regarding the existence and nature of any agreements governing their collaboration with NIH, the design of the proposed combination protocol, and the existence of any obligations that would tend to restrict NCI's participation in the proposed combination protocol.

14.7.4 Each Collaborator shall agree to permit use of the Multi-Party Data from the clinical trial by any other Collaborator solely to the extent necessary to allow said other Collaborator to develop, obtain regulatory approval, or commercialize its own Investigational Agent.

14.7.5 Any Collaborator having the right to use the Multi-Party Data from these trials must agree in writing prior to the commencement of the trials that it will use the Multi-Party Data solely for development, regulatory approval, and commercialization of its own Investigational Agent.

14.7.6 Clinical Trial Data and Results and Raw Data developed under a collaborative agreement will be made available exclusively to Collaborator(s), the NCI, and the FDA, as appropriate. All data made available will comply with HIPAA regulations.

14.7.7 When a Collaborator wishes to initiate a data request, the request should first be sent to the NCI, who will then notify the appropriate investigators of Collaborator's wish to contact them.

14.7.8 Any manuscript reporting the results of this clinical trial must be provided to DCP for immediate delivery to Collaborator(s) for advisory review and comment prior to submission for publication. Collaborator(s) will have 30 days (or as specified in the CTA) from the date of receipt for review. Collaborator shall have the right to request that publication be delayed for up to an additional 30 days in order to ensure that Collaborator’s confidential and proprietary data, in addition to Collaborator(s)’s intellectual property rights, are protected. Copies of abstracts must be provided to DCP for forwarding to Collaborator(s) for courtesy review as soon as possible and preferably at least three days prior to submission, but in any case, prior to presentation at the meeting or publication in the proceedings. Press releases and other media presentations must also be forwarded to DCP prior to release. Copies of any manuscript, abstract, and/or press release/ media presentation should be sent to the Protocol Information Office at [NCI\_DCP\_PIO@mail.nih.gov](mailto:NCI_DCP_PIO@mail.nih.gov).

The Protocol Information Office will forward manuscripts to the DCP Project Officer for distribution to the Collaborator(s). No publication, manuscript or other form of public disclosure shall contain any of Collaborator’s confidential/proprietary information.

## 14.8 Genomic Data Sharing Plan

*If genomic data will be studied, analyzed, collected, and stored in an NIH/NCI Genomic Data Biorepository (*e.g.*, dbGaP, other), please describe the genomic data sharing plan for this trial. Please refer to the* [*NCI Genomic Data Sharing Policy*](https://datascience.cancer.gov/data-sharing/genomic-data-sharing) *for considerations regarding the sharing of data, protection of patient confidential information, and the provision of adequate information in the patient informed consent.*

# 15. STATISTICAL CONSIDERATIONS

## 15.1 Study Design/Description

*Indicate the type of study (*e.g*., phase I, phase II, observational) as applicable. Include justification for the selection of the particular study design. If a randomized study, indicate whether blinding is used and the methodology to ensure the blinding. Indicate whether or not the study employs intent to treat principles. If applicable, indicate both the range of true values of the primary endpoint sufficiently promising to justify further testing of the agent (*e.g*.,* ***true*** *response rate of at least 20%) and a range of values sufficiently discouraging to justify no further testing of the agent (*e.g*.,* ***true*** *response rate no greater than 5%). Consider early testing for sufficiently discouraging results (*e.g*., interim analysis). Indicate the decision rule for declaring the agent promising based on the* ***observed value*** *of the primary endpoint. Provide the probability of a positive result, given that the true value falls within the promising range, and the probability of a negative result (along with the probability of early negative termination), given that the true value falls within the discouraging range.*

## 15.2 Randomization/Stratification

*Methods for randomization and stratification are described and justified. Blocking and/or other techniques used to balance intervention assignments are described completely. Indicate whether interim analysis and efficacy determination will be done for each stratum individually.*

## 15.3Sample Size

*Specify the planned sample size, accrual rate* (e.g*., average number of participants/month), and projected duration of accrual. Accrual rate estimates should reflect staggered activation of accrual sites and the potential for slow accrual in the first months after study activation. Total sample size and sampling strategy are described and justified for testing the primary and secondary hypotheses.*

## 15.4 Primary Objective, Endpoint(s), Analysis Plan

*Describe the primary objective of the study. Define the primary endpoints and indicate how the analysis plan will satisfy the primary objective of the study. Definition of the primary endpoint(s) should indicate time-points considered in computing the primary endpoint from the data observed. The analysis plan should consider the appropriateness for the particular type of endpoint (for example continuous, binary, time-dependent). Analysis plans should indicate the planned statistical test used to evaluate the objectives of the study along with power calculations and sample size requirements. When known, provide pilot or historical data to support power calculations. Clearly state all assumptions for the power calculations and indicate whether significance levels are one- or two-sided values. Consideration should be given to handling missing data if applicable.*

## 15.5 Secondary Objectives, Endpoints, Analysis Plans

*Describe the secondary objectives of the study. Define the secondary endpoints and indicate how the analysis plan will satisfy the secondary objectives of the study. Definition of the secondary endpoint(s) should indicate time-points considered in computing the secondary endpoint from the data observed. The analysis plan should consider the appropriateness for the particular type of endpoint (for example continuous, binary, time-dependent). Analysis plans should indicate the planned statistical test used to evaluate the secondary objectives of the study. Clearly indicate whether significance levels are one- or two-sided values. Consideration should be given to handling missing data if applicable.*

## 15.6 Reporting and Exclusions

*Definition of compliance is clearly stated. Non-compliance is sufficiently addressed. Particular consideration is given to dropouts, drop-ins, and lost-to-follow up. Handling of missing data or data from non-compliers is described. Any methods used to impute missing data should be described.*

## 15.7 Evaluation of Toxicity

*All participants will be evaluable for toxicity from the time of their first dose of [Study Agent].*

## 15.8 Evaluation of Response

*All participants included in the study must be assessed for response to intervention, even if there are major protocol deviations or if they are ineligible.*

*All of the participants who met the eligibility criteria (with the possible exception of those who did not receive study agent) will be included in the main analysis. All conclusions regarding efficacy will be based on all eligible participants.*

*Subanalyses may be performed on the subsets of participants, excluding those for whom major protocol deviations have been identified (*e.g*., early death due to other reasons, early discontinuation of intervention, major protocol violations,* etc*.). However, subanalyses may not serve as the basis for drawing conclusions concerning efficacy, and the reasons for excluding participants from the analysis should be clearly reported. For all measurements of response, the 95% confidence intervals should also be provided.*

## 15.9 Interim Analysis

*If relevant to the study agent and study design, provide a plan for interim analysis and stopping rules. Include plans for monitoring the progress of the trial to implement early termination.*

## 15.10 Ancillary Studies

*Address the following, as appropriate:*

* *If known, indicate the prevalence of the marker*
* *Specify how any cut points will be determined*
* *Specify the statistical power of the correlative study for the endpoint chosen*
* *If relevant, indicate what corrections will be made for multiple comparisons*
* *If appropriate, indicate relevant clinical endpoint, and a plan for how this endpoint will be correlated with the target(s) or marker(s).*

# 16. REGULATORY And ETHICAL CONSIDERATIONS

## 16.1 Required Documents

Besides the regulatory information that will be entered into the Registration and Credential Repository (see Section 5.1), the following documents are also required:

16.1.1 Documentation of Federalwide Assurance (FWA) number for the LAO and all AOs.

* + 1. Signed Investigator’s Brochure/Package Insert acknowledgement form

16.1.3 Delegation of Tasks Log form for the Lead Accruing Organization and all Accruing Sites signed by the PI for each site and initialed by all study personnel listed on the form.

## 16.2 Informed Consent

All potential study participants will be given a copy of the CIRB-approved Informed Consent to review. The investigator will explain all aspects of the study in lay language and answer all questions regarding the study. If the participant decides to participate in the study, he/she will be asked to sign and date the Informed Consent document. The study agent(s) will not be released to a participant who has not signed the Informed Consent document. Individuals who refuse to participate or who withdraw from the study will be treated without prejudice.

Participants must be provided the option to allow the use of blood samples, other body fluids, and tissues obtained during testing, operative procedures, or other standard medical practices for further research purposes. If applicable, statement of this option should be included within the informed consent document.

Prior to study initiation, the informed consent document must be reviewed and approved by NCI, DCP, and the NCI CIRB. The NCI CIRB approves a model consent for each protocol. Each Signatory Institution inserts their CIRB-approved institutional boilerplate language into the model consent to create the CIRB-approved consent. If the model informed consent document is amended, Signatory Institutions must use the revised model informed consent document and insert their CIRB-approved institutional boilerplate language at the time the change becomes active.

The NCI CIRB is the IRB of record and is the only IRB authorized to approve changes to the protocol or informed consent document. Institutions may require additional oversight that involves the local IRB, but the local IRB is not responsible for any regulatorily-required IRB actions.

## 16.3 Collection of Regulatory Documents

Regulatory documents will be collected by the DCP regulatory contractor and reviewed for completeness and accuracy.

## 

## 16.4 Other

This trial will be conducted in compliance with the protocol, the International Conference on Harmonisation’s (ICH) Good Clinical Practice (GCP) guidelines, and the applicable regulatory requirements.

# 17. ROSTER MANAGEMENT

The LAO is responsible for establishing, maintaining, and monitoring all its members that participate in CP-CTNet studies. The LAO must have a “real-time,” comprehensive, consolidated roster of all its members with their relevant Cancer Therapy Evaluation Program (CTEP) institution codes, associated investigators, and research staff. This roster information is used for determining compliance with monitoring requirements

The LAO’s organizational rosters will be managed by the [CP-CTNet Roster Management System website](https://applications.prevention.cancer.gov/cp-ctnet/landing/). Requests to add memberships to a roster will be done via this website. All requests require that the following documents be uploaded:

* Lead Academic Organization Letter of Commitment
* Site Letter of Commitment
* CV/NIH Biosketch

# 18. FINANCING, EXPENSES, AND/OR INSURANCE

*The protocol should describe any expenses incurred by the study participant and/or their insurance carrier. This includes any injuries the participant may have related to their participation in the study.*

# REFERENCES

*Please provide the citations for all publications referenced in the text.*

# APPENDIX A PERFORMANCE STATUS CRITERIA

**ECOG Performance Status Scale**

|  |  |
| --- | --- |
| **Grade** | **Descriptions** |
| 0 | Normal activity. Fully active, able to carry on all pre-disease performance without restriction. |
| 1 | Symptoms, but ambulatory. Restricted in physically strenuous activity, but ambulatory and able to carry out work of a light or sedentary nature (*e.g*., light housework, office work). |
| 2 | In bed <50% of the time. Ambulatory and capable of all self-care, but unable to carry out any work activities. Up and about more than 50% of waking hours. |
| 3 | In bed >50% of the time. Capable of only limited self-care, confined to bed or chair more than 50% of waking hours. |
| 4 | 100% bedridden. Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair. |
| 5 | Dead. |

**Karnofsky Performance Scale**

|  |  |
| --- | --- |
| **Percent** | **Description** |
| 100 | Normal, no complaints, no evidence of disease. |
| 90 | Able to carry on normal activity; minor signs or symptoms of disease. |
| 80 | Normal activity with effort; some signs or symptoms of disease. |
| 70 | Cares for self, unable to carry on normal activity or to do active work. |
| 60 | Requires occasional assistance, but is able to care for most of his/her needs. |
| 50 | Requires considerable assistance and frequent medical care. |
| 40 | Disabled, requires special care and assistance. |
| 30 | Severely disabled, hospitalization indicated. Death not imminent. |
| 20 | Very sick, hospitalization indicated. Death not imminent. |
| 10 | Moribund, fatal processes progressing rapidly. |
| 0 | Dead. |

# *(Include APpendix B if APPRopRiate for AGENt/COhort and utilized in this study)*

# APPENDIX B

## ALCOHOL AND TOBACCO QUESTIONNAIRE INSTRUCTIONS

.

* Data collection will be required for all CP-CTNet studies.
  + Data will be collected at baseline and end of every study. Data may also be collected at follow-up visits as determined by each protocol. If you wish to collect additional information beyond these core elements, you may certainly do so. However, all studies need to collect the basic elements in the attached eCRFs.
  + The eCRFs will be completed by the Site Staff or participant at the time of the designated visit.
* Data will be submitted as part of the final clinical data set.

## ALCOHOL ASSESSMENT-- BASELINE

|  |  |  |  |
| --- | --- | --- | --- |
| REGISTERING INSTITUTION  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | PARTICIPANT ID  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | VISIT TYPE  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | VISIT DATE  (MM/DD/YYYY)  \_\_\_ \_\_\_ / \_\_\_ \_\_\_ / \_\_\_ \_\_\_ \_\_\_ \_\_\_ |

**Instructions:**

**For the following questions about drinking alcoholic beverages, a drink means a 12 oz. beer, a 5 oz. glass of wine, or one and a half ounces of liquor****.**

**When a number is requested in the response, please enter a whole number (i.e. “4”) and not a range or fraction of a number.**

1. In your entire life, have you had at least 12 drinks of any kind of alcoholic beverage?

Yes

No **(End)**

Refuse to answer **(End)**

Don’t know/Not sure

1. In the past 12 months, on average, how often did you drink any type of alcoholic beverage?

\_\_\_\_\_\_\_\_ (Enter the number of days you drank based on the timeframe checked below. Enter 0 if you never drank and skip to Question 6.)

Week

Month

Year

Refuse to answer

Don’t know/Not sure

1. In the past 12 months, on those days that you drank alcoholic beverages, on average, how many drinks did you have per day?

\_\_\_\_\_\_\_\_ (Enter the average number of drinks per day)

Refuse to answer

Don’t know/Not sure

1. In the past 12 months, on how many days did you have 5 or more drinks of any alcoholic beverage?

\_\_\_\_\_\_\_\_\_ (Enter the number of days you had 5 or more drinks or enter 0 if none.)

Refuse to answer

Don’t know/Not sure

1. Was there ever a time or times in your life when you drank 5 or more drinks of any kind of alcoholic beverage almost every day?

Yes

No

Refuse to answer

Don’t know/Not sure

1. If you do not currently drink alcoholic beverages, but did in the past, how long has it been since you last drank regularly?

Within the past month (0 to 1 month ago)

Between 1 and 3 months (1 to 3 months ago)

Between 3 and 6 months (3 to 6 months ago)

Between 6 and 12 months (6 to 12 months ago)

Between 1 and 5 years (1 to 5 years ago)

Between 5 and 15 years (5 to 15 years ago)

More than 15 years ago

Don’t know/Not sure

Never drank regularly

1. At the heaviest point, either now or in the past, on the days when you drank, about how many drinks did you drink a day on the average?

\_\_\_\_\_\_\_\_\_\_ (Enter the number of drinks a day)

Refuse to answer

Don’t know/Not sure

1. How many years have you been drinking (or did drink) regularly?

\_\_\_\_\_\_ years

Refuse to answer

Don’t know/Not sure

1. At what age did you begin drinking regularly?

\_\_\_\_\_\_ years of age

Refuse to answer

Don’t know/Not sure

1. What type(s) of alcohol do you drink? (Mark ALL that apply)

Wine

Liquor

Beer

Wine cooler

Other \_\_\_\_\_\_\_ (enter other type(s) of alcohol you drink)

CRF completed by (*check one*):

Study participant \_\_\_\_\_

Study site staff      \_\_\_\_\_     Staff name (*optional*) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Date \_\_ \_\_ / \_\_ \_\_ / \_\_ \_\_ \_\_ \_\_

*(MM/DD/YYYY)*

## ALCOHOL ASSESSMENT - FOLLOW-UP

|  |  |  |  |
| --- | --- | --- | --- |
| REGISTERING INSTITUTION  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | PARTICIPANT ID  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | VISIT TYPE  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | VISIT DATE  *(MM/DD/YYYY)*  \_\_\_ \_\_\_ / \_\_\_ \_\_\_ / \_\_\_ \_\_\_ \_\_\_ \_\_\_ |

**Instructions:**

**For the following questions about drinking alcoholic beverages, a drink means a 12 oz. beer, a 5 oz. glass of wine, or one and a half ounces of liquor.**

**When a number is requested in the response, please enter a whole number (i.e. “4”) and not a range or fraction of a number.**

1. During the past 30 days, did you drink any alcoholic beverages?

Yes

No **(End)**

Refuse to answer **(End)**

Don’t know/Not sure

2. During the past 30 days, how many days per week or per month did you drink any alcoholic beverages, on the average?

\_\_\_\_\_\_\_\_ (Enter number of days you drank based on the timeframe checked below. Enter 0 if you did not drink.)

Week

Month

Refuse to answer

Don’t know/Not sure

3. On the days when you drank, on average, about how many drinks did you have?

\_\_\_\_\_\_\_\_ (Enter the average number of drinks you had per day.)

Refuse to answer

Don’t know/Not sure

4. In the past 30 days, on how many days did you have 5 or more drinks per day?

\_\_\_\_\_\_\_\_\_\_\_\_\_ (Enter the number of days you had 5 or more drinks or enter 0 if none.)

Refuse to answer

Do not know/Not sure

CRF completed by (*check one*):

Study participant \_\_\_\_\_

Study site staff      \_\_\_\_\_     Staff name (*optional*) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Date \_\_ \_\_ / \_\_ \_\_ / \_\_ \_\_ \_\_ \_\_

*(MM/DD/YYYY)*

## TOBACCO ASSESSMENT – BASELINE

|  |  |  |  |
| --- | --- | --- | --- |
| REGISTERING INSTITUTION  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | PARTICIPANT ID  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | VISIT TYPE  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | VISIT DATE  (MM/DD/YYYY)  \_\_\_ \_\_\_ / \_\_\_ \_\_\_ / \_\_\_ \_\_\_ \_\_\_ \_\_\_ |

**Instructions:**

**When a number is requested in the response, please enter a whole number (i.e. “4”) and not a range or fraction of a number.**

**Section A. Basic Cigarette Use Information**

1. Have you smoked at least 100 cigarettes (5 packs = 100 cigarettes) in your entire life?

Yes

No → **Skip to Section B**

Don’t know/Not sure → **Skip to Section B**

2. How old were you when you first smoked a cigarette (even one or two puffs)?

\_\_\_\_\_\_\_ Years old

3. How old were you when you first began smoking cigarettes regularly?

\_\_\_\_\_\_\_ Years old

Check here if you have never smoked cigarettes regularly.

4. How many total years have you smoked (or did you smoke) cigarettes? Do not count any time you may have stayed off cigarettes.

\_\_\_\_\_\_ Years (If you smoked less than one year, write “1.”)

5. Onaverage when you have smoked, about how many cigarettes do you (or did you) smoke a day?(A pack usually has 20 cigarettes in it).

\_\_\_\_\_ Number of cigarettes per day

6. Do you NOW smoke cigarettes?

Everyday

Some days

Not at all → **Skip to question 8**

7. How soon after you wake up do you smoke your first cigarette?

Within 30 minutes

After 30 minutes

8. How long has it been since you last smoked a cigarette (even one or two puffs)?

*First check which one of the following choices applies to you. Then, if applicable, write a number on the line for how many days, weeks, months, or years it has been since your last cigarette.*

I smoked a cigarette today (at least one puff)

1-7 days → Number of days since last cigarette \_\_\_\_\_\_\_\_

Less than 1 month → Number of weeks since last cigarette \_\_\_\_\_\_\_\_\_

Less than 1 year → Number of months since last cigarette \_\_\_\_\_\_\_\_\_\_

More than 1 year → Number of years since last cigarette \_\_\_\_\_\_\_\_\_\_\_

Don’t know/Don’t remember

**Section B. Use of Other Forms of Tobacco**

9. Have you ever used other forms of tobacco, not including cigarettes?

Yes

No → **Skip to Section C**

10. How often do you/did you use other forms of tobacco?

Every day → Number of times per day \_\_\_\_\_\_\_\_

Some days → Number of days \_\_\_\_\_\_\_ per  Week Month Year

11. Which of the following products have you ever used regularly?

***Check all that apply***

Cigarettes

E-cigarettes or other electronic nicotine delivery system

Traditional cigars, cigarillos or filtered cigars

Pipes

Waterpipe

Hookah

Clove cigarettes or kreteks

Bidis

Smokeless tobacco, like dip, chew, or snuff

Snus

Paan with tobacco, gutka, zarda, khaini

Other, Please specify: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

12. If you do not currently use other forms of tobacco, but did in the past, how long has it been since you last used other forms of tobacco regularly?

Within the past month (0 to 1 month ago)

Between 1 and 3 months (1 to 3 months ago)

Between 3 and 6 months (3 to 6 months ago)

Between 6 and 12 months (6 to 12 months ago)

Between 1 and 5 years (1 to 5 years ago)

Between 5 and 15 years (5 to 15 years ago)

More than 15 years ago

Don’t know/Not sure

Never used other forms of tobacco regularly

**Section C. Second-Hand Smoke Exposure**

13. Are you currently living with a smoker?

Yes

No

14. In the past 30 days, have you lived in a place where other people smoked cigarettes indoors?

Yes

No

15. In the past 30 days, have you worked in a place where other people smoked cigarettes indoors?

Yes

No

16. Thinking of all your childhood and adult years, have you ever lived in a place where other people smoked cigarettes indoors?

Yes In total, for about how many years? \_\_\_\_\_\_\_ If less than 1, write “1.”

No

17. Thinking of all the years you have worked, have you ever worked in a place where other people smoked cigarettes indoors?

Yes → In total, for about how many years? \_\_\_\_\_\_\_ If less than 1, write “1.”

No

CRF completed by (*check one*):

Study participant \_\_\_\_\_

Study site staff      \_\_\_\_\_     Staff name (*optional*) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Date \_\_ \_\_ / \_\_ \_\_ / \_\_ \_\_ \_\_ \_\_

*(MM/DD/YYYY)*

## TOBACCO ASSESSMENT - FOLLOW-UP

|  |  |  |  |
| --- | --- | --- | --- |
| REGISTERING INSTITUTION  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | PARTICIPANT ID  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | VISIT TYPE  \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ | VISIT DATE  *(MM/DD/YYYY)*  \_\_\_ \_\_\_ / \_\_\_ \_\_\_ / \_\_\_ \_\_\_ \_\_\_ \_\_\_ |

**Instructions:**

**When a number is requested in the response, please enter a whole number (i.e. “4”) and not a range or fraction of a number.**

1. Do you NOW smoke cigarettes?

Everyday

Some days

Not at all → **Skip to Question 3.**

Never smoked **→ Skip to Question 4**

2. On average, when you smoked, about how many cigarettes do you (or did you) smoke a day? (A pack usually has 20 cigarettes in it)

\_\_\_\_\_ Number of cigarettes per day

3. How long has it been since you last smoked a cigarette (even one or two puffs)?

*First check which one of the following choices applies to you. Then, if applicable, write a whole number on the line for how many days, weeks, months, or years it has been since your last cigarette.*

I smoked a cigarette today (at least one puff)

1-7 days → Number of days since last cigarette \_\_\_\_\_\_\_\_

Less than 1 month → Number of weeks since last cigarette \_\_\_\_\_\_\_\_\_

Less than 1 year → Number of months since last cigarette \_\_\_\_\_\_\_\_\_\_

More than 1 year → Number of years since last cigarette \_\_\_\_\_\_\_\_\_\_\_

Don’t know/Don’t remember

4. Since your last visit, have you used other forms of tobacco, not including cigarettes?

Yes

No (**End)**

5. How often do you/did you use other forms of tobacco?

Every day → Number of times per day \_\_\_\_\_\_\_\_

Some days → Number of days \_\_\_\_\_\_\_ per  Week Month Year

6. Since your last visit, which of the following products have you used? ***Check all that apply***

Cigarettes

E-cigarettes or other electronic nicotine delivery system

Traditional cigars, cigarillos or filtered cigars

Pipes

Waterpipe

Hookah

Clove cigarettes or kreteks

Bidis

Smokeless tobacco, like dip, chew, or snuff

Snus

Paan with tobacco, gutka, zarda, khaini

Other, Specify\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

7. If you do not currently use other forms of tobacco, but did in the past, how long has it been since you last used other forms of tobacco regularly?

Within the past month (0 to 1 month ago)

Between 1 and 3 months (1 to 3 months ago)

Between 3 and 6 months (3 to 6 months ago)

Between 6 and 12 months (6 to 12 months ago)

Between 1 and 5 years (1 to 5 years ago)

Between 5 and 15 years (5 to 15 years ago)

More than 15 years ago

Don’t know/Not sure

Never used other forms of tobacco regularly

The following instructions pertain to questions 8 - 10. During each of the following time frames, please indicate whether you smoked cigarettes every day, some days, or not at all.

8. During study treatment

Smoked every day

Smoked some days

Did not smoke at all

Don’t know/not sure

Not applicable

9. After the end of study treatment

Smoked every day

Smoked some days

Did not smoke at all

Don’t know/not sure

Not applicable (I have not completed the study treatment)

10. Since your last visit to this clinic

Smoked every day

Smoked some days

Did not smoke at all

Don’t know/not sure

CRF completed by (*check one*):

Study participant \_\_\_\_\_

Study site staff      \_\_\_\_\_     Staff name (*optional*) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Date \_\_ \_\_ / \_\_ \_\_ / \_\_ \_\_ \_\_ \_\_

*(MM/DD/YYYY)*

## NATIONAL AND LOCAL RESOURCES TO HELP WITH ALCOHOL ABUSE AND ALCOHOLISM

is written for individuals, and their family and friends, who are looking for options to address alcohol problems. It is intended as a resource to understand what treatment choices are available and what to consider when selecting among them. <https://pubs.niaaa.nih.gov/publications/treatment/treatment.htm>

**Other resources:**

**National Institute on Alcohol Abuse and Alcoholism** [www.niaaa.nih.gov](http://www.niaaa.nih.gov)   
301–443–3860

**National Institute on Drug Abuse** [www.nida.nih.gov](http://www.nida.nih.gov)   
301–443–1124

**National Clearinghouse for Alcohol and Drug Information** [www.samhsa.gov](http://www.samhsa.gov)   
1–800–729–6686

**Substance Abuse Treatment Facility Locator** [www.findtreatment.samhsa.gov](http://www.findtreatment.samhsa.gov)   
1–800–662–HELP

**Alcoholics Anonymous (AA)** [www.aa.org](http://www.aa.org)   
212–870–3400 or check your local phone directory under “Alcoholism”

**Moderation Management** [www.moderation.org](http://www.moderation.org)  
212–871–0974

**Secular Organizations for Sobriety** [www.sossobriety.org](http://www.sossobriety.org)   
323–666–4295

**SMART Recovery** [www.smartrecovery.org](http://www.smartrecovery.org)   
440–951–5357

**Women for Sobriety** [www.womenforsobriety.org](http://www.womenforsobriety.org)   
215–536–8026

**Al-Anon Family Groups** [www.al-anon.alateen.org](http://www.al-anon.alateen.org)   
1–888–425–2666 for meetings

**Adult Children of Alcoholics**  [www.adultchildren.org](http://www.adultchildren.org)  
310–534–1815

## NATIONAL AND LOCAL RESOURCES TO HELP WITH QUITTING SMOKING

NCI’s [Smokefree.gov](http://www.smokefree.gov) offers science-driven tools, information, and support that has helped smokers quit. You will find state and national resources, free materials, and quitting advice from NCI.

Smokefree.gov was established by the [Tobacco Control Research Branch](https://cancercontrol.cancer.gov/brp/tcrb/) of NCI, a component of the National Institutes of Health, in collaboration with the Centers for Disease Control and Prevention and other organizations.

Publications available from the Smokefree.gov website include the following:

* [Clearing the Air: Quit Smoking Today](http://smokefree.gov/sites/default/files/pdf/clearing-the-air-accessible.pdf) for smokers interested in quitting.
* [Clear Horizons](https://smokefree.gov/sites/default/files/pdf/clear-horizons-accessible.pdf) for smokers over age 50.
* [Staying Smoke-Free for Good](https://smokefree.gov/stay-smokefree-good) for smokers who have recently quit.
* [Smoke-free](https://women.smokefree.gov/) for women, including pregnant women.
* [Smoke-free](https://espanol.smokefree.gov/) information in Spanish
* [Pathways to Freedom: Winning the Fight Against Tobacco](https://archive.cdc.gov/#/details?url=https://www.cdc.gov/tobacco/quit_smoking/how_to_quit/pathways/index.htm) for African American smokers.

**NCI’s Smoking Quitline** at **1–877–44U–QUIT (1–877–448–7848)** offers a wide range of services, including individualized counseling, printed information, referrals to other resources, and recorded messages. Smoking cessation counselors are available to answer smoking-related questions in English or Spanish, Monday through Friday, 8:00 a.m. to 8:00 p.m., Eastern time. Smoking cessation counselors are also available through [LiveHelp](https://livehelp.cancer.gov), an online instant messaging service. LiveHelp is available Monday through Friday, 8:00 a.m. to 11:00 p.m., Eastern time.

Your state has a toll-free telephone quitline. Call **1–800–QUIT–NOW (1–800–784–8669)** to get one-on-one help with quitting, support and coping strategies, and referrals to resources and local cessation programs. The toll-free number routes callers to state-run quitlines, which provide free cessation assistance and resource information to all tobacco users in the United States. This initiative was created by the [Department of Health and Human Services](http://www.hhs.gov). For more information about quitlines, [speak to an expert](http://smokefree.gov/talk-to-an-expert) on the Smokefree.gov website.

# APPENDIX C

# PARTICIPANT DRUG INTERACTIONS HANDOUT AND WALLET CARD

***Instructions for PARTICIPANT drug interactions handout and wallet card Template***

*Participant Drug Interactions Handout and Wallet Card is a requirement that must meet DCP Policies & Procedures for non-marketed investigational agents. The instructions below specify which template to use. Please note the drug interactions handout and wallet card require IRB approval before distribution to participants.*

***Instructions to authors:*** *Refer to the table below to determine which template (Template A or Template B) you should use and fill out the appropriate information as instructed by the template. Use or delete sections below as appropriate.****Only edit the fillable text fields – do not alter any text outside of the fillable fields. The bracketed instruction text will disappear once you begin typing.***

* 1. ***Template A: Participant Drug Interactions Handout and a Participant Drug Interactions Wallet Card*** 
     1. *To be given at the time of enrollment and when updated.*
     2. *A protocol that has a non-marketed investigational agent with drug interactions will have a drug interactions handout and drug interactions wallet card for each agent.*
     3. *Assign a letter or a Roman numeral to the Appendix.*
     4. *A convenient wallet-sized information card for the Participant to cut out and retain at all times.*
     5. ***Suggested text to complete the templates are on the next page.***
     6. ***Use the fillable template and enter information in the fillable fields****.*
  2. ***Template B: Participant Clinical Trial Wallet Card only***
     1. *To be given to the participant at the time of enrollment.*
     2. *A convenient wallet-sized information card for the participant to cut out and retain at all times.*
     3. *Assign a letter or a Roman numeral to the Appendix.*
     4. ***Suggested text to complete the template are on the next page****.*
     5. ***Use the fillable template and enter information in the fillable fields.***

*When the Participant Drug Interactions Handout and Wallet Card is required and who is responsible for the authorship is summarized in table below:*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| *Clinical Trial Sponsor* | *Is Agent Marketed?*  *Yes (Y)/No (N)* | *Does Agent Have Drug-Interactions Potential? (Y/N)* | *Is a Participant Drug Interactions Handout and Wallet Card required? (Y/N)* | *Who is responsible for authorship?* | *Template Required* |
| *DCP-IND* | *N* | *Y* | *Y* | *DCP* | *A* |
| *DCP-IND* | *N* | *N* | *N* | *N/A* | *B* |
| *DCP-IND* | *Y* | *Y or N* | *N* | *N/A* | *B* |
| *Non-DCP IND* | *N* | *Y* | *Y* | *Lead Organization* | *A* |
| *Non-DCP IND* | *N* | *N* | *N* | *N/A* | *B* |
| *Non-DCP IND* | *Y* | *Y or N* | *N* | *N/A* | *B* |

***Template A****:* **PaRTICIPANT drug interactions handout and paRTICIPANt drug interactions wallet card**

**APPENDIX      : PARTICIPANT DRUG Interactions handout and wallet card**

**Information for Participants, Their Caregivers and Non-Study Healthcare Team on Possible Interactions with Other Drugs and Herbal Supplements**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Participant Name:** |  | **Diagnosis/Condition:** |  | **Trial #:** |  |
| **Study Doctor:** |  | **Study Doctor**  **Phone #:** |  | **Study Drug(s):** |  |

Please show this paper to all your healthcare providers (doctors, physician assistants, nurse practitioners, pharmacists), and tell them you are taking part in a clinical trial sponsored by the National Cancer Institute.

**These are the things that your healthcare providers need to know:**

*[Insert study drug]* interacts with [certain specific enzyme(s) in your liver or other tissueslike the gut],[certain transport proteins that help move drugs in and out of cell]*,* [the heart’s electrical activity (QTc prolongation)]*.*

|  |  |
| --- | --- |
|  | **Explanation** |
| CYP isoenzymes | The enzyme(s) in question is/are *[enter name of CYP isoenzyme(s)]*. [Insert brief, easy explanation of the nature of the interaction, i.e., for substrates: “[insert study drug name] is broken down by this enzyme and may be affected by other drugs that inhibit or induce this enzyme.”] |
| Protein transporters | The protein(s) in question is/are *[enter name of transporter(s)]*. [Insert brief, easy explanation of the nature of the interaction, i.e., for substrates: “[insert study drug name] is moved in and out of cells/organs by this transport protein.”] |
| Heart’s electrical activities | The heart’s electrical activity may be affected by [Insert study drug]*.* The study doctor may be concerned about QTc prolongation and any other medicine that is associated with greater risk for having QTc prolongation. |

**These are the things that you need to know:**

The study drug [Insert study drug],may interact with other drugs which can cause side effects. For this reason, it is very important to tell your doctors about all your medicines, including: (a) medicines you are taking before this clinical trial, (b) medicines you start or stop taking during this study, (c) medicines you buy without a prescription (over-the-counter remedy), (d) herbals or supplements (*e*.*g*. St. John’s Wort). It is helpful to bring your medication bottles or an updated medication list with you.

Before you enroll onto the clinical trial, your study doctor will work with your regular health care providers to review any medicines and herbal supplements that are considered *[“strong inducers/inhibitors or substrates] of [name(s) of CYP isoenzyme(s)], [transport protein(s), or any medicine associated with greater risk for having QTc prolongation.”]*

* Please be very careful! Over-the-counter drugs (including herbal supplements) may contain ingredients that could interact with your study drug. Speak to your doctors or pharmacist to determine if there could be any side effects.

* + [Add other specific medications here, if necessary. Examples include acid suppressing drugs, NSAIDS, St. John’s Wort.]
* Make sure your doctor knows to avoid certain prescription medications.

* + [Add other specific medications here, if necessary. Examples include acid suppressing drugs, anticoagulants, NSAIDS.]
* Your regular health care provider should check a frequently updated medical reference or call your study doctor before prescribing any new medicine or discontinuing any medicine.

Version *mmm/yyyy*

(Next page: Participant Drug Interaction Wallet Card)

***TEMPLATE A*:**  **PARTICIPANT DRUG INTERACTION WALLET CARD**

****

|  |  |  |  |
| --- | --- | --- | --- |
| **National Cancer Institute** | **National Cancer Institute** | **National Cancer Institute** | **National Cancer Institute** |
| **EMERGENCY INFORMATION** |  | **dRUG INTERACTIONS** | |
| **Show this card to all of your healthcare providers. Keep it with you in case you go to the emergency room.** | Tell your doctors **before** you **start** or **stop** any medicines.  **Check with your doctor or pharmacist if you need to use an over-the-counter medicine or herbal supplement!** | **Carry this card with you at all times**  [insert study drug] interacts with [a specific enzyme in your liver or other tissues like the gut, transport proteins that help move drugs in and out of cells, the heart’s electrical activity,] and must be used very carefully with other medicines. | |
| **Participant Name:** | **Use caution and avoid the following drugs if possible:**  [List specific medications here. Examples: OTC drugs, herbal supplements, vitamins, acid suppressing drugs, anticoagulants, NSAIDs, digoxin.] | Your healthcare providers should be aware of any medicines that are [strong inducers/inhibitors/substrates of [insert CYP isoenzymes], interact with [insert transport proteins], or affect your heart’s electrical activity]. | |
| **Diagnosis/Condition:** |
| **Study Doctor:** |
| **Study Doctor Phone #:** |
| **NCI Trial #:** | **Before prescribing new medicines**, your health care provider should check a **frequently-updated medical reference** for a **list of drugs to avoid** or contact your study doctor. | |
| **Study Drug(S):** |
|  | Versionmm/yyyy |
| **For more information:** 1-800-4-CANCER | **For more information:** 1-800-4-CANCER | **For more information:** 1-800-4-CANCER | **For more information:** 1-800-4-CANCER |
| cancer.gov | clinicaltrials.gov | cancer.gov | clinicaltrials.gov | cancer.gov | clinicaltrials.gov | cancer.gov | clinicaltrials.gov |

|  |  |  |  |
| --- | --- | --- | --- |
| *Fold at dotted lines*: |  |  |  |

***TEMPLATE B*: PARTICIPANT CLINICAL TRIAL WALLET CARD**

**Appendix** [enter letter/number]**: Participant clinical trial wallet card**

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| --- |
| **National Cancer Institute** |
| **cliniCal trial wallet card** |
| **Show this card to all of your healthcare providers and keep it with you in case you go to the emergency room.** |
| **Participant Name:** |
| **Diagnosis/Condition:** |
| **Study Doctor:** |
| **Study Doctor Phone #:** |
| **NCI Trial #:** |
| **Study Drug(S):** |
|
| **For more information:** 1-800-4-CANCER |
| cancer.gov | clinicaltrials.gov |