Division of Cancer Prevention
National Cancer Institute

Version 2.1

Investigator Technical Progress Reports

Chemoprevention Clinical Trials

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CHANGE MANAGEMENT SUMMARY

The following summary details the changes or updates that have been made to the current version of the instruction document.

Version	Page	Section	Summary of Change
2.0	4	Which clinical trials use ITPR?	Contracts with protocols that are currently in the protocol development phase will use the ITPR administrative sections and the progress comment worksheet to report progress.
2.0	6	How does the ITPR differ from the old report?	Relatedness has been added as a mandatory field on the Cumulative Adverse Event worksheet of the Excel Workbook.
2.0	7	What are the steps for ITPR submission and processing?	The Study Principal Investigator (if different than the Contract/Grant Principal Investigator), Site Coordinator, NCI Contracting Officer (if applicable), NCI Procurement Technician (if applicable), the Medical Monitor (if different than the Project Officer/Program Director) and the DCP Nurse Specialist will be copied on the e-mail that is sent to the site from Westat one month prior to the template due date.
2.0	7	What are the steps for ITPR submission and processing?	For protocols funded by contracts: The ITPR submission from the site should be e-mailed to the DCP Project Officer, Medical Monitor, Nurse Specialist, Contracting Officer, Linda Parreco at the Protocol Information Office (PIO) and the DCP Help Desk. The site can simply use the "Reply to All" feature of their e-mail system and reply to the original e-mail that was sent to the site by the DCP Help Desk to ensure all appropriate personnel are included.
2.0	7	What are the steps for ITPR submission and processing?	For protocols funded by grant or cooperative agreement: The ITPR submission from the site should be e-mailed to the DCP Program Director, Medical Monitor, Nurse Specialist, Linda Parreco at the PIO and the DCP Help Desk. The site can simply use the "Reply to All" feature of the e-mail system and reply to the original e-mail that was sent to the site by the DCP Help Desk to ensure all appropriate personnel are included.
2.0	8	What are the steps for ITPR submission and processing?	A list of suggestions on how to avoid loading and QC discrepancies has been added.
2.0	13	Administrative Information	Definitions of protocol versions and dates have been added.
2.0	15 & 20	Cumulative Participant Accrual	Definition of Registration Number has been modified.
2.0	22	Cumulative Adverse Event Table	Instructions for coding missing days in the Event Onset Date field have been added.
2.1	7-11	Add documentation regarding the Discrepancy Cycle process	More information as to the Discrepancy resolution cycle has been added.

2.1	21	Cumulative Adverse Event Table	New instruction on how to handle specific AE worksheet fields (Agent Type, Agent Dose at AE, Dose Units, Agent Frequency) has been added.

Investigator Technical Progress Reports

DCP Chemoprevention Clinical Trials

Overview

The technical progress report, hereafter referred to as the "Investigator Technical Progress Report" (ITPR), is currently the primary resource of clinical trial data for the Division of Cancer Prevention (DCP). DCP serves as the Investigational New Drug Application (IND) sponsor for many of the chemoprevention trials funded by DCP. The Code of Federal Regulations 21 (CFR) §312 requires the IND sponsor to submit annual reports to the Food and Drug Administration (FDA) on the progress of clinical investigations. Further, 21 CFR §312.60 requires the Principal Investigator (PI), who has committed by signing Form FDA 1572, personally to conduct or supervise the described investigations under applicable regulations, and to report the conduct and progress of the clinical investigation to the authorized representative(s) of the Government and the sponsor of the clinical investigation—the National Cancer Institute (NCI), DCP.

In the past, clinical data were prepared by the investigator and submitted to DCP using the DCP Chemoprevention Progress Report Template. This report was required for studies funded by contracts, but was not required for studies funded by grants or cooperative agreements. DCP is updating the data reporting process to ensure that complete clinical information on all DCP-sponsored IND studies is available to fulfill the regulatory requirements. This new process is described in this document. The major change in the reporting process is that investigators will enter the clinical data into Microsoft Word and Excel templates created by DCP.

The DCP monitoring contractor, Westat, will support DCP in this effort.

This new process benefits investigators and DCP in several ways:

- Decreases the amount of effort required by the site to prepare the report
    - Many of the data fields are "pre-populated" by DCP and the site simply verifies the data. This reduces data entry time required by the site.
    - The Accrual Summary Table and the Demographic Information Tables have been eliminated.
    - DCP tracks the due dates for ITPRs and sends the site a template 1 month in advance of the ITPR due date.
- Standardized definitions and '"drop-down" menus take the guesswork out of data entry and minimize the burden of learning a new system.
- Improved data quality results through a standardized system of edit checks, data query, and data resolution.

- DCP clinical trial data are maintained in a central database at DCP. This facilitates comparing toxicities or results across protocols, cohorts, or agents.

Purpose of this document

The purpose of this document is to:

- Orient investigators and site staff to this new process
- Highlight changes in data elements and data definitions
- Provide examples and instructions to assist data management staff
- Describe the data submission process
- Identify resources to assist with the transition

Question and Answer

Which clinical trials use ITPR?

- Phase I, II, and III clinical trials funded by DCP contracts awarded before 10/01/02, regardless of IND status, will report progress to DCP via the ITPR (see exemptions below). The updated ITPR replaces the existing DCP Chemoprevention Progress Report Template as required by the NCI Research Contracts Branch (RCB). Contracts with protocols that are currently in the protocol development phase will use the ITPR administrative sections and the progress comment worksheet to report progress and will begin adding participant data to the cumulative accrual worksheet following protocol initiation.

- Other clinical trials (regardless of funding mechanism) for which DCP is the IND sponsor will be phased into the ITPR format for progress reports. This includes studies funded by grants or cooperative agreements. The NCI's DCP Program Director will communicate details of the change in the Terms and Conditions of Award.

Are any trials exempt from ITPR reporting?

- Clinical trials that have completed accrual of all participants will continue to use the existing DCP Chemoprevention Progress Report Template.

- Clinical trials testing multiple agents or agent combinations will continue to report using the existing DCP Chemoprevention Progress Report Template.

- Studies with no human subjects (e.g., archival tissue specimens) are not required to use the ITPR. They will continue to report using the existing DCP Chemoprevention Progress Report Template.

- Cooperative agreements and grants funded by DCP but not conducted under a DCP IND use the annual progress report format described in the Terms and Conditions of Award.

Who prepares and submits the ITPR data?

- Data should be collected, prepared, and submitted by the "lead organization." The lead organization is defined as the institution that receives funds directly from DCP for the purpose of

conducting the clinical trial. The term "participating organization" is used for all other sites contributing work in a multi-institutional study. As in the existing system, the lead organization is responsible for entering all the study data in the ITPR.

How does the ITPR differ from the old report?

- In updating the progress reporting process, DCP has ensured that the minimum amount of data possible is requested to reduce the burden of report preparation. The required data elements are essential to DCP for the purpose of fulfilling its regulatory, scientific, and administrative responsibilities. The updated ITPR does not require that more data be reported; however, titles and/or definitions of some existing data elements have been changed for the purpose of clarity.

- The existing report method requires the site to prepare several summary tables (Accrual Summary Table, Gender and Race Cumulative Accrual, Age Distribution). Since the updated ITPR tool collects information for each participant (age, gender, registration date, etc.) these tables can quickly be generated by DCP. Preparation of these tables is no longer required in the ITPR.

- Participant initials are now eliminated in compliance with the requirements of the Health Information Portability and Accountability Act (HIPAA). Only the year of birth is requested; the month of birth has been dropped.

- The previous field "Duration of Agent Prior to Event" is deleted.

- NCI, Common Toxicity Criteria (CTC), Version 2.0 Adverse Event Category is an optional field. DCP will continue to collect the "verbatim" adverse event description as it did previously but, in addition, requests that the corresponding CTC term be indicated where possible.

- Certain fields in the ITPR are designated as required fields. These fields are marked with an "*" in this document and on the ITPR template. The required fields are:

    - Reporting Period Start Date
    - Reporting Period End Date
    - NCI Protocol Number
    - Registration Number
    - Registration Date
    - Randomization Number
    - Birth Year
    - Gender
    - Race
    - Adverse Event Description
    - Event Onset Date
    - Event Grade
    - Relatedness (Attribution)

- Reported as SAE?
- Blind Broken due to this AE?

- **Please note that race and ethnicity codes are changed to comply with new NIH guidelines**. This change applies to only those clinical trials activated after January 1, 2002. This reporting change is discussed in detail in Section 3, Cumulative Participant Accrual, in this document.

What is ITPR?

The ITPR will reflect cumulative data for the clinical trial. ITPR refers to the set of documents needed to complete the required reporting to DCP:

- Cover Page: Microsoft Word document with fields prepopulated from the DCP database.
- Section 1: Administrative Information: Microsoft Word document with fields pre-populated from the DCP database.
- Section 2: Progress Comments: First worksheet in a Microsoft Excel Workbook.
- Section 3: Cumulative Participant Accrual Table: Second worksheet in a Microsoft Excel Workbook.
- Section 4: Cumulative Adverse Event Table: Third worksheet in a Microsoft Excel Workbook.

Each of the above ITPR sections is discussed in detail in the "Data Element Descriptions" section of this document. A sample of the Microsoft Excel template is available on the DCP PIO web page: http://www3.cancer.gov/prevention/pio/instructions.html

What are the steps for completing the first set of ITPR templates?

- DCP provides Westat with a schedule of due dates for all studies for which ITPR submission is required.
- Approximately 1 month prior to the due date of the ITPR, Westat e-mails the ITPR templates, including "Guidelines for Completing the ITPR Excel Template," to the Contract/Grant Principal Investigator with a copy to the Study Principal Investigator (if different than the Contract/Grant PI), the Site Coordinator, DCP Protocol Information Office, NCI Contracting Officer (if applicable), NCI Procurement Technician (if applicable), the DCP Project Officer/Program Director, the DCP Medical Monitor (if different than the Project Officer/Program Director) and the DCP Nurse Specialist. The template consists of the documents previously described.
- The Contract/Grant Principal Investigator or designee reviews the prepopulated ITPR data in the Word document. If data discrepancies are identified, the ITPR is revised by typing the corrected data into the ITPR data field.
    - The ITPR has the Microsoft Word "track changes" function enabled. This tool will automatically highlight changes as they are typed into the ITPR. Please do not turn off the "track changes" function.
- The Contract/Grant Principal Investigator or designee completes the remaining fields the ITPR Excel template.
- Tips regarding the use of the ITPR Excel Template:

- Help Text: The Excel Workbook provides the definition for each data element in the form of "help text" that appears when the user clicks on any field.

- Drop-down lists: A drop-down list appears when clicking in each field requiring a specific term or "value." The user simply "clicks" on the correct term to select the appropriate value for each field.

- The ITPR Excel file will have the first row of each worksheet pre-populated with the Reporting Period Dates and the Protocol Number. These values should be copied into all new data rows that are added to the template.

- Mandatory fields are denoted by an asterisk. (Required fields must be complete before the report can be processed).

- Tips to help minimize discrepancies in the ITPR Excel Template:

  - Review the "Guidelines for Completing the ITPR Excel Template" document prior to submitting the template. This document outlines all of the QC checks that are run on the data.

  - Be sure that every row in the Excel template that contains data has the current reporting period start date, reporting period end date and the protocol number.

  - Do not delete any columns that do not apply to the protocol. Simply leave those columns blank.

  - Do not enter text in a field that is expecting a date. For example, NA, Not Done or Unknown typed into a field expecting a date will cause discrepancies that prevent the ITPR from loading into the database.

  - Key all unknown or missing days as "01" within any date fields. "00" is not a valid day and will prevent the ITPR from loading into the database. A note to file must be included in the participant's study file and the assumed date must be documented in the Progress Comments worksheet as an "Other" comment.

  - Key unknown or missing month values as "06". A note to file must be included in the participant's study file and the assumed date must be documented in the Progress Comments worksheet as an "Other" comment.

  - If cutting and pasting from another source, be sure to use the Paste Special function or the formatting of the Excel template will be lost causing loading errors.

- Note: If a site does not have access to Microsoft Word and/or Excel the site should notify Linda Parreco at DCP to make other arrangements. It is strongly encouraged that sites acquire these tools if they are not available.

What are the steps for completing subsequent ITPR templates?

- **Within the same reporting quarter,** Westat may request another ITPR submission if there are data discrepancies or review issues that need to be resolved before the ITPR can be loaded into DCP's database and accepted by the PO.

  - This subsequent submission request will be distributed via email along with the Discrepancy Report (PDF format) and the ITPR Excel File

- Following instructions in the Discrepancy Report, the Contract/Grant Principal Investigator (or designee) will review the previously submitted data in the ITPR Excel File and add additional data or modify existing data as needed.

- All corrections to the previously submitted ITPR Excel data values need to be documented with comments. These correction verification comments should be added to the Progress Comment worksheet. The comment should be given the type value of "Correction"

- Once all queries listed in the Discrepancy Report have been addressed, the site forwards the corrected file to the appropriate individuals (these contacts are listed below in the Submission section)

- **In subsequent ITPR quarters**, the site will receive the previous quarter's last submission (the one containing the data that the PO accepted previously) updated with the new quarter's reporting period dates.

- If the ITPR cycle remains on schedule, the site can expect to receive the Templates one month before the scheduled ITPR due date. If the processing of the previous ITPR quarter has taken longer than expected, the schedule of the subsequent quarter may be affected.

- The site will add data that has been collected since the last quarter to the new quarter's ITPR Excel Template.

What are the steps for submitting the ITPR templates?

- The Contract/Grant Principal Investigator submits the completed ITPR to DCP by one of the two following methods, depending on the funding mechanism of the study.

    - Protocols funded by contracts

        - Submit the ITPR as an e-mail attachment to the DCP Project Officer, (as named in the contract award document), Medical Monitor, Nurse Specialist, Contracting Officer, Linda Parreco at the DCP Protocol Information Office (parrecol@mail.nih.gov), and the DCP Help Desk (NCI-DCPmonitoring@westat.com). In order to include all of the appropriate DCP personnel in the return submission, the site can simply use the "Reply to All" feature of the e-mail program and reply to the original e-mail sent to the site by the DCP Help Desk.

    - Protocols funded by Grants or Cooperative Agreements

        - Submit the ITPR as an e-mail attachment to the DCP Program Director (as named in the Terms and Conditions of Award), Medical Monitor, Nurse Specialist, Linda Parreco at the DCP PIO (parrecol@mail.nih.gov) and the DCP Help Desk (NCI-DCPMonitoring@westat.com). In order to include all of the appropriate DCP personnel in their return submission, the site can simply use the "Reply to All" feature of their e-mail program and reply to the original e-mail sent to the site by the DCP Help Desk.

- The Contract/Grant PI or designee returns the completed ITPR to NCI/DCP according to the process described previously by the deliverables deadline date specified in the contract, grant, or cooperative agreement award document.

- **If a site does not have the ability to send the report as an e-mail attachment, the site should notify Linda Parreco at DCP to make other mailing arrangements. It is strongly encouraged that sites acquire this tool if it is not available.**

What happens to the ITPR templates once they are submitted to DCP and Westat?

- The ITPR data goes through a series of quality checks (QC) at Westat to ensure all of the required data in the Word document and the Excel workbook are present and to ensure the data that requires specific values are valid.

    - The ITPR must successfully load into the database to allow the automated quality checks to be run against the data.. Refer to the tips on page 7 to help ensure that the ITPR will not fail the loading process.

    - Any ITPRs that fail the loading process will be sent back to the Contract/Grant PI or designee for changes before the process can proceed:

- The DCP Help Desk is always available to answer any technical questions and can be contacted prior to submitting data in order to avoid unnecessary discrepancies. The number is 1-888-662-8354, Monday through Friday. 8:00 a.m. to 4:00 p.m. ET.

- After the data has gone through these quality checks, Westat will process all of the data or contact the study site for revisions to the data.

    - If corrections to the data are required, Westat e-mails a discrepancy report to the Project Officer and the DCP regulatory contractor, CCSA for review. If there is patient level data and the study is a DCP sponsored IND, CCSA will review the Adverse Event data for completeness. CCSA then forwards any queries to the Project Officer, PIO and Westat. The Project Officer will review the data and the discrepancies generated from the QC checks. They will then add any additional queries to the discrepancy report, if necessary. The complete discrepancy report is then e-mailed to Westat.

    - Westat e-mails the complete discrepancy report to the site. The Contract/Grant PI or designee makes the corrections in the original Excel workbook and resubmits the revised Excel workbook to Westat via e-mail.

    - The corrected ITPR is due to Westat, via e-mail, before the due date specified in the Discrepancy Report email.

    - If the resubmitted data passes all quality checks (QC), Westat will process the data and will notify the Project Officer that the data is ready for final review. If the resubmitted data does not pass the QC, Westat will continue to work with the site to resolve data issues.

- The DCP Project Officer/Program Director reviews and accepts the ITPR or requests additional corrections within 2 weeks.

- The entire ITPR must be accepted by the Project Officer/Program Director before it is considered final. Once this acceptance is completed Westat does one of the following:

    - If only Progress Comments were submitted on the ITPR, a Notification of Acceptance e-mail is distributed. This email will state that the ITPR Comments have been accepted by the Project Officer.

    - If the ITPR contains patient data the Complete ITPR (described below) will be attached to the Notification of Acceptance email distributed by Westat.

- All Acceptance Notification emails go to the following list of individuals: the Contract/Grant Principal Investigator, the Study Principal Investigator (if different than the Contract/Grant PI), the Site

Coordinator, the Project Officer/Program Director, Medical Monitor (if different than the Project Officer/Program Director), Nurse Specialist, the NCI Procurement Technician, the Contracting Officer, CCS Associates (CCSA) and the DCP PIO.

What is the Complete ITPR?

- The Complete ITPR is a set of reports generated from the DCP ITPR database after the ITPR submission has been loaded and accepted by the PO.
- The Complete ITPR is distributed by Westat in PDF format and it contains the following reports:
    - Cover Page
    - Administrative Information
    - Progress Comments
    - Cumulative Participant Accrual
    - Cumulative Adverse Events
    - Demographics (Gender and Age)
    - Demographics (Gender and Race)
    - Accrual Summary

What else is the ITPR data used for?

- The DCP regulatory support contractor, CCSA, accesses the ITPR information through the DCP central database to prepare the FDA IND Annual Reports (for studies where DCP has sponsored IND)

When should data be submitted?

- The ITPR should be submitted according to the schedule stated in the funding document.
- Protocols funded by contracts
    - Article F.1 Deliveries contains the specific schedule for data submission. Typically the contract requires delivery of the progress report on a quarterly basis. However, some contracts require monthly submission.
    - The Annual Investigator Technical Progress Report, as required by the contract, is in the same format as the Quarterly (or monthly) Investigator Technical Progress Report. Narrative sections represent a compilation and summary of progress made over the past year.
    - The Contracting Officer should be contacted with any questions regarding the reporting schedule.
    - The new ITPR should be submitted on the first progress report due date for 2003.

- If the protocol is currently in the 'protocol development phase' and has not started accruing participants, only the applicable portions of the ITPR should be completed (Cover page and Section 1: Administrative Information of the Word document and Section 2: Progress Comments of the Excel document). Participant information (Section 3: Cumulative Participant Accrual Table and Section 4: Cumulative Adverse Event Table) is reported once accrual commences.

- Protocols funded by grants or cooperative agreements

  - The Terms and Conditions of Award document gives the annual progress report due date.

  - The Program Director may specify a due date for the submission of the ITPR to coincide with the preparation of DCP's annual report to the FDA.

  - The Program Director can answer questions regarding the reporting schedule.

- ITPR submissions are required until the period of performance, as defined by the award document, is complete.

- Additional information will be provided regarding the process for submitting the Draft Final Report and the Final Report data at the end of the study.

Data Element Descriptions

Cover Page

The Cover Page is a template created with Microsoft Word. The Cover Page contains administrative information regarding the awarded project, i.e., the contract, grant or cooperative agreement. All but the final two fields on this page will arrive with information prepopulated from the DCP database (prepopulated fields are indicated with a plus sign below). The prepopulated data should be checked for accuracy and any changes indicated by typing directly in the field.

The data elements on the cover page are:

+**Title**	Title of the contract, grant, or cooperative agreement as stated on the funding document (e.g., Phase I Clinical Trials of Vitamin A in High Risk Populations). The title of the contract, grant or cooperative agreement may be the same or different than the protocol title.
+**NCI Contract, Grant, or Cooperative Agreement number**	The number as stated on the funding document (Ex: N01-CN-12345, U19-CA-12345, R01-CA-12345).
+**Contract Principal Investigator (PI)**	Name of physician who has organizational and fiscal responsibility for the use of Federal funds to conduct a clinical study or cooperative agreement as stated on the funding document.
+**Lead Organization**	The institution that receives funds directly from DCP for the purpose of performing the work described in the award document.
+**NCI Contracting Officer**	Contracting Officer as stated in the contract award document. (Not applicable for grants or cooperative agreements).
+**DCP Project Officer** (for contracts) or **DCP Program Director** (for grants or cooperative agreements)	DCP employee identified in the award document. The DCP "Project Officer" provides scientific and technical oversight of contract projects, whereas the DCP "Program Director" serves the same function for grants and cooperative agreements.
+**Reporting Period**	The time period presented in this report (i.e., 1/15/2003 through 3/15/2003). Contract-funded studies: the reporting period is specified in the contract award document. The reporting period is updated if a contract modification changes the reporting periods.
Date of report	Date report was **completed** by the site (i.e., 3/15/2003).
Prepared by	Name of individual who prepared the report; with title, address, phone number and e-mail. Included

Section 1 Administrative Information

The Administrative Information page contains detailed information about the protocol being performed under the contract, grant, or cooperative agreement. While most contracts, grants, or cooperative agreements are awarded to conduct a single protocol, some projects will be awarded to conduct more than one protocol. This scenario is most common with awards to conduct Phase I clinical trials. This page is provided to the PI as a Microsoft Word document template. The fields indicated with a plus sign in the table below will be prepopulated with data from the DCP database. The prepopulated data should be checked for accuracy and any changes indicated.

****If one funding agreement (contract, grant, or cooperative agreement) results in multiple protocols, submit Sections 1 to 4 for <u>each</u> protocol that is in development or actively accruing participants.***

The data elements in the Administrative Information section are:

+NCI Protocol Number	The number assigned by NCI, DCP to identify the protocol. The NCI protocol number will be used on all correspondence from NCI to the site. In some cases the NCI protocol number may be the same as the funding mechanism number (i.e., N01-CN-12345), a modification of the funding number (i.e., N01-CN-12345 breast), or the same as the local protocol number.
+Local Protocol Number	The unique number/name assigned by the lead organization to identify this protocol within their institution.
+Protocol Title	Title of the protocol document (e.g., Phase I Clinical Trials of Vitamin A in Oral Leukoplakia). This may be the same or different than the title of the grant, contract or cooperative agreement.
Number Screened	<u>Cumulative</u> number of participants evaluated for potential admission to the protocol.
+Study Status/Status Date	The study status listing shows a chronology of study status(s) and status date(s). The study status listing should be verified. It will include one of the following: • Protocol Development (final protocol has not been approved by DCP) • Approved by DCP • Disapproved by DCP • Active • Temporarily closed to accrual • Closed to accrual • Temporarily closed to intervention • Closed to intervention • Follow-up • Data analysis • Complete • Withdrawn
+Protocol Versions and Dates	All document versions submitted to DCP are listed. The

prepopulated information needs to be verified and any comments or corrections inserted as needed. The terms are defined as follows:

- Local Version Date - The date that appears on the protocol document submitted to DCP.
- Local Change # - The document "identifier" that appears on the protocol document (e.g., version 2 or Amendment 1)
- DCP Receipt Date - The date the document is received by the DCP PIO
- DCP Change # - An internal DCP tracking number assigned by the database.

+IND Number/IND Sponsor

The IND number assigned by the FDA and the sponsor of the IND under which the protocol is submitted. This field is blank for a non-IND protocol.

Participating Organizations

The names of all institutions that have been approved by IRBs to participate in this study should be listed.

Section 2 Progress Comments: One per protocol

Note: The Microsoft Excel Workbook, Worksheet 1 is used to record this information. The "*" next to items below indicates a required field. The first submission of the ITPR will reflect comments for the current reporting period only (i.e., 1/15/03 through 4/14/03). It is not necessary to reflect cumulative/historical comments on the first ITPR. The fields indicated with a plus sign in the table below will be prepopulated with data from the DCP database.

+*Reporting Period Start Date	A row is prepopulated with the reporting period start date. For ease of data entry, this can be copied into the subsequent rows, if necessary.
+*Reporting Period End Date	A row is prepopulated with the reporting period end date. For ease of data entry, this can be copied into the subsequent rows, if necessary.
+*NCI Protocol Number:	The NCI-defined protocol number is prepopulated for copying into the subsequent fields, if necessary.

Note: the above fields must be completed for each participant to allow data loading into the DCP database.

Comment Type:	The appropriate term should be selected from the drop-down list that appears when clicking on any cell in the "Comment Type" column. • Accrual • Agent Supply • Staffing • Other • Correction Comments After selecting the appropriate Comment Type, text should be entered in the Comments Field. Multiple comment entries may be added and should reflect activities during the reporting period. If different multiple comments of the same comment type are reported, each different comment can be listed on a separate row and the Comment Type simply repeated.
Comments:	Specific comments relating to the type of category chosen.

For Example:

Accrual Comments	If actual accrual is less than planned accrual, reasons should be given and action provided for correcting accrual. Plans should be included for adding new sites.
Agent Supply Comments	If applicable, the problem and any impact on accrual and conduct of the study should be described.

Staffing Comments	If applicable, the problem and any impact on the conduct of the study should be described.
Other Comments	Any observed trends related to adverse events, deviations, etc should be addressed. The overall progress of the trial, planned activities, and any problems encountered should be discussed. Comments related to the status of protocol development activities should be added.
Corrections Comments	Note any changes in data that were reported on a previous ITPR. This includes discovery of errors or other discrepancies occurring since the data was submitted.

Section 3 Cumulative Participant Accrual: One per protocol

Note: The Microsoft Excel Workbook, Worksheet 2 is used to enter the following data for each participant on the trial. One row is entered for each study participant. Each row contains the following columns for data entry. The "*" next to items below indicates a required field. This report reflects cumulative data; all ITPR submission requires inclusion of all participants previously reported and those participants accrued during the reporting period. The fields indicated with a plus sign in the table below will be prepopulated with data from the DCP database.

+*Reporting Period Start Date A row will be prepopulated with the reporting period start date. This date can be copied into the subsequent rows, if necessary.

+ *Reporting Period End Date A row will be prepopulated with the reporting period end date. This date can be copied into the subsequent rows, if necessary.

+ *NCI Protocol Number The NCI-defined protocol number will be prepopulated for copying into the subsequent fields, if necessary.

Note: the above fields must be completed for each participant to allow data loading into the DCP database.

***Registration Number** Unique identifying number assigned to the participant. Institutions may use other names for this identifier, including "Subject Number," "Patient ID," etc. In the previous DCP Chemoprevention Progress Report template, this was referred to as "Subject ID." The Registration Number is defined with a maximum length of 10 characters.

***Registration Date** Date (MM/DD/YYYY) the participant signed the Informed Consent.

***Birth Year** Format YYYY is used for birth year.

***Gender** Male, Female, or Unknown. The appropriate term is selected from the drop-down list that appears when clicking in each cell of the "Gender" column.

Ethnicity This field is applicable only for protocols approved by the NCI after 1/1/02. These protocols must report an ethnicity category to comply with the new race and ethnicity reporting requirements guidelines set forth by the Department of Health and Human Services (DHHS), Office of Management and Budget (OMB). The guidelines require designation of the patient's ethnicity (Hispanic or Latino, Non-Hispanic, or Unknown). The participant's ethnicity is provided using the code and descriptions below. It does not permit a multiple response that would indicate an ethnic heritage that is both Hispanic/Latino and non-Hispanic/non-Latino.

The appropriate term should be selected from the drop-down list that appears when clicking in each cell of the "Ethnicity" column.

If the clinical trial was approved by NCI prior to 1/1/02, this field is left blank.

One of the following ethnicity categories is selected for each study participant:

Hispanic or Latino: A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin, regardless of race.
Non-Hispanic: A person NOT meeting the definition for Hispanic or Latino.
Unknown: Ethnicity unknown.

***Race**

All study participants must be reported by race. However, the race category selections differ under the old and new reporting criteria. The "Race" field on the ITPR spreadsheet displays a drop-down list when the user clicks on each cell in the race column. The drop-down menu contains a list of all race codes (for both the old and new reporting systems). This list is referred to as the "superset." Race is selected from the categories described below depending on the date of study approval.

Studies approved after 1/1/02: Based on the new DHHS, OMB guidelines participants have the ability to report multiple race categories. For example, a person of European and Chinese origins is classified as "White" and "Asian." The individual categories are collected on the Case Report Form. However, for the purpose of ITPR reporting, use the term below, "more than one race" is used to identify participants who report themselves as multiracial. The selection is made from the following race codes on the superset:
01-American Indian or Alaskan Native: A person having origins in any of the original peoples of North and South America (including Central America), and who maintains tribal affiliation or community attachment.
06-Asian: A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and Vietnam.
07-Native Hawaiian or Other Pacific Islander: A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.
08-Black or African-American: A person having origins in any of the black racial groups of Africa.
09-White: A person having origins in any of the original peoples of Europe, the Middle East, or North Africa.
10-More than one race: This category is used for participants who select multiple races on the CRF.
12-Unknown or not reported

Studies approved before 12/31/01: These protocols will continue to report according to the old criteria. That is, ethnicity is not captured as a separate category and the participant may select only one race. The following categories may be selected in the race superset to describe the participant's racial category. These requirements are unchanged from the old DCP Chemoprevention Progress Report Template:

01-American Indian or Alaskan Native: A person having origins in any of the original peoples of North and South America (including Central America), and who maintains tribal affiliation or community attachment.
02-Asian or Pacific Islander: A person having origins in any of the original peoples of the Far East, Southeast Asia, or the Indian subcontinent including, for example, Cambodia, China, India, Japan, Korea, Malaysia, Pakistan, the Philippine Islands, Thailand, and

Vietnam. A person having origins in any of the original peoples of Hawaii, Guam, Samoa, or other Pacific Islands.
03-Black, not of Hispanic Origin: A person having origins in any of the black racial groups of Africa.
04-Hispanic: A person of Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin.
05-White, not of Hispanic Origin
11-Other or Unknown

Begin Run-In Date

Date (MM/DD/YYYY) that prerandomization placebo trial period (run-in) began, if applicable. If the trial does not use a run-in period this field is left blank.

End Run-In Date

Date (MM/DD/YYYY) that prerandomization placebo trial period (run-in) ended, if applicable. If not applicable, this field is left blank.

***Randomization Number**

Number given to the participant when assigned to a study arm, if applicable. If the trial does not assign a randomization number NA is entered.

Randomization Date

Date (MM/DD/YYYY) that participant was assigned to study arm; the date may be the same or different than the Registration Date. If the trial does not assign a randomization number, this field is left blank.

Start Study Agent Date

Date (MM/DD/YYYY) participant received first dose of the agent/placebo while on study.

End Study Agent Date

Date (MM/DD/YYYY) participant received last dose of the agent/placebo. Note: this date will either be the day the participant completed the protocol prescribed intervention or the date that the participant stopped taking the agent before completing the protocol intervention.

If the participant continues on agent, this field is left blank. For temporary agent stops, an end study agent date is entered and the reason stopped is selected. When the agent is started again, a new row with a start study agent date is entered.

Off Agent Reason

"Off Agent Reason" is a new field and is not a required field. Since the ITPR is a cumulative report, this field may be left blank for participants previously reported under the old system. "Off Agent Reason" refers to reasons that the participant stopped taking the study agent. The reason may be that the participant completed the protocol-prescribed agent or the participant may have stopped the agent early for other reasons. If the participant stopped taking agent, <u>one</u> of the following is specified. If the participant continues to receive agent leave this field blank. If the participant also goes "Off Study" at the same time that he or she stops the agent, the "Off Study" field is completed.

The user selects the appropriate term from the drop down list that appears when clicking on any cell in the "Off Agent Reason" column.

- Completed protocol-prescribed intervention
- AE/SAE
- Inadequate agent supply (e.g., patient had no agent or site had no agent)

- Noncompliant participant (includes refused treatments and/or assessments)
- Concomitant medication
- Medical contraindication (e.g., pregnancy)
- (Death is an “off study” reason rather than an “off agent” reason; see below)
- Other (must provide a value in Off Agent Comments)

Off Agent Comments

If the “Off Agent Reason” is “Other,” the details in this text field must be specified.

Begin Follow-up Date

Date (MM/DD/YYYY) that the post-treatment, protocol-defined observation period began, if applicable. If not applicable, the template field is left blank.

End Follow-up Date

Date (MM/DD/YYYY) that the post-treatment, protocol-specific observation period ended, if appropriate. If not applicable, the field is left blank.

Off Study Date

Date (MM/DD/YYYY) participant completed the study (treatment or treatment with follow-up) or the last date of contact.

Off Study Reason

“Off Study Reason” was captured on the old template; however, additional categories have been added to facilitate improved data analysis. The new categories are indicated in the list below. This is not a required field. Since the ITPR is a cumulative report, this field may be left blank for participants reported under the old system. If a participant goes off study, one of the following reasons is selected.

The categories below appear on a drop-down list when clicking in any of the cells in the “Off Study Reason” column.

- Completed (completed protocol intervention and any protocol–specified follow-up period or evaluations)
- AE/SAE
- Lost to follow-up
- Noncompliant participant--new category (includes refused treatment, assessments)
- Concomitant medication--new category
- Medical contraindication-new category (e.g., pregnancy)
- Withdraw consent
- Death
- Other (must provide a reason in Off Study Comments)

Off Study Comments

If “Other” is selected as the Off Study Reason, details are specified in this text field.

Other Comments

Text field for adding any other pertinent details regarding the individual participant.

Section 4 Cumulative Adverse Event Table

Note: The Microsoft Excel Workbook, Worksheet 3 is used to enter the following data for each adverse event experienced by participants on the trial. One row is entered for each adverse event. Each participant may have multiple adverse events. Each row contains the columns listed below for data entry. The "*" next to items below indicates a required field. This report reflects cumulative data; all ITPR submission requires inclusion of all adverse events previously reported and those adverse events observed during the reporting period. The fields indicated with a plus sign in the table below will be prepopulated with data from the DCP database.

+*Reporting Period Start Date The first date of the reporting period is entered in format MM/DD/YYYY. For ease of data entry, the date is entered in the first row and copied into the subsequent rows, if necessary.

+*Reporting Period End Date The final date of the reporting period is entered in format MM/DD/YYYY. For ease of data entry, the date is entered in the first row and copied into the subsequent rows, if necessary.

NCI Protocol Number The NCI-defined protocol number is entered and copied into the subsequent fields, if necessary.

Note: the above fields must be completed for each participant to allow data loading into the DCP database.

***Registration Number** Unique identifying number assigned to the participant. Institutions may use other names for this identifier including "Subject Number," "Patient ID," etc. In the previous DCP Chemoprevention Progress Report template, this was referred to as "Subject ID." The Registration Number is defined with a maximum length of 10 characters.

***Randomization Number** Number given to the participant when assigned to a study arm, if applicable. If the trial does not assign a randomization number, NA Is entered.

Agent Type The agent name is not required. If the intervention arm is known, "active" or "placebo" should be specified. If the study is blinded, then "blinded" should be specified. If the study is blinded, the following dosing information fields (Agent Dose at AE, Dose Units, and Agent Frequency) must be left blank.

Agent Dose at AE If known, the actual dose of study agent (e.g., "100") that the participant was receiving at the time of the event is indicated in the spreadsheet column. If the actual dose is not known (i.e. the study is blinded) this is left blank.

Dose Units The dosing units (e.g., mg, ml) of the study agent the participant was receiving at the time of the adverse event are indicated. The unit (e.g. mg, ml) may be selected from the drop-down list that appears when clicking in any cell in the "Dose Units" column. If the study is blinded, this is left blank.

Agent Frequency The dosing schedule for the agent (e.g., qd, bid, qid) is indicated. The frequency term is selected from the drop-down list on the Excel spreadsheet. If the study is blinded, this is left blank.

***Adverse Event Description**

Overview:

Definition--An adverse event (AE) is any condition that appears or worsens after the participant is enrolled in an investigational study.

Procedure/diagnostic exam: An invasive procedure is not AE. However, if an AE occurs in the process of performing a procedure it should be reported. Example: excessive bleeding following a colonoscopy is reported as an AE.

This is a required field. All adverse events must be noted, whether or not they are related to the study agent, and must be reported during the reporting cycle in which they occurred. Each event is listed separately. Several events may not be in one record or entry. AE reporting is mandatory for all studies assigned to ITPR reporting.

Instruction: The event is recorded as described verbatim by the participant and collected/reported by the site personnel (e.g., headache, nausea, dizziness).

CTC Term

This is a new field. This field is optional but strongly encouraged.

Overview: The NCI ++Common Toxicity Criteria (CTC) was developed in 1982 for use in adverse drug experience reporting, creating adverse event summaries, IND reports to the FDA, and publications. The primary organization of the CTC is based on pathophysiological (e.g., Allergy/Immunology) and anatomical (e.g., Dermatology/Skin) categories. Within each of these categories, specific adverse events are listed alphabetically and graded.

The CTC contains terms for toxicities resulting from cancer treatment modalities. Some adverse events that occur in chemoprevention trials (ocular conditions related to retinoids) are not listed in the CTC. In addition, the CTC does not contain medical conditions that may be necessary to report. However, it is important to collect data regarding events unique to cancer prevention agents so that the CTC may be modified in the future to include these events.

For a number of years, DCP has required use of the CTC for *grading* adverse events, but did not require use of the actual CTC terms to describe the AE. At this time, use of the CTC term to describe the AE is strongly encouraged but not required. To assist in this process, the CTC terms appear in the Excel spreadsheet and can be viewed and selected by scrolling through the drop-down list.

Instruction:

1. The CTC term is selected that corresponds to the term entered in the spreadsheet field “AE Description” (e.g., fatigue, weight gain, corneal opacity). The user scrolls through the dropdown list in the spreadsheet to find the CTC term that most closely corresponds to the verbatim term (e.g., AE description = fatigue, CTC term = Constitutional Symptoms: fatigue (lethargy, malaise, asthenia).
2. If the CTC list does not contain the exact term needed (e.g., corneal opacity), the user scrolls through the CTC list to identify the most related higher level “category” (e.g.,

Ocular/Visual) and selects "Other (Specify, _____))"(e.g., Ocular/Visual-Other (Specify, ___). The next spreadsheet column captures the specific information.

CTC "Other—Specify"

If "Other-Specify" is selected as the AE term, the details must be provided in this field. This may be the same term captured in the adverse event description field. This field is optional.

***Event Grade**

Event grade represents the severity of the AE and is a required field. Each reported AE must be assigned an event grade. The required source for assigning grades to AE is the NCI Common Toxicity Criteria. Due to the extensive nature of the listing, the CTC grades are not available as a drop-down menu on the Excel spreadsheet. The CTC table should still be used for the event grade definitions. The table is available at (http://ctep.info.nih.gov/reporting/ctc.html).

The user should refer to he protocol for any agent-specific event grading scale that may be included in the protocol document and use the protocol-defined grading scale when one is provided.

Events not listed in the NCI CTC or in the protocol may be graded using a generic grading system. The generic grades may be selected from the dropdown list on the spreadsheet.

- 0 = No adverse event or within normal limits
- 1 = Mild adverse event (causing no limitations of usual activities)
- 2 = Moderate adverse event (causing some limitation of activity)
- 3 = Severe adverse event (severe and undesirable, causing inability to carry out usual activities)
- 4 = Life-threatening or disabling adverse event
- 5 = Fatal adverse event

****NOTE: In the past, DCP used a three-tiered generic grading system. Ongoing trials will continue to use this system to maintain consistent methodology. New trials will transition to the five-tiered grading system. DCP will discuss these changes with the Contract PI during the protocol development phase.**

***Event Onset Date**

The user should specify the date (MM/DD/YYYY) an event started. If the exact day is unknown, the day is reported as "01" and the date assumption is documented as an "Other" Progress Comments should be made on the Progress Comments worksheet. The date assumption should be documented in the participant's study file with a note to file.

Event Ended Date

The date (MM/DD/YYYY) that the event ended should be specified. If the event is ongoing, this field is left blank.

Event Status

The resolution status is indicated for each reported adverse event at the time of this report:

- Resolved (must enter an Event Ended Date)

- Not resolved
- Unknown

***Relatedness (Attribution)**

The site's Principal Investigator's assessment of relationship between event and study agent/placebo. The following categories of relatedness, which are based on the European Organization for Research and Treatment of Cancer (EORTC) guidelines, should be used. The appropriate value is selected from the drop-down list in each cell.

- Unrelated (There is no evidence of causal relationship). Previous term was "Not Related."
- Unlikely (There is *little* evidence to suggest there is a causal relationship (e.g., the event did not occur within a reasonable time after administration of the trial medication). There is *another reasonable explanation* for the event (e.g., the patient's clinical condition, other concomitant treatments).
- Possible (There is *some* evidence to suggest a causal relationship (e.g., the event occurred within a reasonable time after administration of the trial medication). However, the influence of *other factors may have contributed* to the event (e.g., the patient's clinical condition, other concomitant events).
- Probable (There *is evidence* to suggest a causal relationship, and the influence of other factors is *unlikely).*
- Definite (There is *clear* evidence to suggest a causal relationship, and other possible contributing factors can be *ruled out).*

Dropped due to this AE?

Specify whether participant dropped out of the study due to this adverse event. Select either "Yes" or "No" from the drop down list.

***Reported as SAE?**

If the AE meets one of the following criteria it must be reported to DCP as a Serious Adverse Event. This field indicates whether an SAE form was completed and submitted to DCP. The user selects "Yes" (SAE form submitted) or "No" (SAE form not submitted) from the drop-down list. The ICH Guideline 2A defines an SAE as an adverse experience, occurring at any dose that includes the following:

- Results in death
- Is life threatening
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- May not meet these criteria, but which the investigator finds very unusual and/or potentially serious.

The SAE reporting policy in the protocol document gives further details on the SAE reporting requirements.

***Blind Broken due to this AE?**

"Yes" or "No" are entered to indicate if the SAE for this participant required the study blind to be broken. If not applicable, NA is entered into this field.

Resources

DCP Help Desk Phone Number:	1-888-662-8354, Monday-Friday, 8:00 a.m. to 4:00 p.m. ET
DCP Help Desk E-mail:	NCI-DCPMonitoring@westat.com
DCP Web Site\ITPR Information:	http://www.cancer.gov/prevention/pio (The ITPR instruction document, definitions, and sample templates are available on this DCP Protocol Information Office web site: click on "Instructions, Templates, and Reference Materials"
DCP Web Site\IContact Information:	http://www.cancer.gov/prevention (This web site has contact information for the DCP Project Officers/ Program Directors, the Organ Group Nurse Specialists and the Protocol Information Office: click on "About the Division of Cancer Prevention").
NCI Research Contracts Branch:	http://rcb.cancer.gov/rcb-internet/