Division of Cancer Prevention
National Cancer Institute

Version 4.0

Investigator Technical Progress Reports (ITPR)

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
4.0	5	Are any trials exempt from ITPR reporting?	This section was removed from the current version.
4.0	5	What are the steps for completing the first set of ITPR templates?	Removed information regarding site's that do not have access to MS Word or Excel.
4.0	7	What happens to the ITPR templates once they are submitted to DCP and Westat?	Updated the information regarding CCSA's review of ITPRs.
4.0	9	When should data be submitted?	Removed information regarding monthly reporting.
4.0	12	Administrative Information	Updated the definition of "Number Screened" field.
4.0	25	Resources	Updated websites and phone numbers for resources.
4.0	26	Flow chart of ITPR process	Updated to reflect current process.

Investigator Technical Progress Reports

Division of Cancer Prevention 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) Master Agreement Holder contracts and for some grants. The ITPR enables DCP to ensure participant safety and study integrity throughout the duration of the Clinical Trial by establishing a consistent data format that allows study data to be uploaded and reviewed from DCP's database. Additionally, as DCP serves as the Investigational New Drug Application (IND) sponsor for many of the chemoprevention trials funded by DCP, the ITPR allows DCP to generate reports to satisfy the requirements of the Code of Federal Regulations 21 (CFR) §312 which requires the IND sponsor to submit annual reports to the Food and Drug Administration (FDA) on the progress of clinical investigations. 21 CFR §312.60 requires the Principal Investigator (PI) to personally 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. This is documented by having the PI sign Form FDA 1572 and the ITPR satisfies the latter requirement.

DCP, in creating the ITPR, has established a reporting process to ensure that complete clinical information on all DCP-sponsored IND studies is available to fulfill the regulatory requirements. This is accomplished by having the investigators or their designees 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 ITPR process benefits investigators and DCP in several ways:

- Decreases the amount of effort needed 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 by the site.
    - DCP tracks the due dates for ITPRs and sends the site a template approximately one month in advance of the ITPR due date.
- Standardized definitions and '"drop-down" menus take the guesswork out of data entry.
- 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 the ITPR process
- 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 Master Agreement Holder (MAH) contracts awarded before 10/01/2002, regardless of IND status, will report progress to DCP via the ITPR (see exemptions below). 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.

- Phase I, II, and III clinical trials funded by DCP MAH contracts awarded after 10/01/2002, regardless of IND status, may report progress to DCP via the ITPR at the discretion of DCP. 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 for which DCP is the IND sponsor includes studies funded by grants or cooperative agreements.

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 for all sites into the ITPR.

What is ITPR?

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

- Cover Page: Microsoft Word document with fields pre-populated 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://www.cancer.gov/prevention/pio/instructions.html

What is the difference between the terms "mandatory" and "required" as used for ITPR?

- The term "mandatory" refers to data fields that the database depends on for data loading. The consequence of this is that fields that are labeled as "mandatory" must in all cases be completed, even if a "real value" is not collected. An example of this is the ITPR data field Randomization Number. If a randomization number is not available for a participant, the value "N/A" is captured in the data field for that accrual record on the ITPR excel template.

- The term "required" refers to data fields that are of high importance for collection, however, they may not be available at all stages of the trial. An example of this is the ITPR data field Start Study Agent Date. This field is especially important for FDA reporting, however due to the way in which the DCP database is designed, and due to the fact that this value may not be available for all participants, it cannot be labeled as "mandatory". Start Study Agent Date is therefore labeled "required", and sites are expected to report this value as it becomes available. If a participant has not yet started study agent, the Start Study Agent Date field would remain blank for that participant.

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 will be the progress reporting method.

- Approximately 1 month prior to the due date of the ITPR, Westat emails 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 from 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 pre-populated 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 in the ITPR Excel template.

- Tips regarding the use of the ITPR Excel Template:

    - Help Text: The Template 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 Template 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. All mandatory fields must be completed before the report can be processed. Regardless of whether or not a field is labeled as "mandatory" data should be added for all applicable fields as it becomes available. Tips to help minimize discrepancies in the Template:

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

- Be sure that every row in the 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 row's Comment field (either the Other Comments field in the Cumulative Participant Accrual sheet, or the AE Comments field in the Cumulative Adverse Event sheet, as applicable).

- 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 row's Comment field (either the Other Comments field in the Cumulative Participant Accrual sheet, or the AE Comments field in the Cumulative Adverse Event sheet, as applicable).

- 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.

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 approximately 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.

- **Out of Cycle Updates,** If an update to a previous reporting period is discovered, an email should be forwarded to the DCP Helpdesk (nci-dcpmonitoring@westat.com). Westat will communicate with DCP to determine on a case by case basis what the site will need to do in order to submit updated data. In some cases, it may be decided to hold updates for the next ITPR reporting period.

What are the steps for submitting the ITPR templates?

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

    - Protocols funded by contracts

        - Submit the ITPR as an email attachment to the DCP Project Officer, (as named in the contract award document), Contracting Officer, the DCP Protocol Information Office (PIO) (nci_dcp_pio@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 their email program in reply to the original email sent to the site by the DCP Help Desk.

    - Protocols funded by Grants or Cooperative Agreements

        - Submit the ITPR as an email attachment to the DCP Program Director (as named in the Terms and Conditions of Award), the DCP PIO (nci_dcp_pio@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 email program in reply to the original email sent to the site by the DCP Help Desk.

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

- The ITPR data goes through a series of quality control (QC) checks at Westat to ensure all of the required data in the Word document, and the Excel workbook, are present, and to ensure the data in fields that require specific values are valid. See Appendix A for an ITPR process Diagram that outlines the entire process.

- The ITPR must successfully load into the database to allow the automated quality checks to be run against the data.

- 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 available to answer any technical questions, and can be contacted prior to submitting data, in order to avoid unnecessary discrepancies. Hours of operation: Monday - Friday, 8:00 AM. to 4:00 PM. ET. Phone number: 1-888-662-8354.

- 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 and safety contractor, CCS Associates (CCSA) for review. If Westat does not identify any data errors, the ITPR excel template is forwarded to the Project Officer and CCSA to review.

    - If there is subject level data, CCSA will review the Adverse Event data for completeness and compare the data against any SAE forms. CCSA then forwards any queries to the Project Officer, PIO and Westat. The Project Officer will review the data and if necessary 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 emailed to Westat.

    - Westat emails 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.

- 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 email is distributed. This e-mail will state that the ITPR Comments have been accepted by the Project Officer.

    - If the ITPR contains participant data, the Complete ITPR (described below) will be attached to the Notification of Acceptance e-mail distributed by Westat.

- All Acceptance Notification emails are sent 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, 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?

- CCSA accesses the ITPR information through the DCP central database to prepare the FDA IND Annual Reports (for studies where DCP has sponsored IND) or for other tasks as directed by DCP.

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.
    - The Annual Investigator Technical Progress Report, as specified by the contract, is in the same format as the Quarterly 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.
    - 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 necessary 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

What should I do if the answer values on my CRF don't exactly match the selections in the ITPR drop-down menus?

- If a value on a CRF does not exactly match one of the values available in an ITPR drop-down field, each value that does not match will need to be "translated" into an ITPR value. This translation process is referred to as data "mapping."
- Mapping is only needed when the list of values of an ITPR field does not match a specific value on the protocol specific CRF.
- For Example: If the status of an adverse event is marked as "Ongoing" on the CRF, but the only ITPR options for the AE Event Status are "Resolved", "Not Resolved", and "Unknown ", then the "Ongoing" CRF selection should be mapped to the ITPR value of "Not Resolved".
- When in doubt of the proper mapping of study specific values to ITPR values, the Principal Investigator should consult with the protocol Project Officer.
- Any mapping between study specific terms and an ITPR list of values should be documented internally at the site, in accordance with site specific rules.
- In the ITPR, all mapping should be documented with either Progress Comments or, in the case of SAE/AE records, General comments on the record itself.

How do I map my SAE form "Outcome of events" to the ITPR "Event Status"?

- See the table below for event resolution mapping between the NCI, DCP paper SAE form and the ITPR list of values.
- Instructions for completing the field EVENT STATUS are on page 25 of this Instruction Document.

SAE form Outcome of Event	ITPR Event Status
Resolved	Resolved
Improved	Not Resolved
Unchanged	Not Resolved
Worse	Not Resolved
Not Available	Unknown
Fatal	Resolved

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 (pre-populated fields are indicated with a plus sign below). The pre-populated data should be checked for accuracy, and any changes should be indicated by typing directly in the field.

The data elements on the cover page are:

+Title	The 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)	The name of a person (usually a 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	The 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)	The 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 represented in the report (i.e., 1/15/2007 through 3/15/2007). 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	The date the report was **completed** by the site (i.e., 3/15/2007).
Prepared by	The name of the individual who prepared the report; with title, address, phone number and email 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

The 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

The cumulative number of participants evaluated for protocol eligibility.

+Study Status/Status Date

The study status listing shows a chronology of study status(es) 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

Note: The Microsoft Excel Workbook, Worksheet 1 is used to record this information. The "*" next to items below indicates a required field. The first submitted version of the ITPR reporting period 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 this first version submitted for a new ITPR 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 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 comment to allow data loading into the DCP database. In addition, a minimum of one comment must be included on the ITPR Excel Template.

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 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, if necessary.

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

Note: The Microsoft Excel Workbook, Worksheet 2 is used to enter the following data for each participant on the trial. Generally, one row is entered for each study participant. If a participant had an interrupted dosing regime, this should be captured using multiple rows. 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 submissions require inclusion of all participants previously reported, as well as 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 should be copied into subsequent rows, as new rows become necessary.
+*Reporting Period End Date	A row will be prepopulated with the reporting period end date. This date should be copied into subsequent rows, as new rows become necessary.
+*NCI Protocol Number	The NCI-defined protocol number will be prepopulated for copying into subsequent rows, as new rows become necessary. **Note: the above fields must be completed for each participant to allow data loading into the DCP database.**
***Registration Number**	A unique identifying number assigned to each 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**	The 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 each participant's ethnicity (Hispanic or Latino, Non-Hispanic, or Unknown). The participant's ethnicity is provided using the code and descriptions below. This field 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.
Not Hispanic or Latino: 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, the term below, "more than one race", is used to identify participants who report themselves as multiracial. All selections are 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

The date (MM/DD/YYYY) the participant's pre-randomization 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

The date (MM/DD/YYYY) the participant's pre-randomization placebo trial period (run-in) ended, if applicable. If not applicable, this field is left blank.

***Randomization Number**

The number given to the participant when assigned to a study arm, if applicable. If the trial does not assign a randomization number, NA or N/A is entered.

Randomization Date

The date (MM/DD/YYYY) the participant was assigned to a 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

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

End Study Agent Date

The date (MM/DD/YYYY) the participant received the last dose of the study agent. 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 the new start study agent date is entered.

Off Agent Reason

"Off Agent Reason" is a new field and is not a required field unless an "End Study Agent Date" is given. "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 should also be 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., participant 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 — The date (MM/DD/YYYY) the participant's post-treatment, protocol-defined observation period began, if applicable. If not applicable, this template field is left blank.

End Follow-up Date — The date (MM/DD/YYYY) the participant's post-treatment, protocol-specific observation period ended, if appropriate. If not applicable, this field is left blank.

Off Study Date — The date (MM/DD/YYYY) the 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. 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 should be selected for this field.

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
- Non-compliant 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 — A 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 submissions require inclusion of all adverse events previously reported, as well as 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, as 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, as necessary.

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

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

***Registration Number** A unique identifying number assigned to each 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. This value must match the value given on the participant's accrual record (on the Cumulative Accrual Worksheet) exactly.

***Randomization Number** A number given to each participant when assigned to a study arm, if applicable. If the trial does not assign a randomization number, NA or N/A is entered. This value must match the value given on the participant's accrual record (on the Cumulative Accrual Worksheet) exactly.

Agent Type The agent name is not required. If the intervention arm is known, "active" or "placebo" should be specified in this field. If the study is blinded, then "blinded" should be specified. If the study is blinded, the 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 this field. If the study is blinded, this field 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 in this field. 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 field is left blank.

Agent Frequency

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

This is a required field. All AEs must be reported, regardless of whether or not they are related to the study agent, and should be reported during the reporting cycle in which they occurred (except where this is not possible). Each event is listed separately. Multiple events may not be listed as one record or entry. For instance, if a participant reports a headache and nausea with Event Onset and Ended Date of 11/18/2004, then two events should be listed. One event listing for the headache and one event listing for the nausea. 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 on the AE CRF (e.g., headache, nausea, dizziness).

CTC Term

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

Overview: The NCI CTC was developed in 1982 for use in adverse drug experience reporting, creating AE 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 an AE resulting from cancer treatment modalities. Some AEs 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 the use of the CTC for ***grading*** the severity of AEs, but did not require the use of the actual CTC terms to describe the AE. At this time, the use of the CTC term to describe an 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. As of 12/18/2005 CTC version 2 and CTCAE (version 3) are available for ITPR data entry. Per protocol, the site will receive a template with the drop down listing of CTC version 2, or CTCAE (version 3), on the ITPR template. If the protocol specification of CTC version changes mid-study, the DCP Helpdesk and the NCI-PIO office must be informed so that the ITPR template can be updated accordingly.

Instruction:

1. The CTC term is selected that corresponds to the term entered in the spreadsheet "AE Description" field (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 in the CTC Term field, then the details must be provided in this field. This may be the same term captured in the Adverse Event Description field, if the term is clearly understandable. Otherwise, a more clearly defined AE description should be provided in this field. This field is optional.

***Event Grade**

The 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 AEs is the NCI CTC. Due to the extensive nature of the listing, the CTC grades are not available as a drop-down menu on the Excel spreadsheet. Nevertheless, the CTC table should still be used to determine the appropriate Event Grade assignments. The CTC table is available at http://ctep.cancer.gov/ .

The user should refer to the 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 table, 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 (only available for CTC version 2)
- 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 of the month is unknown, the day is reported as "01" and the date assumption is documented in the "AE Comment" field. The date assumption should also 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 in this field. If the event is ongoing, this field is left blank.

Event Status

The resolution status is indicated for each reported AE at the time of this report: (see "How do I map my SAE form "Outcome of events" to the ITPR "Event Status"?" section for mapping the SAE paper report Outcome of Event to the Event Status to the ITPR)

- Resolved (must enter an Event Ended Date)
- Not resolved (no Event Ended Date)
- Unknown (no Event Ended Date)

***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 participant'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 participant'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 the participant dropped out of the study due to this AE. 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 (SAE). This field indicates whether an SAE report 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.

Note: The CTC Grade assigned to an event does not determine whether this field is marked Yes or No.

	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 the event is not a SAE, or if the study is not blinded, then this field is not applicable, and NA is entered into this field.
AE Comment	Use this field to add comments for discrepancy resolution, or to provide additional information regarding the AE.

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\Contact 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 Office of Acquisitions:	http://rcb.cancer.gov/rcb-internet/

ITPR Process Diagram for Site Personnel

Site submits initial ITPR (data filled) Template.

Westat performs initial review of ITPR Template.

If there are pre-loading data questions that can be resolved over the phone, Westat contacts the site to resolve them. (An example of a discrepancy that can be addressed over the phone is rows propagated only with Period Dates.) It there are pre-loading data questions that cannot be resolved over the phone, Westat will include those in a Discrepancy Report to sites.

After initial review, Westat attempts to load the data into the staging tables in DESK.
If loading errors occur, Westat evaluates whether that data needs to be corrected by site before in can continue to be processes.

If site corrections are needed, Westat issues a Pre-Loading Discrepancy Report and requests that the site submits corrected submission. (An example of a pre-load discrepancy is text values in date fields.)

If data loads successfully into the staging tables (or can continue processing without corrections by site) Westat runs automated and manual checks on data (QC and SAS), and requests the PO and CCSA review that data in the ITPR Excel File.
If during their review, the PO or CCSA find values that need to be queried, they create a Query Report.

The PO and CCSA notify Westat that they have completed their review and attach their Query Report (if needed) to the notification email.

Westat merges all and any of the Query Reports into a Master Discrepancy Report before sending to the site.

The site must respond to all queries and resolve all discrepancies listed in the Master Discrepancy Report.

Any subsequent ITPR submissions are reviewed by CCSA and DCP to verify that all queries were addressed by the site.
If no Query Reports were generated (from Westat, CCSA, nor from PO), Westat will request that the PO performs a final review of the ITPR in DESK.

The PO will review the ITPR in DESK.
If during the final review the PO finds discrepancies, then PO will push "Delete ITPR Details". Westat will create a discrepancy report for the site.
If during the final review the PO finds no discrepancies, and if no further queries remain, the PO will add the "Accepted" status to DESK and Westat will generate the ITPR Complete Report.

Westat notifies the site (via email) that the data has been Accepted and attaches the ITPR Complete Report (if applicable).

CCSA runs the AE auto-coder on the accepted ITPR data in DESK.
If Additional data errors are discovered, CCSA creates a Query Report (which will be merged into next quarter's Master Discrepancy Report) and sends the report (via email) to PO, Westat, and DCP.