National Cancer Institute

AACI – NCI CLINICAL TRIALS REPORTING PROGRAM (CTRP) STRATEGIC SUBCOMMITTEE REPORT

CTRP Reporting Objectives and Implementation Timeline

July 2011

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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I. Executive Summary

The need for a single central repository of National Cancer Institute (NCI)-supported clinical trials has been long-standing. In 2005, the Clinical Trials Working Group (CTWG) recommended the development of "a shared foundation of comprehensive, up-to-date information about the status of cancer clinical trials." The NCI has no electronic database for more than half of its clinical trials portfolio, accounting for more than 20,000 patients each year, most of which are conducted with grant support (e.g., R01s, R21s, P01s, SPOREs, those taking place in NCI-designated Cancer Centers, etc.). Thus, currently available databases do not allow NCI to monitor accrual for all NCI-supported trials. A comprehensive database of the entire NCI portfolio would help to identify gaps in clinical research and duplicative studies, as well as facilitate effective clinical trial prioritization. The April 2010 Institute of Medicine report "A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program" reiterated the need for a comprehensive database of cancer clinical trials.

In 2010, the Clinical Trials Reporting Program (CTRP) Strategic Subcommittee, co-chaired by Dr. Kevin Cullen, Director, University of Maryland Greenebaum Cancer Center, and Dr. Sheila Prindiville, Director, Coordinating Center for Clinical Trials, NCI, was formed in collaboration with members of the NCI cancer research community, leadership of NCI-designated Cancer Centers and the AACI. The charge of the subcommittee was to identify current and estimated future workload and timeframe to meet CTRP information requirements for: 1) registration; 2) accrual (summary, patient level with demographics, disease coding); and 3) outcomes. Specific agenda topics included: 1) summary of experience with CTRP registration; 2) review of data elements for registration, amendments, updates, accrual, and outcomes; 3) report on the status of vendor integration and their estimates to automate registration and accrual reporting (e.g., Forte Research Systems, Velos); 4) timeline for adoption of reporting requirements; and 5) policy on reporting by trial type.

The subcommittee met by teleconference six times between August 2010 and February 2011. During the first several meetings, the subcommittee reviewed the rationale and current status of CTRP. It was agreed that the primary goal of CTRP is to be a central repository of all NCI-supported clinical trials with accrual data that will enable NCI to efficiently manage its clinical research portfolio. Each trial that is submitted to CTRP is abstracted by CTRP staff. These abstracts are indexed with terminology that optimizes retrieval of cancer clinical trials that are made available to the public through the NCI's Web site (http://www.cancer.gov).

During the initial development of CTRP, concern arose in the extramural community that CTRP would increase the workload for cancer clinical researchers and would duplicate the clinical trial reporting to Clinicaltrials.gov required by the Food and Drug Administration

Amendments Act of 2007 (FDAAA) and as a condition of subsequent publication by the International Committee of Medical Journal Editors (ICMJE). However, the development of CTRP began several years before the enactment of the FDAAA, Title VIII, Section 801, which mandates that a "responsible party" (i.e., the sponsor or designated principal investigator) register and report results of certain "applicable clinical trials." [1] Furthermore, CTRP is designed to meet the unique needs of those searching for and/or monitoring cancer clinical trials, whereas Clinicaltrials.gov includes clinical trials for all types of illness. Since the enactment of FDAAA, CTRP provides institutions that submit trials with a data file suitable for submission to Clinicaltrials.gov after independent review and validation by the responsible party, eliminating the need for duplicate entry of required data elements to both systems.

The subcommittee then reviewed the workflow, including the required data elements, for listing trials in CTRP. The subcommittee concurred that the scope of trials for registration in CTRP should include NCI-supported interventional cancer clinical trials open to patient accrual as of or after January 1, 2009. The scope of NCI-supported interventional trials includes all interventional cancer clinical trials taking place in NCI-designated Cancer Centers, as well as other NCI-supported trials, such as NCI Cooperative Group trials and trials conducted as part of an NCI grant. There are two types of trials registered in CTRP: 1) clinical trials managed by the Cancer Therapy Evaluation Program (CTEP) and Division of Cancer Prevention (DCP) Protocol and Information Offices (PIOs), and clinical trials conducted in the Center for Cancer Research (CCR), and 2) other NCI-supported trials. Registration data for clinical trials managed by the CTEP and DCP PIOs will be transferred within NCI to CTRP; thus investigators of these trials do not need to register these trials in CTRP. Other NCI-supported trials will be registered directly in CTRP by the NCI-supported entity. At the time of registration, clinical trials will be categorized in one of the four Summary 4[2] categories: 1) National, 2) Peer-Reviewed, 3) Institutional, or 4) Industrial.

The subcommittee discussed the type and frequency at which changes to a clinical trial protocol should be submitted to CTRP. Amendments should be submitted to CTRP within 20 days of the approval of the change in a protocol document by the Institutional Review Board (IRB), and updates should be submitted annually. Status changes should be submitted as soon as possible, but no later than 30 days after the status change has taken place.

The subcommittee reviewed the accrual data proposed for submission to CTRP. CTRP is building an accrual module to capture patient-level data elements based on CTEP's Clinical Data Update System (CDUS) Abbreviated.[3] Currently, accrual data can be entered manually via the CTRP Web site; batch submission and web service specifications are targeted for

[1] (http://prsinfo.clinicaltrials.gov/fdaaa.html)
[2] Summary 4 is an annual clinical trials reporting requirement required by the NCI in order to qualify for a Cancer Center Support Grant. (http://cancercenters.cancer.gov/documents/Summaries6_06.pdf)
[3] Clinical Data Update System (CDUS) Abbreviated (http://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/cdus_inst_guidev20.pdf)

completion in September 2011. After these specifications are published, software vendors providing clinical data management system (CDMS) support and organizations with in-house systems will be able to develop applications to support automated reporting of accrual data to CTRP. For National, Peer-Reviewed, and Institutional trials, the Lead Organization will report patient accrual for all participating sites on a trial. For Industrial trials, summary accrual information will be reported by the Participating Organization. For all trials, patient accrual will be reported quarterly. Accrual reporting specifications for CTRP will be designed so that each cancer center's accrual to a study is appropriately counted.

The subcommittee then reviewed the timeline for CTRP registration and accrual reporting. Initial registration of trials conducted by NCI-designated Cancer Centers should be complete by October 2011. Other grantee institutions conducting NCI-supported trials should develop processes and complete initial trial registration by January 2012.

Data elements and specifications for automated submission of amendments, updates, and trial status changes are targeted for completion in June 2011. Amendments, updates, and status changes are to be submitted within 9 months after the communication of the specification. NCI-designated Cancer Centers should develop processes and begin submitting amendments, updates, and status changes by March 2012. Other grantee institutions conducting NCI-supported trials should begin submitting amendments, updates, and status changes for NCI-supported trials by June 2012.

Data elements and specifications for submission of patient accrual data are targeted for completion in September 2011. Automated reporting of accrual is anticipated 12 months after the accrual specification is made available. NCI-designated Cancer Centers should develop processes and begin submitting accrual by September 2012. Other grantee institutions conducting NCI-supported trials should develop processes and begin submitting accrual by January 2013.

The subcommittee recommended the creation of a working group, to include representatives from interested clinical data management systems (CDMSs) vendors, plus sites developing and/or maintaining in-house CDMSs, as well as representatives of NCI and at least two participating cancer centers. This working group would evaluate the cost and timeline for implementation of future changes to registration, amendment, update, status and accrual specifications.

Although the original CTWG report discussed the desirability of outcome reporting, including toxicity and adverse event reporting, based on CDUS Complete, the CTRP Strategic Subcommittee concluded that it is premature to define outcome reporting requirements and timelines for CTRP. Instead, they recommended deferring capture of outcomes data in CTRP for 3-5 years. They recommended that during that time, a group, with extramural representation, should work with NCI to identify the outcomes data elements, the implementation and cost, and the timeframe for implementation.

NCI reiterated its continued support to grantees and software vendors to facilitate registration and accrual reporting. Examples of NCI support included funding supplements to NCI-designated Cancer Center grants to support start-up costs for CTRP reporting requirements; professionally written abstracts following clinical trial registration and a data file suitable for posting in Clinicaltrials.gov after review; and technical support, user calls, etc., to support the CTRP community.

The subcommittee acknowledged that there were areas that would require continued consideration and discussion, including the reporting of non-interventional trials in CTRP, patient-level disease coding, the design and implementation of CTRP-generated Summary 4-type reports, and how to support or adjust timelines for centers without a CDMS.

Finally, the subcommittee suggested broad dissemination of the CTRP Strategic Subcommittee final report and recommendations, through channels including: 1) NCI's CTRP Web site; 2) Cancer Center Administrators Forum; and 3) Association of American Cancer Institutes' Clinical Research Initiative.

II. Introduction

a. Background

In January 2004, the director of the National Cancer Institute (NCI) established the Clinical Trials Working Group (CTWG) to advise the National Cancer Advisory Board (NCAB) on whether and in what ways the NCI-supported national clinical trials enterprise should be restructured to realize the promise of molecular medicine for advancing oncologic clinical practice in the 21st century. The result of the CTWG's work was a compendium of 22 initiatives detailed in the group's 2005 report "Restructuring the National Cancer Clinical Trials Enterprise."[4] First and foremost in the report is a series of coordination initiatives. As the report notes:

> The CTWG envisions an enhanced cancer clinical trials enterprise in which increased participation by the extramural community in the prioritization process more effectively focuses resources on those trials judged most likely to facilitate advances in treatment. The success of this strengthened prioritization process depends on a shared foundation of comprehensive, up-to-date information about the status of cancer clinical trials.

[4] "Restructuring the National Cancer Clinical Trials Enterprise" (http://transformingtrials.cancer.gov/files/ctwg-report.pdf)

The CTRP fulfills a major initiative of the CTWG report, to provide a shared foundation of information by establishing a comprehensive database containing regularly updated information on all NCI-supported clinical trials. The expected benefits articulated by the CTWG include:

- Investigators would be aware of other NCI-supported clinical trials already completed or underway that are addressing similar questions when preparing new trial concepts and proposals.
- Prioritization would be enhanced by having available a full picture of the cancer clinical trials enterprise.
- Patient accrual to trials may be enhanced because physicians and patients would be aware of relevant opportunities for participation in clinical trials.

In April 2010, the Institute of Medicine released a report titled "A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program"[5] which reiterated the need for a complete database of clinical trials, with a standardized and accessible infrastructure supporting electronic data capture.

The CTRP Strategic Subcommittee, co-chaired by Dr. Kevin Cullen, Director, University of Maryland Greenebaum Cancer Center, and Dr. Sheila Prindiville, Director, Coordinating Center for Clinical Trials, NCI, was formed in 2010. Members of the CTRP Strategic Subcommittee include individuals from cancer centers who are responsible for the day-to-day operations of cancer center clinical trials offices as well as physicians who conduct clinical trials. The subcommittee identified appropriate data elements for registration and accrual reporting, suggested appropriate timelines for instituting automated processes for CTRP reporting, proposed resources that will be required for implementation of CTRP, and noted other issues requiring additional consideration. This report summarizes the work of the CTRP Strategic Subcommittee.

III. CTRP Trial Registration

a. Scope

All NCI-supported interventional trials open to patient accrual as of or after January 1, 2009, are to be registered in CTRP, including all trials in the following Summary 4[6] clinical research categories:

1) Clinical trials involving *an agent or device*

[5] "A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program" http://www.iom.edu/Reports/2010/A-National-Cancer-Clinical-Trials-System-for-the-21st-Century-Reinvigorating-the-NCI-Cooperative.aspx

[6] Summary 4 is an annual clinical trials reporting requirement required by the NCI in order to qualify for a Cancer Center Support Grant. (http://cancercenters.cancer.gov/documents/Summaries6_06.pdf)

2) Clinical trials involving *other types of interventions* (i.e., behavioral modification, nutritional protocols, etc.)

Note: Trials in the following Summary 4 clinical research categories are not currently in scope for CTRP:

1) Epidemiologic, outcome, or other observational studies
2) Ancillary or correlative studies associated with a clinical trial and other biological studies using clinical specimens that can be linked to individual patients or participant data

NCI-supported trials include:

- All NCI Cooperative Group trials
- Any trial conducted at an NCI-designated Cancer Center (with P30 center core grant), including all industrial trials
- Trials conducted under any type of contract, grant, or cooperative agreement supported by the NCI (e.g., R01, N01, SPOREs, P01, U01, U10)

Timing: Trials open to patient accrual as of or after January 1, 2009. Trials are to be registered prior to the enrollment of the first patient.

There are two types of trial registration:

1) **Trials Managed by the Cancer Therapy Evaluation Program (CTEP) or Division of Cancer Prevention (DCP) Protocol and Information Offices (PIO) and Trials Managed by the Center for Cancer Research (CCR):** These trials will be registered by the NCI and do not need to be registered separately in CTRP by the institution conducting the trial. Examples of trials managed by the CTEP or DCP PIO include:

    - Phase I trials under CTEP Investigational Drug Branch grants (U01s)
    - Phase II trials under CTEP Investigational Drug Branch contracts (N01s)
    - DCP Chemoprevention contracts
    - DCP Community Clinical Oncology Program (CCOP) trials
    - NCI Cooperative Groups trials

2) **Other NCI-supported trials:** All other NCI-supported trials will be registered directly in CTRP by the institution conducting and/or participating in the trial.

b. Categorization

At time of registration, trials will be categorized in one of the following categories, consistent with Summary 4 reporting guidelines:

- **National**: National Cooperative Group Trials.
- **Externally Peer-Reviewed**: R01s, SPORES, U01s, U10s, and P01s or other trial mechanisms supported by the NIH or supported by other peer-reviewed funding organizations.
- **Institutional**: In-house trials authored or co-authored by cancer center investigators and undergoing scientific peer-review solely by the Protocol Review and Monitoring System of the center. The center investigator should have primary responsibility for conceptualizing, designing, and implementing the trial and reporting results. It is acceptable for industry and other entities to provide some support (e.g., drug, device, other funding) but the trial should clearly be the intellectual product of the center investigator.
- **Industrial**: Design and implementation of the study is controlled by the pharmaceutical company.

c. Data Elements - Complete Registration (National, Externally Peer-Reviewed, Institutional Trials)

Registration Data Elements[7]	Mandatory = M Optional = O Conditional = C
Lead Organization	M
NCT Number[8]	O
Other Identifiers	O
Title	M
Phase	M
Trial Type	M
Purpose	M
Principal Investigator	M
Sponsor and Responsible Party	C (Mandatory if XML[9] is requested)
Trial Submission Category	M
Summary 4 Funding Sponsor	M
Program Code	O
NIH Grant Information	O
Current Trial Status and Status Dates	M
IND/IDE Information	O
Protocol Document	M
IRB Approval	M
List of Participating Sites	O
Informed Consent Document	M
Regulatory Information[10]	C (Mandatory if XML is requested)

[7] Definitions of the data elements can be found in Appendix C

[8] Clinicaltrials.gov registry number

[9] XML is Extensible Markup Language, e.g., an electronic data file suitable for submission to Clinicaltrials.gov after review

[10] Regulatory Information includes trial oversight authority country; trial oversight authority organization name; FDA regulated intervention indicator; Section 801 indicator; delayed posting indicator; and data monitoring appointed indicator. See http://prsinfo.clinicaltrials.gov/definitions.html

d. Data Elements - Abbreviated Registration (Industrial Trials)

Registration Data Elements[11]	Mandatory = M Optional = O Conditional = C
Lead Organization	M
NCT Number[12]	O
Lead Organization Trial Identifier Number	M
Title	M
Submitting Organization Name	M
Submitting Organization Local Trial Identifier	M
Phase	M
Trial Type	M
Purpose	M
Site Principal Investigator	M
Confirmation that Trial Submission Category is Industrial	M
Summary 4 Funding Sponsor Type	M
Site-Specific Program Code	O
Current Site-Specific Trial Status	M
Date Reporting Site Open to Accrual	C (M when date known)
Date Reporting Site Closed to Accrual	C (M when date known)
Trial related documents[13]	O

e. Methods for CTRP Trial Registration

Clinical trials may be registered via one of the following three mechanisms:

1) CTRP Registration Web Site (https://trials.nci.nih.gov/registry/home.action)
2) Batch file submission (http://www.cancer.gov/clinicaltrials/ctrp/page11)
3) Web Services (http://www.cancer.gov/clinicaltrials/ctrp/page11)

[11] Definitions of the data elements can be found in Appendix C
[12] Clinicaltrials.gov registry number
[13] Trials-related documents include other documents that the submitter may want to provide, e.g., completion of an abbreviated trial submission template, etc.

f. Amendments/Status Changes/Updates

1) Definitions:

Amendments: Amendments include changes that: 1) substantively alter the treatment administered; and/or 2) the study design; and/or 3) the sites in which patients are being enrolled on the trial. Amendments are to include all changes (including updates) since the last change to the protocol was submitted. Examples of amendments include:

- **Dose Escalation Amendment** (e.g., change in the number of patients treated at a given dose level)
- **Change in Sites Open to Patient Accrual**
- **Change in Principal Investigators**
- **Change in Risk to Participants** (e.g., new risk identified [new CAEPR], changes made as a result of an updated Severe Adverse Event)
- **Scientific Change** (e.g., opening an arm, adding a new arm, closing an arm, changing objectives, changing statistical analysis, adding correlative studies, increase or decrease in the accrual goal, changing from Phase I to Phase II, additional data points)
- **Correction of Typographical Errors which Change Scientific Meaning** (e.g., mg vs. mcg)
- **Eligibility Change** (change to the inclusion or exclusion criteria)
- **Therapy Change** (e.g., change in dose, adding another agent, change in administration, change in route)

Status Changes: Status changes include changes in the overall status of the trial (e.g., a change from active to temporarily closed to accrual, a change from temporarily closed to accrual to complete, etc).

Updates: Updates are defined as other changes to the protocol that do not substantively affect the scientific conduct of the study, the study design, and/or the sites in which patients are being enrolled on the trial. The following types of changes will be considered updates:

- **Editorial, Administrative Changes** (correction of minor typographical errors; clarifications made to previously approved descriptions of research)
- **Data, Data Collection, and Data Collection Materials** (revised study diaries; revised questionnaires or QOL surveys given to participants)
- **Recruitment of Subjects** (changes in the way subjects are recruited; new or revised advertisement)

- **Change in Principal Investigator Contact Information**

2) Frequency for submission:

Amendments: All amendments are to be submitted within 20 days of the approval of the change in the protocol by the institution's IRB. An amendment submission is to include all changes to the clinical trial (including any updates) since the last submission.

Status Changes: Trial owners are asked to submit these changes as quickly as possible, so that publicly available Web sites reflect the correct status of the trial. However, these changes are to be submitted to CTRP no later than 30 days after they have taken place.

Updates: Updates are to be submitted annually.

3) Documentation to be submitted with amendments, updates, or status changes:

Amendments: The submitter is asked to submit the following:

- A copy of the revised protocol document showing the changes since the last submission; or
- A copy of the revised protocol document that was sent to the IRB clearly indicating these changes and/or a document that lists all changes since the last submission; or
- For centers with an electronic IRB approval system and/or centers that do not have a change memo readily available for submission, a redline and strikeout protocol document showing the changes in the document itself is an acceptable alternative.

Updates: Once each year, the submitter is to provide:

- A list of all changes made to the protocol since the last amendment or update was submitted, or
- For a study that provides an annual update to the IRB, a copy of this annual update will meet this requirement, or
- For centers with an electronic IRB approval system and/or centers that do not have a change memo readily available for submission, a redline and strikeout protocol document showing the changes in the document itself is an acceptable alternative.
- Updates are to be submitted at least once each year, even if no changes have occurred. A copy of the annual report to the IRB will suffice.

Status Changes:

- These can be entered in the CTRP user interface.
- The attachment of a revised protocol document or change memo is optional.

IV. CTRP Patient Accrual Reporting

a. Data Elements - Complete Registration (National, Externally Peer-Reviewed, Institutional Trials)

Protocol Administrative Data Elements[14]	**Mandatory = M Optional = O Conditional = C**
NCI Protocol Number	**M**
CTEP/DCP Protocol Number	**C (Mandatory if CTEP/DCP PIO managed trial)**
Date Report Submitted	**M**
Cut-Off Date for Data	**M**
Current Protocol Status	**M**
Submitter Name and Contact Information	**O**
Patient Demographic Information	**Mandatory = M Optional = O Conditional = C**
Patient ID	**M**
Patient Zip Code	**C (Mandatory if US)**
Patient Country Code	**C (Mandatory if not US)**
Patient Birth Date (Month/Year)	**M**
Patient Gender	**M**
Patient Ethnicity	**M**
Patient Method of Payment	**O**
Date of Patient Entry	**M**
Patient Disease Code[15]	**C (Mandatory for all trials except DCP PIO trials registered in CTRP by NCI**
Patient Race	**M**

[14] Definitions of the data elements can be found in Appendix D

[15] Either CTEP Simplified Disease Codes (SDC) or ICD-9 codes are acceptable

b. Data Elements - Abbreviated Registration (Industrial Trials)

Protocol Administrative Data Elements[16]	**Mandatory = M** **Optional = O** **Conditional = C**
NCI Protocol Number	**M**
CTEP/DCP Protocol Number	**C (Mandatory if CTEP/DCP PIO managed trial)**
Date Report Submitted	**M**
Cut-Off Date for Data	**M**
Current Protocol Status	**M**
Submitter Name and Contact Information	**O**
Accrual During Reporting Period	**Mandatory = M** **Optional = O** **Conditional = C**
Number of patients accrued at site	**M**

c. Methods for Patient Accrual Reporting

The CTRP system was enhanced in the beginning of 2010 to allow submission of patient accrual through the CTRP Accrual Web Site based on the CDUS Abbreviated specification. This was tested by CTRP pilot sites with most sites requesting an automated method (i.e., batch or services) for reporting patient accrual rather than doing so manually. The specification for automated patient accrual reporting is targeted for finalization in September 2011. Accrual is to be submitted within 12 months after the specification is made available. NCI will partner with the key CDMS vendors used by the cancer centers community (e.g., Medidata, Forte Research Systems, and Velos) to develop an automated mechanism for delivering registration and accrual information to NCI. CDUS reporting guidelines are not changed and accrual data reported to NCI via CDUS will be transferred within NCI to CTRP.

d. Guidelines for Patient Accrual Reporting

There are two types of CTRP trials for which patient accrual will be reported:

1) **Trials managed by the CTEP or DCP PIOs and CCR** - Accrual for these trials will be entered in CTRP by the NCI. Examples of trials managed by the CTEP or DCP PIO include:

[16] Definitions of the data elements can be found in Appendix D

- Phase I trials under CTEP Investigational Drug Branch grants (U01s)
- Phase II trials under CTEP Investigational Drug Branch contracts (N01s)
- DCP Chemoprevention contracts
- DCP Community Clinical Oncology Program (CCOP) trials
- NCI Cooperative Groups trials

2) **Other NCI-Supported trials** - Accrual for all other NCI-supported trials will be entered in CTRP as outlined below:

- **Patient-Level Accrual** will be reported for National, Externally Peer-Reviewed, and Institutional Trials. **The Lead Organization** will report patient accrual for its site and all participating sites.
- **Summary Accrual** (cumulative count only) will be reported for Industrial trials by participating sites.

Accrual data will be reported quarterly.

V. CTRP Outcomes Reporting

a. Outcome Reporting Requirement

The CTWG report discussed elements of outcome reporting, including toxicity and adverse event reporting. The CTRP Strategic Subcommittee recommended deferring capture of outcome data for 3-5 years. During that time, a group, with extramural representation, should work with NCI to identify the outcomes data elements, the proposed implementation and cost, and the timeframe for implementation.

VI. Timelines: (See Appendix B)

Institution workload assessments and estimated time for vendors of CDMSs (e.g. Velos, Forte Research Systems) to implement automated reporting were taken into account in developing timelines.

a. Timelines for Registration

1) **NCI-designated Cancer Centers:** initial registration of trials conducted by NCI-designated Cancer Centers should be complete by October 2011.
2) **Other Grantee Institutions** conducting NCI-supported trials should develop processes and complete initial trial registration by January 2012.

b. Timelines for Reporting Amendments, Updates, and Status Changes

The specification for automated amendments, updates, and status changes is targeted for finalization in June 2011. The reporting of amendments and updates is to begin 9 months after the specification is made available.

1) **NCI-designated Cancer Centers** should develop processes and begin submitting amendments, updates, and status changes by March 2012.
2) **Other Grantee Institutions** conducting NCI-supported trials should develop processes and begin submitting amendments, updates, and status changes by June 2012.

c. Timelines for Reporting Patient Accrual

The specification for automated patient accrual is targeted for finalization in September 2011. The reporting of accrual is to begin one year after the specification is made available.

1) **NCI-designated Cancer Centers** should develop processes and begin submitting accrual by September 2012.
2) **Other Grantee Institutions** conducting NCI-supported trials should develop processes and begin submitting accrual by January 2013.

d. Workload Estimate for CTRP Registration and Accrual Reporting

The CTRP Strategic Subcommittee prepared an assessment of the workload required to register and provide accrual data to CTRP, based on the data elements for registration and patient accrual reporting. Staffing estimates ranged from 1/2 to 2 Full Time Equivalents (FTEs) to support CTRP reporting. The upper estimates assumed more manual data reporting; the lower estimates assumed automated reporting through vendor system integration.

VII. Support

a. NCI Support

The NCI will continue to support NCI grantees and software vendors to facilitate registration and the reporting of accrual. Examples of NCI support include funding supplements to NCI-designated Cancer Center grants to support start-up costs of CTRP reporting requirements, professionally written abstracts following clinical trial registration, and a data file suitable for posting in Clinicaltrials.gov after review.

Furthermore, the NCI continues to provide technical support, user calls, etc., to support the CTRP community.

VIII. Topics Requiring Additional Consideration

a. Reporting Non-Interventional Trials in CTRP

The subcommittee noted that two categories of trials required for preparation of Summary 4 are not currently registered in CTRP: 1) epidemiologic, outcome, or other observational studies and 2) ancillary or correlative studies associated with a clinical trial and other biological studies using clinical specimens that can be linked to individual patient or participant data. The subcommittee agreed that reporting these trials to CTRP requires additional deliberation. It recommended that registration of these trials be deferred until complete registration of all interventional trials has been achieved and after NCI, in collaboration with the extramural community, has determined the value of registering these types of trials in CTRP.

b. Patient-Level Disease Coding for Accrual

Cancer center members of the subcommittee strongly endorsed using ICD-9 codes for reporting patient-level accrual, to be consistent with the coding required for preparation of Summary 3 and coding frequently used for other patient data management applications. However, CTEP requires patient-level coding from CTEP's Simplified Disease Code (SDC) list. Rather than require cancer centers to use CTEP SDC for coding patient-level accrual data, the committee suggested that cancer centers report their data using ICD-9 and that those reporting data to CTEP continue to use CTEP SDC. Mappings, if necessary, between CTEP SDC and ICD-9 might take place within NCI to standardize patient-level coding on all data reported to CTRP.

c. CTRP Summary 4 Reports

The subcommittee noted that it will be critical to design the accrual reporting specifications in such a way that each cancer center's accrual to a study is appropriately counted. It will also be critical for system-generated reports to accurately attribute those institution(s) responsible for data management (typically the Lead Organization) and those institution(s) which have provided the intellectual capital for devising and implementing the study.

The subcommittee recognized that the accrual reported to CTRP for CTEP and DCP trials will need to be reviewed to ensure that it is harmonized with that which is needed for Summary 4 reports.

d. Institutions without Automated Systems

The subcommittee noted that some institutions have no CDMS and may need additional support or more liberal timelines for meeting reporting guidelines.

NCI will work with these sites to modify timelines and seek to provide additional support to these sites in the form of making available NCI-furnished CDMSs to these sites and potentially provide support for data entry personnel to fill the gap until suitable CDMSs are in place at all centers as appropriate.

e. Process for Changing CTRP Technical Specifications

The subcommittee recommended the creation of a working group, to include representatives from any interested vendors of CDMSs, plus any sites developing and/or maintaining in-house CDMSs, as well as representatives of NCI and at least two participating cancer centers. This working group would evaluate any future changes to registration, amendments, updates, and accrual specifications and work with affected stakeholders to ensure timely and accurate implementation.

f. Report Dissemination

1) The CTRP Strategic Subcommittee final report and presentations will be communicated in various forums, including:

    - CTRP Web site
    - Cancer Center Administrators Forum
    - Association of American Cancer Institutes' Clinical Research Initiative

2) The NCI Office of Communications and Education will be consulted regarding the communication of the contents of this report.

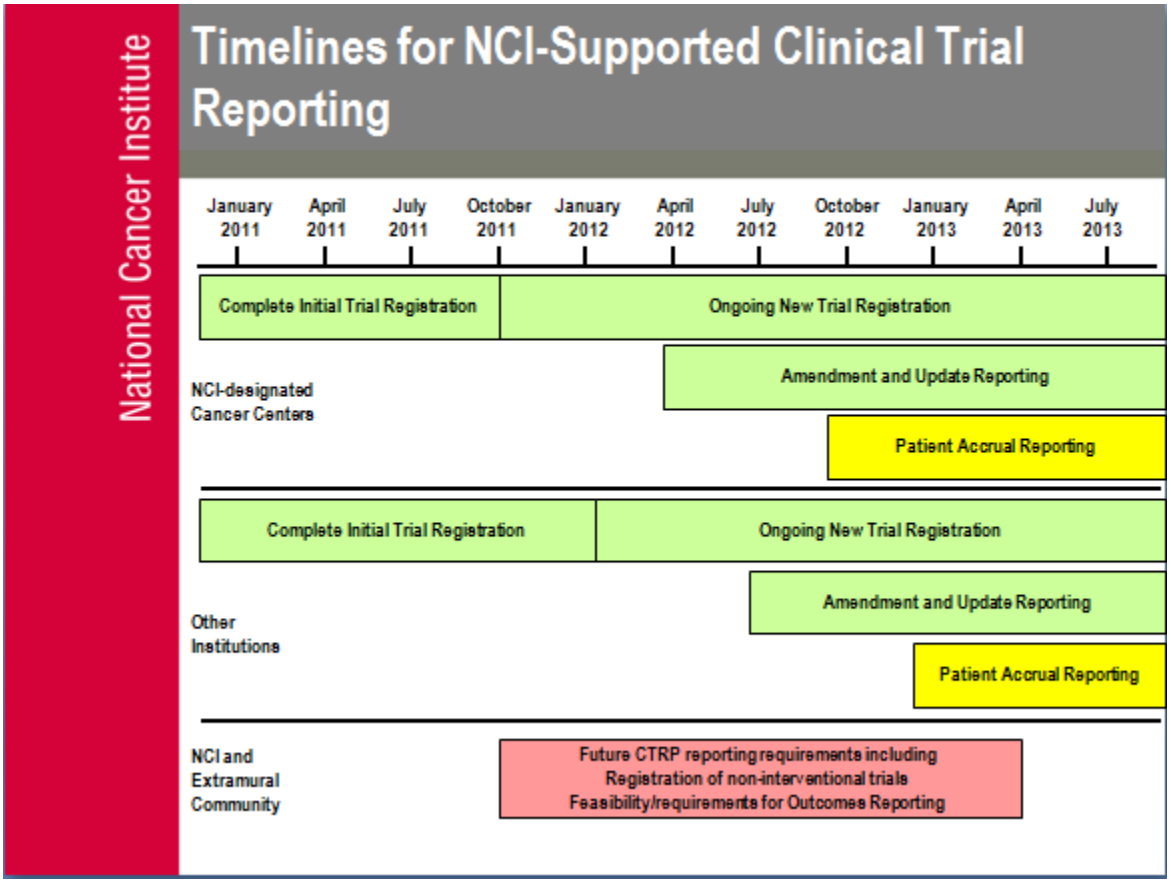
IX. Appendices

a. Appendix A: Members of the CTRP Strategic Subcommittee

Kevin Cullen, M.D., Co-Chair, Director, University of Maryland Greenebaum Cancer Center
Sheila Prindiville, M.D., M.P.H., Co-Chair, Director, Coordinating Center for Clinical Trials, National Cancer Institute
Rhoda Arzoomanian, M.S.M., Associate Director, Administration, University of Wisconsin Carbone Cancer Center
Jan Buckner, M.D., Professor of Oncology, Mayo Clinic College of Medicine
Rob DuWors, M.P.A., Deputy Director, Administration and Finance, Jonsson Comprehensive Cancer Center, UCLA
Alyssa K. Gateman, M.P.H., C.C.R.P., Deputy Director, Quality Assurance Office for Clinical Trials, Dana-Farber/Harvard Cancer Center
Collette Houston, Director, Clinical Research Operations, Office of Clinical Research, Memorial Sloan-Kettering Cancer Center
Nicholas J. Petrelli, M.D., Medical Director, Helen F. Graham Cancer Center at Christiana Care
Daniel M. Sullivan, M.D., Executive Vice President/Associate Center Director for Clinical Investigations, Moffitt Cancer Center
James Thomas, M.D., Ph.D., Associate Director, Clinical Investigation, Medical College of Wisconsin Cancer Center

AACI Liaison:
Janie Hofacker, R.N., M.S., Director of Programs, Association of American Cancer Institutes

b. Appendix B: Timelines



c. Appendix C: Data Elements for Registration

Data Elements for Registration of National, Externally Peer-Reviewed, Institutional Trials

COMPLETE REGISTRATION DATA ELEMENTS	Mandatory = M Optional = O Conditional = C	Definition
Trial Identifiers		
Lead Organization Identifier	M	The ID exactly as it appears in the protocol document. For Inter-Group trials, type the Lead Group's trial number. For multisite trials that have no assigned single center, use the protocol ID.
NCT Number	O	The NCT number assigned to trials that have been submitted to ClinicalTrials.gov previously.
Other Identifier	O	Additional trial identifier(s) such as unique identifier from other registries, NIH grant numbers, or protocol numbers assigned by the review board.
Trial Details		
Title	M	Official name of the protocol provided by the study principal investigator or sponsor (same as in the protocol document).
Phase	M	Select from list: Phase 0, I, I/II, II, II/III, III, IV, N/A, Pilot Trial.
Trial Type	M	Select Interventional or Observational.
Purpose	M	Select from list: Treatment, Prevention, Supportive Care, Screening, Diagnostic, Health Services Research, Basic Science, Other – Any other type of trial not included in this list If Other, is it a pilot trial? Y/N.
Lead Organization/Principal Investigator		
Lead Organization	M	Organization responsible for the overall scientific and administrative coordination, study monitoring, and data management activities of a given clinical trial.
Principal Investigator	M	Appointed investigator responsible for conducting clinical trial, or for multisite trials, the study chair.
Sponsor/Responsible Party *Only if XML Requested		
Sponsor	C	Mandatory if XML Requested. Sponsor of the clinical trial (as defined in 21 CFR 50.3 or successor regulation).
Responsible Party	C	Mandatory if XML Requested. Sponsor of the clinical trial (as defined in 21 CFR 50.3 or successor regulation) - or – Principal investigator of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee, so long as the principal investigator is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right and ability to publish the results of the trial.
Responsible Party Email Address	C	Mandatory if XML Requested.
Responsible Party Phone Number	C	Mandatory if XML Requested.

Summary 4 Information (for trials at NCI-designated Cancer Centers)		
Trial Submission Category	M	National, Peer-Reviewed, Institutional, Industrial.
Summary 4 Funding Sponsor	M	Group/Sponsor/Funding Source**:** Provide the name of the external sponsor or funding source.
Program Code	O	Cancer center-specific program code.
NIH Grant Information (for NIH-supported Trials)		
Funding Mechanism	O	NCI code used to identify areas of extramural research activity applied to various funding mechanisms.
Institute Code	O	The name of the primary organization responsible for funding the trial.
Serial Number	O	The 5- or 6-digit number generally assigned sequentially to a series within an Institute, Center, or Division.
NCI Division Code	O	
Status/Dates		
Current Trial Status	M	Select the current stage or state of the trial or study.
Why Study Was Stopped	O	Required for Administratively Complete and Temporarily Closed statuses only.
Current Trial Status Date	M	Enter the date on which the current trial status became effective.
Trial Start Date	M	Select Anticipated or Actual.
Primary Completion Date	M	Select Anticipated or Actual.
FDA IND/IDE Information for Applicable Trials		
IND/IDE Types	O	Select IND (Investigational New Drug Application) or IDE (Investigational Device Exemption).
IND/IDE Number	O	For IND trials, type the trial's FDA-assigned IND number.
IND/IDE Grantor	O	Select one of the following grantors: For IND trials, • CDER: Center for Drug Evaluation and Research • CBER: Center for Biologics Evaluation and Research For IDE trials, • CDRH: Center for Devices and Radiological Health
IND/IDE Holder Type	O	Select one of the following types: Investigator, Organization, Industry, NIH, NCI.
NIH Institution, NCI Division/Program Code	O	
Expanded Access	O	If an experimental drug or device is available outside any clinical trial protocol, select Yes.
Expanded Access Type	O	Select one of the following access statuses: Available, No Longer Available, Temporarily Not Available, Approved for Marketing.
Exempt	O	Select Yes only if the IND/IDE is exempt from reporting in ClincalTrials.gov.
Regulatory Information *Only if XML Requested		
Trial Oversight Authority Country	C	Mandatory if XML Requested. Select the country responsible for trial oversight.
Trial Oversight Authority Organization Name	C	Mandatory if XML Requested. Select the oversight organization.
FDA Regulated Intervention Indicator	C	Mandatory if XML Requested. Yes or No. If the trial includes a non-exempt IND/IDE, select Yes.

Section 801 Indicator	C	Mandatory if XML Requested. Yes or No. Only if the FDA Regulated Intervention Indicator = Yes.
Delayed Posting Indicator	C	Mandatory if XML Requested. Yes or No. Only if the Section 801 Indicator = Yes.
Data Monitoring Committee Appointed Indicator	C	Mandatory if XML Requested. Yes or No.
Trial-Related Documents		
Protocol Document	M	
IRB Approval	M	
List of Participating Sites	O	
Informed Consent Document	M	
Other	O	

Data Elements for Registration of Industrial Trials

ABBREVIATED REGISTRATION DATA ELEMENTS	Mandatory = M Optional = O Conditional = C	Definition
Trial Identifiers		
Lead Organization	M	Organization responsible for the overall scientific and administrative coordination, study monitoring, and data management activities of a given clinical trial.
Lead Organization Trial Identifier	M	The ID exactly as it appears in the protocol document. For Inter-Group trials, type the Lead Group's trial number. For multisite trials that have no assigned single center, use the protocol ID.
Submitting Organization Name	M	
Submitting Organization Local Trial Identifier	M	
NCT Number	O	The NCT number assigned to trials that have been submitted to ClinicalTrials.gov previously.
Trial Details		
Title	M	Official name of the protocol provided by the study principal investigator or sponsor (same as in the protocol document).
Phase	M	Select from list: Phase 0, I, I/II, II, II/III, III, IV, N/A, Pilot Trial.
Trial Type	M	Select Interventional or Observational.
Purpose	M	Select from list: Treatment, Prevention, Supportive Care, Screening, Diagnostic, Health Services Research, Basic Science, Other – Any other type of trial not included in this list. If Other, is it a pilot trial? Y/N.
Site Principal Investigator	M	
Summary 4 Information (for trials at NCI-designated Cancer Centers)		
Trial Submission Category	M	National, Peer-Reviewed, Institutional, Industrial.
Summary 4 Funding Sponsor	M	
Program Code	O	Cancer center-specific program code.
Status/Dates (site specific)		
Site Recruitment Status	M	The current stage or state of the trial or study.
Site Recruitment Status Date	M	The date on which the current trial status became effective.
Date Opened For Accrual	C	If known, enter the date on which the trial was opened for accrual.
Date Closed For Accrual	C	If known, enter the date on which the trial was closed for accrual.
Trial-Related Documents		
Abbreviated Trial Template	O	An Abbreviated Trial Template document is required if the NCT number was not provided.
Other	O	

Complete information on CTRP registration is available in the CTRP Site Registration User's Guide on the CTRP Resources page:
http://www.cancer.gov/clinicaltrials/ctrp/page11

d. Appendix D: Data Elements for Accrual

Data Elements for Reporting Accrual for National, Externally Peer-Reviewed, Institutional Trials

PROTOCOL ADMINISTRATIVE DATA ELEMENTS	Mandatory = M Optional = O Conditional = C	Definition
NCI Protocol Number	M	This is the number assigned to the protocol registered in CTRP.
DCP/CTEP Protocol Number	C	Mandatory if this is a protocol managed by the CTEP or DCP PIO.
Date Report Submitted	M	
Current Protocol Status	M	
Submitter Name and Contact Information	O	
PATIENT DEMOGRAPHIC INFORMATION	**Mandatory = M Optional = O Conditional = C**	**Definition**
Patient ID	M	Unique identifier (numeric or alphanumeric) assigned to participants in a study.
Patient Zip Code (Only first 5 digits)	C	If U.S.
Patient Country Code	C	Non-U.S. only.
Patient Birth Date (Month/Year)	M	The month and year on which the person was born.
Patient Gender	M	To be harmonized with CRF Demography.
Patient Ethnicity	M	To be harmonized with CRF Demography.
Patient Method of Payment	O	To be harmonized with CRF Demography.
Date of Patient Entry	M	Provide the date the patient entered the study. Defined as date the patient signed the Informed Consent form.
Patient Disease Code	C	Based on the CTEP standard Simplified Disease Code (SDC); can be reported using ICD-9 codes used for Summary 3. Optional for studies managed by the DCP PIO that are transferred directly from DCP to CTRP.
Patient Race	M	To be harmonized with CRF Demography.

Data Elements for Reporting Accrual for Industrial Trials

PROTOCOL ADMINISTRATIVE DATA ELEMENTS	Mandatory = M Optional = O Conditional = C	Definition
NCI Protocol Number	M	This is the number assigned to the protocol registered in CTRP.
DCP/CTEP Protocol Number	C	Mandatory if this is a protocol managed by the CTEP or DCP PIO.
Date Report Submitted	M	
Current Protocol Status	M	
Submitter Name and Contact Information	O	
PATIENT DEMOGRAPHIC INFORMATION	**Mandatory = M Optional = O Conditional = C**	**Definition**
Number of patients accrued at site	M	Summary count of patients accrued on protocol at site.