

**Report of the Clinical Trials Informatics Working Group (CTIWG) of the
National Cancer Institute (NCI) Clinical Trials and Translational
Research Advisory Committee (CTAC)
on Recommendations for the Clinical Trials Reporting Program (CTRP)**

**Working Group Report
November 1, 2017**

The report was accepted at the November 1, 2017 CTAC Meeting.

REPORT OF THE CLINICAL TRIALS INFORMATICS WORKING GROUP (CTIWG) OF THE NATIONAL CANCER INSTITUTE (NCI) CLINICAL TRIALS AND TRANSLATIONAL RESEARCH ADVISORY COMMITTEE (CTAC) ON RECOMMENDATIONS FOR THE CLINICAL TRIALS REPORTING PROGRAM (CTRP)

WORKING GROUP REPORT, NOVEMBER 1, 2017

EXECUTIVE SUMMARY

In 2015, the National Cancer Institute (NCI) Clinical Trials Advisory Committee (CTAC) established the Clinical Trials Informatics Working Group (CTIWG) to provide advice on the implementation of NCI's clinical trials informatics initiatives. The CTIWG initially focused on NCI's Clinical Trials Reporting Program (CTRP), which maintains a comprehensive database of information on all NCI-supported cancer clinical trials. CTRP was developed in response to the 2005 report of the Clinical Trials Working Group (CTWG) of the NCI National Cancer Advisory Board, which highlighted the value of complete and consistent information on NCI-supported cancer clinical trials and called for the creation of a repository of such data.

The CTIWG was charged with advising the NCI on refining CTRP as a clinical trials portfolio management resource; increasing the usability and accessibility of clinical trial information for physicians, patients, and the public by enhancing clinical trial search capabilities; and enhancing the utility of CTRP as a clinical trials information resource for the cancer research community. CTIWG members were chosen for their expertise which represents a wide range of perspectives on the cancer clinical trials enterprise and the uses of clinical trials information.

Following a series of face to face and webinar meetings conducted over a two-year period, in October 2017 the CTIWG finalized recommendations in seven areas:

- A. CTRP Data Access
- B. CTRP Participant-Level Accrual Reporting
- C. CTRP Data Expansion
- D. CTRP-Based Clinical Trials Searching
- E. Resolving CTRP Data Inconsistencies and Ambiguities
- F. Implementation of a CTRP-Generated Data Table 4
- G. Communicating the Value of CTRP

The recommendations in each of these areas, described in detail in this report, are summarized below.

A. CTRP DATA ACCESS

- A1. Data Table 4 Study Source should be public
- A2. CTRP information on biomarkers essential to trial conduct should be public
- A3. Participant-level accrual data should not be public

- A4. Aggregate accrual data for trials open and closed to accrual should be public under certain conditions
- A5. Aggregate accrual data by demography should be public for trials closed to accrual
- A6. Develop query and reporting tools to facilitate access to CTRP data

B. CTRP PARTICIPANT-LEVEL ACCRUAL REPORTING

- B1. Continue to collect participant-level data elements
- B2. Emphasize submission of proper zip code data
- B3. Map NCI Thesaurus disease codes to CTRP accrual data

C. CTRP DATA EXPANSION

- C1. NCI should require CTRP registration and accrual reporting for observational studies
- C2. NCI should not require CTRP registration and accrual reporting for ancillary/correlative studies at this time
- C3. NCI should not implement real-time reporting of serious adverse events to CTRP
- C4. NCI should not implement reporting of outcome data to CTRP

D. CLINICAL TRIAL SEARCHING

- D1. Create clinical trials search interfaces tailored for defined user populations and drawing on a unified clinical trials search engine
- D2. Facilitate automated trial matching based on genetic analysis reports and/or data from electronic medical records
- D3. Continue the structuring of biomarker eligibility criteria
- D4. Structure additional eligibility criteria as feasible

E. RESOLVING CTRP DATA INCONSISTENCIES AND AMBIGUITIES

- E1. Adopt ClinicalTrials.gov clinical trial status categories, definitions and, as possible, titles
- E2. Adopt and promulgate a standard definition for “accrued subject/enrolled participant”
- E3. Record screening accruals for precision medicine trials separately from accruals to intervention arms
- E4. Clarify primary purpose definitions in CTRP user support materials

F. IMPLEMENTATION OF CTRP-GENERATED DATA TABLE 4

- F1. Implement a CTRP-generated Data Table 4 for non-competing renewals in October 2017 and for competing renewals in October 2018

G. COMMUNICATING THE VALUE OF CTRP

- G1. Pursue efforts to increase awareness of the value of CTRP
- G2. Continue efforts to increase understanding of the Clinical Trials Search API utility

This report provides background information on CTRP and describes the background and rationale for each of the recommendations. For some recommendations, the report also describes implementation guidance or additional commentary provided by the CTIWG.

INTRODUCTION

The National Cancer Institute (NCI) Clinical Trials Advisory Committee (CTAC) formed the Clinical Trials Informatics Working Group (CTIWG) to provide extramural expertise and advice on the implementation of NCI's clinical trials informatics initiatives. The goals of these initiatives are to (1) improve the value of cancer clinical trial data, (2) increase the usability and accessibility of clinical trials information for physicians, patients, and the public, (3) minimize the burden of cancer clinical trials data management and (4) increase the impact of clinical trials by streamlining initiation, conduct, data analysis and reporting.

NCI's Clinical Trials Reporting Program (CTRP) addresses the first three of these goals through the development and operation of a comprehensive database of information for all NCI-supported interventional trials. CTRP has four important roles. First, it provides NCI, the leadership of NCI-Designated Cancer Centers and other cancer clinical research organizations with a clinical trials portfolio management tool. Second, it serves as a clinical trials information resource for NCI, the Cancer Centers¹ and the broader cancer research community. Third, CTRP serves as the data source for NCI-supported clinical trials search tools that assist patients, physicians, patient advocates and the public in identifying clinical trials for which individuals may be eligible or that are otherwise of interest. Finally, CTRP supports regulatory compliance for NCI-sponsored trials and facilitates registration of NCI-supported trials to ClinicalTrials.gov. With these roles as organizing themes, the CTIWG was charged with advising the NCI on improving CTRP operations and enhancing the accessibility and value of CTRP data.

CTIWG members (see Appendix 1) were selected for their expertise in clinical trial conduct and management and represent a wide range of perspectives on the cancer clinical trials enterprise and the uses of clinical trial information. Working Group meetings were conducted primarily via webinar, with in-person plenary meetings held in November 2016 and October 2017. A full schedule of meetings and webinars is provided in Appendix 2.

In preparation for its deliberations, the CTIWG requested information on user perceptions of CTRP and its operations. As a result, in the Fall of 2015 the IDA Science and Technology Policy Institute conducted individual, confidential discussions with staff directly involved in CTRP reporting at Cancer Centers. Several operational concerns and desired improvements were identified through this user feedback exercise. Steps to address the technical and operational issues identified in these discussions were incorporated into NCI's planned CTRP development, and many have been implemented in parallel with

¹ Throughout the remainder of this report, the term "Cancer Center" refers to an NCI-Designated Cancer Center.

the CTIWG's deliberations. Feedback that raised broader issues of policy was incorporated into the topics deliberated on by the Working Group.

To facilitate its work, the Working Group convened two subgroups tasked with detailed analysis of selected topics. These subgroups met independently via periodic web conferences and reported their recommendations to the full Working Group for discussion and ratification. One subgroup addressed the usability and accessibility of CTRP data by patients, treating physicians and the public. This subgroup focused on the clinical trials search tool on NCI's Cancer.gov website, which draws on CTRP data. The second subgroup addressed the value of CTRP data for the cancer research community, with a dual focus on resolving inconsistencies and ambiguities in existing CTRP data and advising NCI on potential expansions of scope. The remaining topics were addressed by the Working Group during plenary sessions. These topics included envisioning CTRP data analyses that would provide value to the extramural community, facilitating access to CTRP information, transitioning to a CTRP-generated Cancer Center Support Grant (CCSG) Data Table 4 for interventional trials, reviewing NCI's progress in addressing CTRP operational issues and improving communication concerning the rationale and value of CTRP.

This report describes the purpose, development and current status of CTRP and presents the Working Group's recommendations.

CTRP PURPOSE AND DEVELOPMENT

CTRP's origin can be traced to the 2005 report of the Clinical Trials Working Group (CTWG) of the NCI National Cancer Advisory Board. In the report, the CTWG noted the incomplete and fragmented character of NCI's clinical trial information resources and highlighted the value and importance of complete and consistent clinical trials information. Such information would support the work of individuals charged with managing the cancer clinical trials enterprise, investigators planning and conducting trials and patients and physicians seeking opportunities to participate in trials. The CTWG also noted the importance of timely information on efficacy and toxicity findings from trials. To address these needs, the CTWG recommended establishing "a comprehensive database containing regularly-updated information on all NCI-funded clinical trials."² The importance of such a database was reiterated in the 2010 report by the Institute of Medicine on NCI's Cooperative Group Program.³

Development of the National Institutes of Health (NIH) ClinicalTrials.gov website over the past 20 years, under the leadership of the National Library of Medicine, has brought wider attention to the value of and need for clinical trials information databases. ClinicalTrials.gov, which grew out of the Food and Drug Administration (FDA) Modernization Act of 1997, commenced operations in February 2000. Since then, reflecting the continued evolution of legislation and policy, its scope has expanded considerably to accommodate increasingly comprehensive clinical trial reporting requirements. In keeping with the vision articulated by the Clinical Trials Working Group, CTRP goes beyond ClinicalTrials.gov,

² *Restructuring the National Cancer Clinical Trials Enterprise*, Report of the Clinical Trials Working Group of the National Cancer Advisory Board, June 2005, p. 12.

³ Institute of Medicine, *A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program*. Washington, DC: The National Academies Press, April 2010, p. 8.

implementing several unique features designed to address research program management, scientific planning and clinical practice needs distinctive to cancer. These unique features include:

- Consistent terminology and standardized data elements to optimize search and retrieval of *cancer* clinical trial information
- Inclusion of structured biomarker information
- Quarterly reporting of accrual for ongoing interventional clinical trials, including participant-level demography
- Standard representation of persons and organizations
- Identification of associated NCI contracts and awards
- Daily updating of participating sites for all clinical trials managed by NCI

Implementation of CTRP began with a pilot in 2009, requiring registration of interventional clinical trials taking place at Cancer Centers. NCI continues to develop CTRP to meet the needs of the cancer research community, coordinating where possible with the National Library of Medicine to harmonize practices across ClinicalTrials.gov and CTRP and minimize the burden of cancer clinical trials registration and reporting. Appendix 3 provides an overview of CTRP operations, functions and data accessibility.

Extramural⁴ stakeholders have played an important role in shaping CTRP implementation. A CTRP Strategic Subcommittee was convened in 2010 under the auspices of NCI and the Association of American Cancer Institutes (AACI). The group included representatives of nine cancer research centers that conduct NCI-supported clinical trials. The July 2011 report⁵ laid out a near-to-mid-term roadmap identifying (1) trial registration, amendment, update, and accrual data elements to be collected by CTRP; (2) the periodicity of required reporting and (3) the timeline for implementation of reporting. In addition, they identified several aspects of the CTRP vision that were deferred until CTRP was more mature. These outstanding items included those described in the current report: toxicity, adverse event and outcomes data, reporting of non-interventional trials and participant-level disease coding for accrual.

TOPICS FOR WORKING GROUP DELIBERATIONS

The Working Group was charged to provide guidance and recommendations to minimize the burden of cancer clinical trials data management, improve the value of those data and increase the impact of clinical trials as originally envisioned by the CTWG. To this end, drawing on both the 2011 AACI-NCI Subcommittee report and CTRP user feedback, the following topics were presented to the CTIWG for consideration:

1. Access to CTRP data
2. Requirements for reporting participant-level demographic data

⁴ For the purposes of this report, an extramural stakeholder is defined as any individual or organization other than NCI program staff. This includes leadership and investigators from NCI-Designated Cancer Centers, other cancer research organizations and industry; NCI intramural investigators; patient advocacy groups and the general public

⁵ AACI-NCI Clinical Trials Reporting Program (CTRP) Strategic Subcommittee Report: CTRP Reporting Objectives and Implementation Timeline, National Cancer Institute, July 2011.

3. Challenges posed by the use of multiple disease coding systems in reporting participant-level accrual
4. Reporting of observational studies to CTRP
5. Reporting of ancillary and correlative studies to CTRP
6. Capture of adverse events and outcomes data in CTRP
7. Cancer clinical trials searching
8. Optimizing the efficiency and efficacy of trial reporting and the accuracy and usability of CTRP data
9. Efficient use of CTRP data to support generation of the Data Table 4 reports for Cancer Center Support Grants (CCSG) applications
10. Improving stakeholder communications about the value CTRP

The remainder of this report describes the CTIWG’s recommendations on each of these topics.

A. RECOMMENDATIONS ON CTRP DATA ACCESS

Key data elements collected by CTRP for each trial include:

- Title
- Brief summary
- Lead organization
- Detailed trial description
- Trial design information⁶
- Disease condition(s)
- Anatomic site(s)
- Intervention(s)
- Biomarker(s)
- Arms
- Sub-groups
- Participating sites
- Data Table 4 Study Source
- Accrual information (participant-level and cumulative)

Data Table 4 is an element of the Cancer Center Support Grant (CCSG) annual renewal application that is used for reporting a Cancer Center’s clinical trial activity. The following Study Source definitions are used in the table:⁷

- **National:** National Clinical Trials Network (NCTN) and other NIH-supported national trial networks

⁶ Trial design information includes model, masking, allocation, target accrual, outcome measures and eligibility criteria.

⁷ P30 Cancer Center Support Grant Data Table Guide, <https://cancercenters.cancer.gov/Documents/CCSGDataGuide508C.pdf>, accessed October 6, 2017.

- **Externally Peer-Reviewed:** R01s, SPORes, U01s, U10s, P01s, CTEP, and any other clinical research study mechanism supported by NIH, or an approved peer-reviewed funding organization
- **Institutional:** In-house clinical research studies authored, or co-authored, by Cancer Center investigators and undergoing scientific peer-review solely by the Protocol Review and Monitoring System of the Cancer Center. The Cancer Center investigator has primary responsibility for conceptualizing, designing, and implementing the clinical research study and reporting results
- **Industrial:** The design and implementation of these clinical research studies is controlled by a pharmaceutical company or for profit organization

All of these CTRP data elements are available to the public⁸ except for (1) Data Table 4 Study Source, (2) biomarker information outside of the inclusion/exclusion eligibility criteria and (3) accrual data. The CTIWG was asked to consider whether these data elements should be available, who should have access to them if they are made available and how that access should be facilitated.

DATA TABLE 4 STUDY SOURCE

Recommendation A1. Data Table 4 Study Source should be public.

Public availability of Data Table 4 Study Source information from CTRP enables analyses of the distribution of trials by Study Source across the clinical trials portfolio, including analyses by disease, intervention type and Cancer Center.

The CTIWG acknowledged that Cancer Center Directors may have concerns about having data on their trials by Study Source publicly available. However, the Working Group concluded that these data should be made available to all stakeholders. The Working Group therefore recommended that access to Study Source designations for trials reported to CTRP not be limited to NCI program staff but rather that these designations be made available to the public.

NON-ELIGIBILITY BIOMARKER INFORMATION

Recommendation A2. CTRP information on biomarkers essential to trial conduct should be public

CTRP currently collects information on biomarkers (e.g., molecular markers, imaging markers) used for purposes essential to trial conduct:

1. **Eligibility criteria:** Biomarkers measured to help determine if patients can participate in the research trial (inclusion/exclusion)

⁸ Access is provided via NCI's Clinical Trials Search API which is a set of tools designed to provide communication between a software application and a computer operating system or between applications. It is used within NCI to provide information to the Cancer.gov website and is available as well to any other interested parties. It should be noted that the Clinical Trials Search API requires the development of specialized software applications in order to retrieve CTRP data in a format directly useful by patients, providers and researchers.

2. **Treatment assignment:** Biomarkers measured to help determine what treatment is administered (or how much is given)
3. **Stratification factor:** Biomarkers measured to help classify patients into strata as part of the randomization process or for purposes of data analysis
4. **Response assessment:** Biomarkers measured to characterize the effect of treatment

While information on biomarkers used as eligibility criteria is currently publicly available, information on those used for treatment assignment, stratification or response assessment is not.

The CTIWG acknowledged that CTRP biomarker information not currently public could include proprietary information. However, the Working Group also noted that this non-public information could (1) enable more comprehensive analyses of biomarkers in NCI-supported trials, (2) permit identification of trials using a particular biomarker and (3) allow investigators to assess more accurately the utility of proposed biomarker studies or avoid duplicative studies. As a result, the CTIWG recommended that CTRP biomarker information essential to the conduct of a clinical trial be made available to all stakeholders.

ACCRUAL DATA

Accrual targets for trials reported to CTRP are currently public, available through the clinical trials search tool on NCI's Cancer.gov website and the Clinical Trials Search API⁹, but actual accrual data are not available for actively accruing studies or studies closed to accrual.

Recommendation A3. Participant-level accrual data should not be public

The CTIWG noted that the release of participant-level data could violate informed consent agreements. In some situations, demographic information such as date of birth and zip code, in combination with clinical attributes, could be sufficient to reidentify a participant. Such situations are especially likely in, but are not restricted to, trials addressing rare tumors. Therefore, out of respect for participant confidentiality, the Working Group recommended not making participant-level accrual data public. However, the CTIWG also suggested that NCI create mechanisms by which researchers could gain access to specific participant-level data sets for approved research purposes.

Recommendation A4. Aggregate accrual data for trials that are open and closed to accrual should be public under certain conditions

The CTIWG noted that aggregate accrual data are useful for patient advocates assessing clinical trial opportunities, as well as for NCI staff and clinical researchers conducting clinical trial portfolio and other analyses. The CTIWG therefore recommended that aggregate accrual data be publicly available for National, Externally Peer-Reviewed and Institutional trials, not only after these trials are closed to accrual but also while they are actively accruing.

⁹ Application Programming Interface: Set of tools designed to provide communication between a software application and a computer operating system or between applications.

However, the CTIWG noted that many Institutional trials involve collaborations with industry, and in such cases accrual reporting on actively accruing trials may violate contractual agreements. As a result, the CTIWG suggested that CTRP develop a mechanism by which submitters could opt out of making aggregate accrual available for actively accruing trials, in cases where such reporting would violate a contractual agreement. Because CTRP is unlikely to receive permission to release aggregate accrual data for actively accruing Industrial trials, the CTIWG recommended that CTRP make aggregate accrual data for Industrial trials public at the same time as basic results reporting to ClinicalTrials.gov (i.e., within one year of the primary completion date of a trial).¹⁰

Recommendation A5. Aggregate accrual data by demography should be public for trials that are closed to accrual.

Demographic data elements include the participant’s zip code or country of residence, date of birth, gender, race and ethnicity. The Working Group concluded that the demographic data elements contained in CTRP are valuable in aggregate on a per trial level, noting that such data (1) enable accrual analyses by gender, age, race, ethnicity and geography for individual trials and for specific diseases, (2) indicate whether accrual is representative of the population and incidence of the disease under study and (3) enable identification of eligibility criteria and/or other trial characteristics that influence the demographic distribution of accrual. However, the Working Group recommended that CTRP make demographic data available only after trials are closed to accrual, only in aggregate format and only if doing so does not enable participant identification. The Working Group noted that preventing participant identification in some instances may be difficult.

QUERY AND REPORTING TOOL

Recommendation A6. Develop query and reporting tools to facilitate access to CTRP data

CTRP data can be used for diverse purposes and has high potential value for extramural stakeholders. In theory, CTRP data are public to any user through the Clinical Trials Search API. In practice, the need for programming expertise to effectively utilize the API constitutes a barrier to access. CTRP data are also available through the clinical trials search tool on NCI’s Cancer.gov website. However, the user interface for this tool is designed for finding clinical trials relevant to a specific participant and is therefore sub-optimal for general data analysis. NCI has begun development of a query and reporting tool that would facilitate access to CTRP data for such general data analyses. The CTIWG recommended that NCI proceed with development of this tool and suggested that NCI consider developing customized tools and access portals to meet the needs of specific stakeholder groups:

1. NCI program staff
2. Cancer Center leadership and administrators
3. Cancer research community
4. General public

¹⁰ It should be noted that accrual to Industrial trials will be only that provided by Cancer Centers and therefore cannot be used to assess overall accrual to Industrial trials or to any particular Industrial trial. These data can only be used to assess the degree of Cancer Center accrual to this category of trials.

The data source for these different tools would be identical, but the query process, the data presented and the format in which the data are presented might vary by stakeholder group. Tools for the public, for example, could include more explanatory material and format search results in ways designed to reduce the potential for misinterpretation by lay users. The CTIWG further recommended that for all tools other than those aimed at the public, NCI should provide training materials to educate users on the use and limitations of the results obtained from these tools. Finally, the Working Group recommended that NCI develop these tools sequentially, starting with the tool designed for NCI program staff and working toward a tool that would be available to the public. Staggering tool releases in this way provides the opportunity to address any issues that may arise and develop necessary training materials prior to broad public release.

B. RECOMMENDATIONS ON CTRP PARTICIPANT-LEVEL ACCRUAL REPORTING

In 2010, NCI enhanced CTRP to support participant-level accrual reporting, and, in 2013, quarterly participant-level accrual reporting became mandatory for interventional trials except for Industry trials, for which only cumulative accrual data are collected. The following participant-level data elements are currently required for CTRP reporting:

- Subject ID
- Zip code for U.S. residents or country of residence for non-U.S. residents
- Gender (Male, Female, Unknown, Unspecified)
- Race (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, Not Reported, Unknown, White)
- Ethnicity (Hispanic or Latino, Not Hispanic or Latino, Not Reported, Unknown)
- Date of birth (YYYYMM)
- Disease code
- Registration date

In view of concerns about reporting burden, the CTIWG was asked to consider the purpose and value of collecting the currently-required participant-level data elements. Weighing the benefits of participant-level data collection against the reporting burden placed on Cancer Centers, the Working Group made recommendations on whether CTRP should continue to collect these elements and on modifications to enhance the utility of the data for NCI and the extramural community.

DEMOGRAPHIC DATA

Recommendation B1. Continue to collect participant-level data elements

Participant level demographic elements include zip code, gender, race, ethnicity and date of birth. The CTIWG acknowledged the importance of these data contained in CTRP. They noted that the availability of such data enables analyses stratified by demographic variables. The Working Group also noted that these data can be used to monitor accrual from minority or underserved populations. However, they acknowledged that these data could, in some situations, be used to identify individual participants.

In discussion, the CTIWG noted that this risk can be mitigated by constraining *access* to participant-level data (see “Recommendations on CTRP Data Access”) and implementing a bucket size minimum for reporting of these data. Nevertheless, some residual risk associated with collecting such data remains, particularly with respect to initial data submission or in the case of a possible data breach. On balance, weighing the value of these data and the analyses that they can inform against the potential risks of compromising participants’ confidentiality, the CTIWG recommended that NCI continue to collect participant-level data on zip code, gender, race, ethnicity and date of birth.

Recommendation B2. Emphasize submission of proper zip code data

The CTIWG noted that there are a number of issues associated with CTRP’s current zip code data. Although CTRP requires reporting of a five-digit zip code for participants who are U.S. residents and reporting of a country of residence for participants who are non-U.S. residents, the data are not always accurate. For example, some foreign accruals are reported with a zip code, while some accruals from U.S. sites are reported without a zip code, with an invalid zip code or with only a three-digit zip code. In addition, accruals are sometimes reported with the zip code of the site at which the subject is enrolled, rather than the zip code of the subject’s residence.

The CTIWG concluded that collection of accurate five-digit zip codes for U.S. participants should remain a priority, as such data provide important information on the geographic distribution of clinical trial participants. Furthermore, they recommended that CTRP emphasize the importance of reporting the zip code of the subject’s residence, rather than the enrolling institution’s zip code. In addition, the Working Group recommended that CTRP training materials be modified as necessary to emphasize these points.

DIAGNOSTIC DISEASE CODES

Recommendation B3. Map NCI Thesaurus¹¹ disease codes to CTRP accrual data

Since 2013, reporting of participant-level disease codes for accruals has been mandatory for National, Externally Peer-Reviewed and Institutional trials except for trials supported by NCI’s Division of Cancer Prevention. Currently, CTRP accepts submissions using four disease coding systems: CTEP Simplified Disease Coding (SDC), a histologic coding system; ICD-9, an anatomic site coding system; ICD-10, an anatomic site coding system that has recently superseded ICD-9 in general use and ICD-O-3, an anatomic site and histologic coding system. However, within any trial, only one disease coding system may be used. Because the disease coding systems differ in their focus (histologic versus anatomic) and structure, it is not possible to analyze CTRP accrual data by disease across trials in a consistent and unambiguous manner. Moreover, assigning disease codes to accruals for non-treatment trials can be problematic because of the inclusion of healthy volunteers. To help resolve some of these inconsistencies, the CTIWG was asked to consider whether the disease coding of accruals in CTRP could be standardized.

¹¹ NCI Thesaurus provides reference terminology for many systems. It covers vocabulary for clinical care, translational and basic research and public information and administrative activities.
<https://ncit.nci.nih.gov/ncitbrowser/>

The CTIWG deemed the idea of requiring all submitters to use the same participant-level disease coding system currently infeasible. The Working Group focused instead on approaches that would allow participant-level codes from all disease coding systems to be mapped to a unified set of terms for inclusion in CTRP. The CTIWG considered two options for a unified CTRP disease-coding system: (a) mapping reported participant-level data to the CCSG Data Table 4 anatomic site codes or (b) mapping reported participant-level data to the NCI Thesaurus disease codes. CCSG Data Table 4 anatomic site coding does not account for histology and/or biologic behavior, nor does it include a term for healthy volunteers, and it is not sufficiently specific for many analysis purposes. In contrast, the NCI Thesaurus codes account for anatomic site, histology and stage.

The CTIWG therefore recommended that NCI standardize CTRP accrual disease coding by mapping all submitted accruals to appropriate NCI Thesaurus disease codes. They also recommended allowing multiple NCI Thesaurus codes for a single accrual, as necessary. This mapping would be done for all accrual data currently in CTRP and prospectively for data reported to CTRP on an ongoing basis. Mapping of NCI Thesaurus disease codes to all accrual data in CTRP would create a consistent, unified set of accrual disease codes for analysis.

C. RECOMMENDATIONS ON EXPANSION OF CTRP DATA

As noted above, the AACI-NCI CTRP Strategic Subcommittee identified certain aspects of the originally-envisioned scope for CTRP that required additional consideration at an appropriate future date. Those topics included reporting of non-interventional (i.e., observational or ancillary/correlative) studies and reporting of toxicity, adverse event and outcome data. With the current progress of CTRP implementation, consideration of these issues by the CTIWG was deemed appropriate.

OBSERVATIONAL STUDIES

Recommendation C1. NCI should require CTRP registration and accrual reporting for observational studies

CTRP currently supports, but does not mandate, registration/accrual reporting for observational studies. Required CTRP registration and accrual reporting for observational studies would have several advantages. It would support required reporting of observational studies in CCSG Data Table 4 for Cancer Centers and enhance the comprehensiveness of portfolio analyses based on CTRP data. It would also support registration of observational studies in ClinicalTrials.gov and promote awareness of observational studies among investigators, patient advocates and the public, who use the clinical trials search tool on NCI's Cancer.gov Website. Based on these advantages, the CTIWG recommended that CTRP be expanded to include observational studies and offered several recommendations relating to implementation of this recommendation.

To ensure uniformity in the observational studies reported to CTRP, the CTIWG recommended that NCI adopt and disseminate the ClinicalTrials.gov definition of an observational study:

Studies in human beings in which biomedical and/or health outcomes are assessed in pre-defined groups of individuals. Participants in the study may receive diagnostic, therapeutic, or other interventions, but the investigator does not assign specific interventions to study participants. This includes when participants receive interventions as part of routine medical care and a researcher studies the effect of the intervention.

The Working Group recommended that this definition be distributed to Cancer Centers and used to define the studies that must be reported to CTRP under this study type.

The CTIWG also provided recommendations on the required data elements and reporting frequency to ensure integration with ClinicalTrials.gov and minimize reporting burden. They recommended that the data required by CTRP for observational studies mirror the data reported for observational studies in Data Table 4. However, if submitters would like to use CTRP data for ClinicalTrials.gov reporting, they could submit the required additional data elements to CTRP as well. To avoid placing undue burden on individual investigators, the CTIWG recommended a phased approach for implementation of required CTRP reporting of observational studies. Initially, implementation would be limited to studies conducted at Cancer Centers, followed by the implementation of reporting for NCI-supported studies at other institutions. For multi-site studies, the Working Group recommended that the Lead Organization be responsible for data submission, as is the policy for interventional trials.

To further minimize burden, the CTIWG recommended that CTRP observational study reporting be required only annually to match the periodicity of current Data Table 4 reporting. The CTIWG further recommended that aggregate, rather than participant-level, accrual data be required. However, the Working Group recommended that CTRP should enable more frequent reporting and submission of participant-level, rather than aggregate, accrual data, if this is desired by the submitting entity.

Finally, the CTIWG recommended that CTRP consistently code observational studies with a primary purpose classification of “other”, as specified for ClinicalTrials.gov.¹² The Working Group also recommended that observational studies in CTRP continue to be coded according to the study model (cohort, case-control, case-only, case-crossover, ecologic/ community, family-based and other), and time perspective (retrospective, prospective, cross-sectional and other) designations used by ClinicalTrials.gov.

ANCILLARY/CORRELATIVE STUDIES

Recommendation C2. NCI should not require CTRP registration and accrual reporting for ancillary/correlative studies at this time

As with observational studies, ancillary/correlative studies with independent protocols are reported by Cancer Centers in Data Table 4. Studies which are secondary aims in clinical protocols are not reported separately from the parent clinical trial in Data Table 4. CTRP also currently supports, but does not require, registration and reporting of ancillary/correlative studies with independent protocols. The

¹² Most but not all observational studies currently in CTRP are coded with a primary purpose of “Other”.

CTIWG was therefore asked whether CTRP should require reporting of these ancillary/correlative studies to support CCSG Data Table 4 reporting.

In discussing this topic, CTIWG members raised a number of questions concerning the inclusion of ancillary/correlative studies in Data Table 4 submissions. These included the meaning of an “accrual” to an ancillary/correlative study and whether both the Cancer Center conducting the study and the Cancer Center(s) supplying the data or specimens should report the study in Data Table 4. In addition, the value of this information for NCI Cancer Center program staff and CCSG reviewers was questioned given that only a subset of a Center’s ancillary/correlative study activity is included in Data Table 4. The Working Group ultimately concluded that NCI should examine the purpose and value of including information on ancillary/correlative studies in Data Table 4, as well as the scope of studies reported and what role a Cancer Center should play in a study to warrant reporting. Until NCI’s analysis of these topics is available, the CTIWG recommended that CTRP reporting of ancillary/correlative studies not be required.

TOXICITIES

Recommendation C3. NCI should not implement real-time reporting of serious adverse events to CTRP

CTRP does not collect information on adverse events (AEs) or serious adverse events (SAEs) associated with registered trials. Such toxicity data are, however, currently collected in various repositories:

- The CTEP Adverse Event Reporting System (AERS) requires AE reporting for all interventional trials with agents under a CTEP, Cancer Imaging Program (CIP) or DCP investigational new drug/investigational device exemption (IND/IDE) and real-time reporting of SAEs as defined for FDA reporting requirements in 21 CFR Part 312.¹³
- ClinicalTrials.gov requires reporting of deaths, SAEs (as defined for FDA reporting requirements in 21 CFR Part 312) and other AEs (AEs not meeting the definition of a SAE) as part of its results reporting for completed trials.
- FDA’s MedWatch program allows providers and consumers to report AEs on FDA-approved products.

Real-time reporting to CTRP of SAE data would provide real-time toxicity information on all NCI-supported clinical trials, rather than only those trials that currently report to AERS and other NCI systems. Collecting such data in CTRP would facilitate analysis of SAEs across multiple ongoing and closed trials and across families of drugs, potentially enabling identification of SAEs that occur at too low a frequency to be detected in individual trials. The Working Group acknowledged these benefits but noted that CTRP reporting would duplicate FDA and sponsor reporting requirements for many trials,

¹³ In 21 CFR Part 312, a serious adverse event is defined as any adverse drug experience occurring at any dose that results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed.

require expansion of current CTRP staffing and technical capabilities, and substantially increase the CTRP reporting burden for Cancer Centers. Moreover, collecting SAE data creates the responsibility to analyze the data for emerging issues. There is currently no clear authority or chain of command for taking action based on the results of a CTRP SAE data analysis. Therefore, despite the potential value of having real-time SAE data for ongoing trials, the CTIWG concluded that the burden of such reporting outweighs the benefits.

The Working Group also acknowledged that the quality and completeness of the current ClinicalTrials.gov SAE/AE data on completed trials are perceived as inadequate. However, members noted that the comprehensiveness of the data is likely to improve due to reporting mandated by the FDA Amendments Act of 2007 and review of compliance with ClinicalTrials.gov reporting requirements during the grant renewal process. The CTIWG encouraged NCI to investigate approaches to improve the quality and timeliness of SAE/AE data from completed trials reported to ClinicalTrials.gov by NCI awardees.

OUTCOMES

Recommendation C4. NCI should not implement reporting of outcome data to CTRP

Outcome data are not currently included in CTRP. However, a subset of these data are housed in other repositories. Summary outcome measures are required by ClinicalTrials.gov as part of basic results reporting; primary outcome measures must be reported within one year of the primary completion date of a trial, while reporting of secondary outcome measures is mandated within one year of the study completion date. The NCTN/NCORP Data Archive will contain de-identified participant-level outcome data for Phase III NCTN and NCORP trials with published results. In addition, clinical outcomes, including participant-level data, may be available upon request from investigators under existing NIH data sharing guidelines. With respect to summary outcome data on completed trials, the Working Group concluded that a broad CTRP reporting requirement would be duplicative of ClinicalTrials.gov reporting and was therefore not recommended.

The Working Group also discussed potential inclusion in CTRP of de-identified participant-level outcome data on trials that have reached their primary completion date, as participant-level data are not included in ClinicalTrials.gov. The members acknowledged a trend toward increased access to such detailed clinical trial data, especially given the data access policies of many journals, and noted that providing access to participant-level outcome data is a laudable goal. However, the CTIWG concluded that CTRP collection of participant-level outcome data would impose too high a burden on investigators to prepare and submit de-identified datasets and data dictionaries and on NCI to incorporate these data into CTRP. The need to respect data release restrictions in collaborative agreements with industry was identified as an additional challenge. As a result, the Working Group recommended against required reporting of participant-level outcome data to CTRP, even in summary form and after trial completion.

Although the CTIWG recommended against required CTRP reporting of outcome data, the Working Group did recommend that NCI continue to encourage improvements in the quality and timeliness of outcome data published and submitted to ClinicalTrials.gov by NCI awardees. The Working Group also suggested that NCI facilitate access to outcome data by providing links in CTRP to the ClinicalTrials.gov

summary outcome data, the NCTN/NCORP Data Archive participant-level data and any other relevant source of outcome data for each complete CTRP-registered trial for which such data are available.

D. RECOMMENDATIONS ON CLINICAL TRIALS SEARCHING

The CTIWG was asked to comment on how the clinical trials search tool on the Cancer.gov website can be improved, particularly for patients and other non-specialist users. To do so, Working Group members tested the NCI's Cancer.gov website search tool available in October 2016 and recommended improvements. They also recommended improvements in the structuring of CTRP data to facilitate clinical trials searching.

IMPROVEMENTS TO THE SEARCH PROCESS

Recommendation D1. Create Cancer.gov interfaces tailored for defined user populations and drawing on a unified clinical trials search engine

Because the needs and knowledge of various user populations may vary substantially, the CTIWG recommended that NCI develop tailored user interfaces to improve the ease and efficiency of Cancer.gov clinical trials searching. However, the Working Group specified that the underlying data retrieval engine should be shared across the various user interfaces to assure that identical queries will return the same results.

The Working Group noted that user interfaces should be developed with the respective user groups' knowledge and needs in mind. For example, the CTIWG recommended that clinical trial information retrieved via a participant-oriented interface be prioritized for treatment trials and be presented in simple language that includes links to definitions for terms that might require clarification. The search menu itself might also be tailored to different user groups. A participant-oriented interface might include simplified lists of cancer types and drugs on which a query can be based, whereas an interface tailored to a more specialized user might include more specialized terminology.

Recommendation D2. Facilitate automated trial matching based on genetic analysis reports and/or data from electronic medical records

To improve matching of patients to trials, the CTIWG recommended that NCI facilitate automated trial matching based on genetic analysis reports or data from electronic medical records (EMRs). NCI's role in such an effort might include (1) ensuring that the Clinical Trials Search API is suited for automated trial matching, (2) developing a prototype automated trial matching tool as a proof-of-concept and (3) working in partnership with commercial providers to develop additional trial matching tools. The utility of such matching would depend on the degree to which clinical trials information and patient EMR data are structured. The CTIWG acknowledged that eligibility criteria in CTRP would need to be structured in a consistent and machine-readable format and, similarly, that laboratory or EMR documentation of molecular abnormalities would need to be in a consistent and machine-readable format interoperable with CTRP.

STRUCTURING OF ELIGIBILITY CRITERIA

Structured eligibility criteria enable retrieval of trials for which a patient is more likely to be a candidate. However, the only structured eligibility criteria currently available in CTRP are age, gender, whether the trial accepts healthy volunteers and biomarker inclusion/exclusion criteria for trials open to accrual. Structured biomarker inclusion/exclusion criteria are available through the Clinical Trials Search API but not currently accessible through the clinical trials search tool on NCI's Cancer.gov website.

Recommendation D3. Continue structuring of biomarker eligibility criteria in CTRP

The CTIWG recommended that NCI make structured biomarker eligibility criteria available for searching in the clinical trials search tool on NCI's Cancer.gov website as soon as practical. The Working Group also indicated that (a) it is not necessary to include the assay or institutional standard used to measure the biomarker in the criteria and (b) if biomarker positivity is an inclusion criterion, biomarker negativity need not be listed as a separate exclusion criterion. Finally, the Working Group recommended that the biomarker criteria themselves be listed with as much specificity as possible.

Recommendation D4. Additional eligibility criteria should be structured as feasible

The CTIWG recommended that eligibility criteria be prioritized for structuring based on the following factors:

1. **Clinical Significance:** What is the clinical importance of the attribute or metric captured in the criterion?
2. **Structuring Ease:** How easy is it to structure the criterion across trials?
3. **Practicality:** How easy is it for the typical physician or clinical research staff member to determine whether the criterion is met?
4. **Frequency:** How many trials list the criterion?
5. **Durability:** Is the criterion unlikely to change over time?

The Working Group suggested that NCI conduct a pilot to determine whether the structuring of eligibility criteria will narrow the list of retrieved trials sufficiently to warrant the effort required. They suggested this pilot could involve (a) selecting a subset of trials and several eligibility criteria that would likely narrow the trials retrieved, (b) structuring the selected criteria and (c) determining whether patients and physicians obtain useful trial results through queries based on the structured criteria.

E. RECOMMENDATIONS FOR RESOLVING CTRP DATA INCONSISTENCIES AND AMBIGUITIES

The feedback obtained from CTRP users in the Fall of 2015 identified a number of perceived ambiguities and inconsistencies in CTRP data that were of concern at that time. As noted previously, some of these were judged to be purely technical and could be resolved internally by NCI. However, several points were identified as raising substantive questions for which guidance from the CTIWG was requested.

MISMATCH BETWEEN CTRP AND CANCER CENTER TRIAL STATUS CATEGORIES

Recommendation E1. ClinicalTrials.gov clinical trial status categories, definitions and, as possible, titles should be adopted for CTRP

CTRP has used trial status categories whose definitions and titles differ from those used by ClinicalTrials.gov. In addition, CTRP trial status categories often do not correspond to the trial status data that are routinely collected by Cancer Centers. To fully meet CTRP reporting requirements, many Cancer Centers collect and maintain data beyond what is required by ClinicalTrials.gov and/or their internal clinical trials management systems. Due to this burden, Cancer Centers have sometimes reported trial status data that were incomplete or inconsistent.

NCI analyzed the differences between the CTRP and ClinicalTrials.gov trial status categories and determined that CTRP could use the ClinicalTrials.gov trial status categories and definitions. The CTIWG therefore recommended that CTRP adopt the clinical trial status categories, definitions and, to the degree possible, titles used by ClinicalTrials.gov.

The CTIWG also discussed that trials, especially early phase trials, often open and close repeatedly for short periods and that the resulting frequent status changes are not recorded in all Cancer Center clinical trials management systems. They noted concerns about the accuracy of CTRP trial status data for trials that undergo frequent status changes but elected not to issue a recommendation on this point. ClinicalTrials.gov does not specify a minimum duration of study closure that mandates reporting, and for CTRP to do so might introduce a discrepancy in trial status for trials registered in these two systems.

DIFFERENT DEFINITIONS OF “ACCRUED SUBJECT” ACROSS CANCER CENTERS

Recommendation E2. Adopt and promulgate a standard definition for “accrued subject/enrolled participant” in CTRP

There is substantial variation across Cancer Centers in the definition of when a participant is recorded as accrued to a trial. For example, one Cancer Center may consider a participant accrued when he or she has been screened for eligibility, while others might consider a participant accrued when he or she signs the informed consent, registers for a trial or receives an initial intervention. The lack of a consistently applied definition creates ambiguities in assessing accrual across trials and Cancer Centers. To resolve this inconsistency, the CTIWG recommended that CTRP adopt a standardized definition for “accrued subject,” based on the Food and Drug Administration Amendments Act (FDAAA) Final Rule definition of an “enrolled participant”:

“Enrolled means a participant’s, or their legally authorized representative’s, agreement to participate in a clinical study following completion of the informed consent process. Potential participants who are screened for the purpose of determining eligibility for the study, but do not participate in the study, are not considered enrolled, unless otherwise specified by the protocol.”¹⁴

¹⁴ <https://prsinfo.clinicaltrials.gov/definitions.html#IntEnrollment>

Recommendation E3. Record screening accruals for precision medicine trials separately in CTRP from accruals to the intervention arms

Some precision medicine trials, such as NCI-MATCH, specify a screening intervention requiring informed consent followed by a treatment intervention requiring a separate informed consent. The definition of enrolled participant recommended by the CTIWG thus enables participants to be considered enrolled to each stage of a precision medicine trial independently. For example, a participant who consents to screening can be recorded as an enrolled participant for the screening stage, and if that same participant matches to a treatment arm and consents to participate, the participant can also be recorded as enrolled for that treatment arm. Based on this logic, the CTIWG recommended that screening accruals for precision medicine trials be recorded separately in CTRP from accruals to the interventions arms. However, screening for conformance with general trial eligibility criteria or routine screening for standard of care or genetic markers not associated with a specific trial, should not be reported to CTRP as a screening accrual.

INCONSISTENT APPLICATION OF “PRIMARY PURPOSE” DEFINITIONS

Recommendation E4. Clarify the primary purpose definitions in CTRP user support materials.

The primary purpose categories currently used for coding trials in CTRP are Treatment, Prevention, Supportive Care, Screening, Diagnostic, Health Services Research, Basic Science, Device Feasibility and Other. These categories and their definitions are identical in ClinicalTrials.gov and CTRP, but they have not always been consistently applied for trials in CTRP. The Working Group indicated that clarification of the definitions might be helpful in achieving consistent application and recommended adding further explanatory information concerning the definitions to CTRP user support materials, including examples where appropriate.

F. RECOMMENDATIONS ON IMPLEMENTATION OF A CTRP-GENERATED DATA TABLE 4

Data Table 4 serves as documentation of a Cancer Center’s clinical trial activity for CCSG application review. Data Table 4 includes cancer-relevant, hypothesis-driven studies that meet the definition of clinical research, including interventional, observational and ancillary/correlative studies. To minimize duplicate reporting by Cancer Centers and assure consistency and completeness of the data on NCI-supported clinical trials, NCI has committed to implementing CTRP-generated Data Table 4 reports for interventional trials.

In light of CTRP user concerns, the CTIWG was asked to comment on how the generation of Data Table 4 from CTRP data could be most effectively implemented. The Working Group concluded that their recommendations concerning expansion of CTRP data and resolution of CTRP data inconsistencies and ambiguities, if implemented, as well as several operational improvements currently being implemented by NCI, would address the majority of concerns raised by administrators. In addition, the Working Group

made a recommendation concerning the timeline for implementation of a CTRP-generated Data Table 4 for interventional trials.

Recommendation F1. Generate Data Table 4 for interventional trials from CTRP data for non-competing CCSG renewal submissions beginning in October 2017, and for competing review submissions beginning in October 2018

CTRP began creating Data Table 4 reports for interventional trials for internal NCI review and data reconciliation purposes in May 2014. Interventional trial information in CTRP and Cancer Center generated Data Table 4 reports were extensively reconciled by June 2017. NCI's initial proposal was to implement the use of CTRP-generated Data Table 4 reports for interventional trials in all CCSG application submissions beginning in October 2017. However, the Working Group recommended modifying this timeline to stagger implementation, with CTRP-generated interventional trial Data Table 4 reporting required in October 2017 only for non-competing renewal submissions and implementation for competing applications starting in October 2018. The accuracy of the information contained in Data Table 4 is critical for competing reviews. The recommended implementation timeline provides ample opportunity to address any issues that may arise during the transition (e.g., reconciliation of the quarterly accrual reported to CTRP with the grant year accrual total required for Data Table 4). In addition, this delay enables Cancer Centers to improve the completeness and accuracy of their CTRP reporting through enhanced training and other internal improvements.

G. RECOMMENDATIONS ON COMMUNICATING THE VALUE OF CTRP

The CTIWG recognized the value of CTRP and its potential impact on cancer clinical research. Nevertheless, its value is not widely known, as was evidenced in comments from those submitting data to CTRP in 2015. The CTIWG commented that obtaining buy-in from those responsible for data submission might result in higher quality data. Accordingly, the Working Group made recommendations on ways to improve communications about CTRP, not only to individuals responsible for data submission but to all potential stakeholders.

Recommendation G1. Pursue efforts to increase awareness of the value of CTRP

It is timely to increase outreach to improve awareness of CTRP value among stakeholders. Specific measures recommended include: (1) disseminating information through the American Society of Clinical Oncology and American Association for Cancer Research, (2) conducting a CTRP "roadshow" for Cancer Centers to convey the value of CTRP to Cancer Center leadership and administrators and present CTRP data analysis use cases for investigators, (3) publishing a peer-reviewed article on the value and uses of CTRP data and (4) encouraging publication of CTRP-derived analyses in peer-reviewed journals.

Recommendation G2. Continue efforts to increase understanding of the Clinical Trials Search API

To increase awareness of the Clinical Trials Search API among various stakeholders the CTIWG suggested NCI provide more extensive information about the tool, developing content and selecting communication channels targeted toward specific audiences. They also recommended that NCI make

the information about the Clinical Trials Search API presented on Cancer.gov more understandable and useful for a wide range of audiences. Example software demonstrating usage of the Clinical Trials API is currently available in the GitHub site for the project, but these examples should be refined to reflect the changing capabilities of the API. Finally, the Working Group suggested that NCI communicate on a periodic basis with parties developing software applications using the Clinical Trials Search API to determine how to best meet their needs.

APPENDIX 1 – WORKING GROUP MEMBERS AND OTHER PERSONNEL

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APPENDIX 2 – WORKING GROUP MEETINGS AND WEBINARS

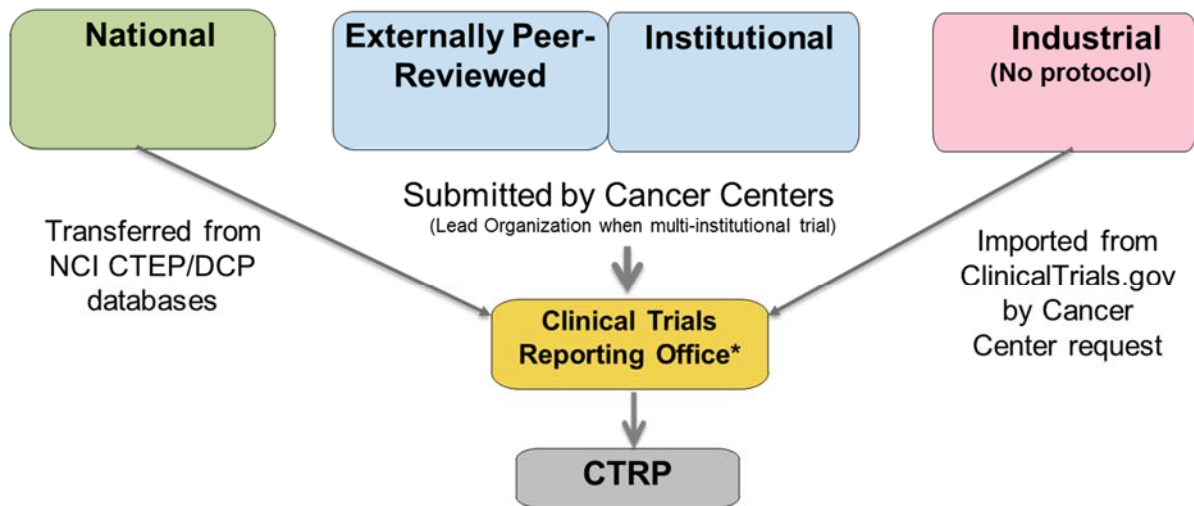
Date	Meeting Type	Topic(s)
December 2, 2015	Plenary Webinar	CTIWG Orientation
February 11, 2016	Plenary Webinar	Background on CTRP
April 26, 2016	Plenary Webinar	Information on CTRP Workflow; User Feedback Results
August 29, 2016	Subgroup 1 Webinar	Subgroup 1 Orientation; Enhancing Clinical Trials Searching
September 23, 2016	Subgroup 1 Webinar	Structured Eligibility Criteria
October 20, 2016	Subgroup 2 Webinar	Inconsistencies and Ambiguities in CTRP Data, Part 1
October 31, 2016	Subgroup 2 Webinar	Inconsistencies and Ambiguities in CTRP Data, Part 2
November 9, 2016	Plenary In-Person Meeting	CTRP as an Information Resource for Researchers; CTRP-Generated Data Table 4; Subgroup Progress
February 3, 2017	Subgroup 2 Webinar	Inconsistencies and Ambiguities in CTRP Data, Part 3
February 8, 2017	Subgroup 1 Webinar	Update on Clinical Trials Search API; Cancer.gov Clinical Trial Search Tool; Structured Eligibility Criteria
March 2, 2017	Subgroup 2 Webinar	CTRP Accrual Reporting
April 6, 2017	Subgroup 2 Webinar	Disease Coding of Accrual
April 19, 2017	Plenary Webinar	Extramural Access to CTRP Data
May 4, 2017	Subgroup 2 Webinar	Inclusion of Observational Studies in CTRP
June 15, 2017	Subgroup 2 Webinar	Inclusion of Ancillary/Correlative Studies in CTRP
August 3, 2017	Subgroup 2 Webinar	Inclusion of Outcome/Toxicity Data in CTRP
September 8, 2017	Plenary Webinar	Refining Conclusions on Extramural Access to CTRP Data
October 4, 2017	Plenary In-Person Meeting	Finalizing and Approving CTIWG Recommendations

APPENDIX 3 – OVERVIEW OF CTRP OPERATIONS

Submission of data to the CTRP database can be viewed as a complex matrix of data flows. On the one hand, each of the Data Table 4 Study Source categories has a distinctive workflow for registering trials and reporting amendments, updates and accrual to CTRP. On the other, each entity that submits data to CTRP conducts clinical trials in a variety of Data Table 4 Study Source categories.

Briefly, information regarding registration, amendments, updates as well as participant-level accrual for trials managed directly by NCI (e.g., CTEP, DCP and CCR), are transferred within NCI to CTRP. During trial registration, NCI abstracts the protocol document and adds further coding, such as study source, anatomic site, cancer type and intervention. Cancer Centers and other NCI awardees register, update and amend their clinical trial information through a website interface and attach the required documents, including the protocol and informed consent form, if separate.¹⁵ Participant-level accrual data for trials originating from Cancer Centers are typically submitted via a batch upload. When the trial is taking place in multiple Cancer Centers, the lead organization is responsible for maintaining the status of all participating sites, as well as reporting the accrual for each of the participating sites. Finally, for Industrial trials conducted at Cancer Centers, the CTRP system can import trial registration and update information from ClinicalTrials.gov at the request of the Cancer Center. Cancer Centers then register participating sites and submit cumulative accrual data for these trials to CTRP. Protocol documents and participant-level data are not provided to CTRP for Industrial trials. For all trials, CTRP staff verify submitted data for consistency and accuracy. These data flows are summarized in Figures 1 and 2 below.

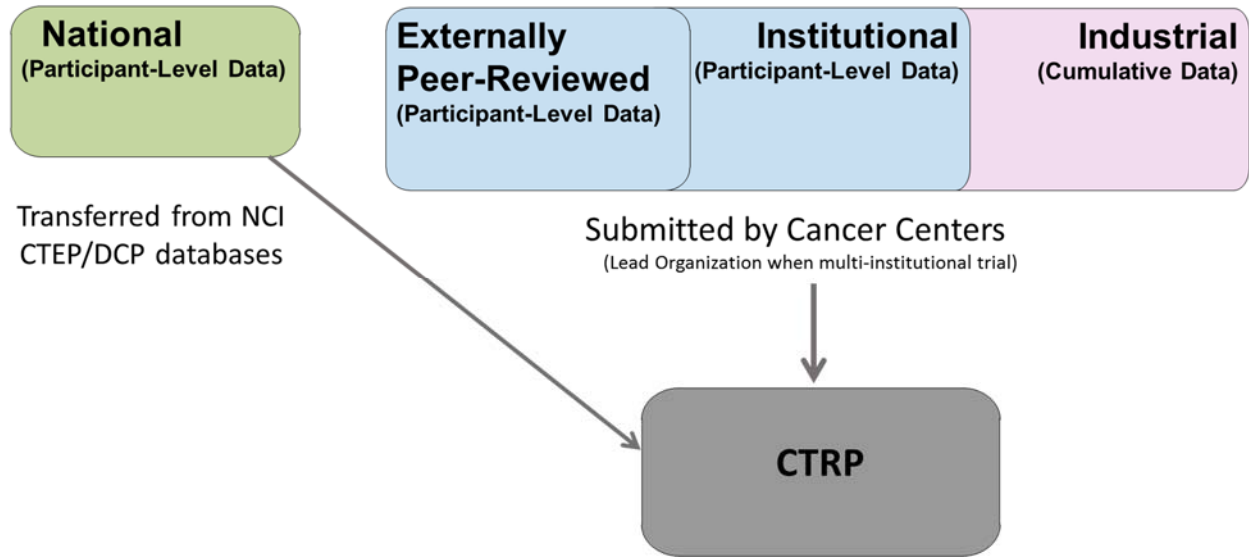
Figure 1: CTRP Workflow: Trial Registration, Amendments and Updates



*NCI staff who abstract, code and review data for entry in CTRP

¹⁵ Although direct transfer of registration and accrual data from the clinical trials management systems of these extramural parties to NCI is possible, this method of reporting has not been widely adopted.

Figure 2: CTRP Workflow: Accrual Information



Information contained in the CTRP database is used for many purposes. NCI uses the data for program management and to fulfill ClinicalTrials.gov reporting requirements for trials for which NCI is the sponsor per FDAAA (e.g. trials supported by NCI contracts, and trials for which NCI holds the IND).¹⁶ Other sponsors can use the “Upload from CTRP” function on the ClinicalTrials.gov website to access a CTRP-generated record to use for ClinicalTrials.gov registration, thereby minimizing duplicative reporting. In addition, a Cancer Center may search CTRP for data on all trials they submitted and trials where they are listed as a participating site. CTRP also serves as the data source for the clinical trials search service on NCI’s Cancer.gov website. Finally, NCI has created a Clinical Trials Search (CTS) API that can be used to access public CTRP information. Taking advantage of this API, extramural parties can build software applications to support a wide range of possible uses for CTRP data. For example, advocacy groups, patients or physicians could use CTS-API-based applications to identify trials of interest, or researchers designing trials could use CTS-API-based applications to obtain a comprehensive view of NCI clinical trial activity in their area of interest.

¹⁶ IND = Food and Drug Administration Investigational New Drug application.