

# NCI Clinical Trials Informatics Working Group Report to CTAC

# Agenda

---

- Background
  - NCI's Clinical Trials Reporting Program (CTRP)
  - CTRP-generated Data Table 4 (DT4)
- Clinical Trials Informatics Working Group (CTIWG)
- Highlights of CTIWG Recommendations
  - Improving Access to CTRP Data
  - Expanding CTRP Data
  - Improving Clinical Trial Search
  - Recording Accruals to Precision Medicine Trials
  - Implementing a CTRP-Generated DT4 for Interventional Trials
- Discussion and Move for Approval of the Report



# NCI's Clinical Trials Reporting Program (CTRP)

***Gisele A. Sarosy, M.D.***

*Medical Officer, Coordinating Center for  
Clinical Trials*

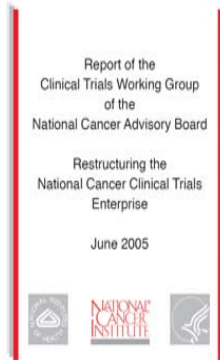
# What is CTRP?

---

- Comprehensive database containing regularly updated information, including accrual, on all NCI-supported interventional trials
- Utilizes standardized data elements and consistent protocol abstraction
- Supports NCI clinical trials portfolio management
  - Identify gaps in portfolio
  - Prioritize clinical research opportunities
- Supports registration and results reporting to ClinicalTrials.gov for NCI sponsored trials in compliance with NIH policies and FDAAA legislation

# CTRP: Rationale for Development

---



- Key conclusions of 2005 Clinical Trials Working Group (CTWG) and 2010 Institute of Medicine reports
  - NCI had no electronic database that captured all NCI supported trials and their accrual
  - Trials supported by grants (R01, R21, P01, SPORE, etc.) and institutionally-supported trials using NCI-funded Cancer Center infrastructure resources were particularly difficult to identify
- Available databases did not allow NCI and the broader cancer community to:
  - Monitor accrual
  - Identify gaps and duplicative studies
  - Effectively prioritize clinical trials

## CTRP: Key Attributes

---

- Existing databases (e.g., ClinicalTrials.gov) do not fulfill all purposes envisioned for an NCI clinical trials database
- CTRP addresses these gaps through unique features:
  - Consistent terminology and standardized data elements to optimize search and retrieval of cancer clinical trials information
  - Inclusion of structured biomarker information
  - Quarterly reporting of accrual, including participant-level demography
  - Standard representation of persons and organizations
  - Identification of associated NCI awards and contracts
  - Regular updates to reflect protocol amendments, as well as participating site and status changes

# CTRP: Scope and Content

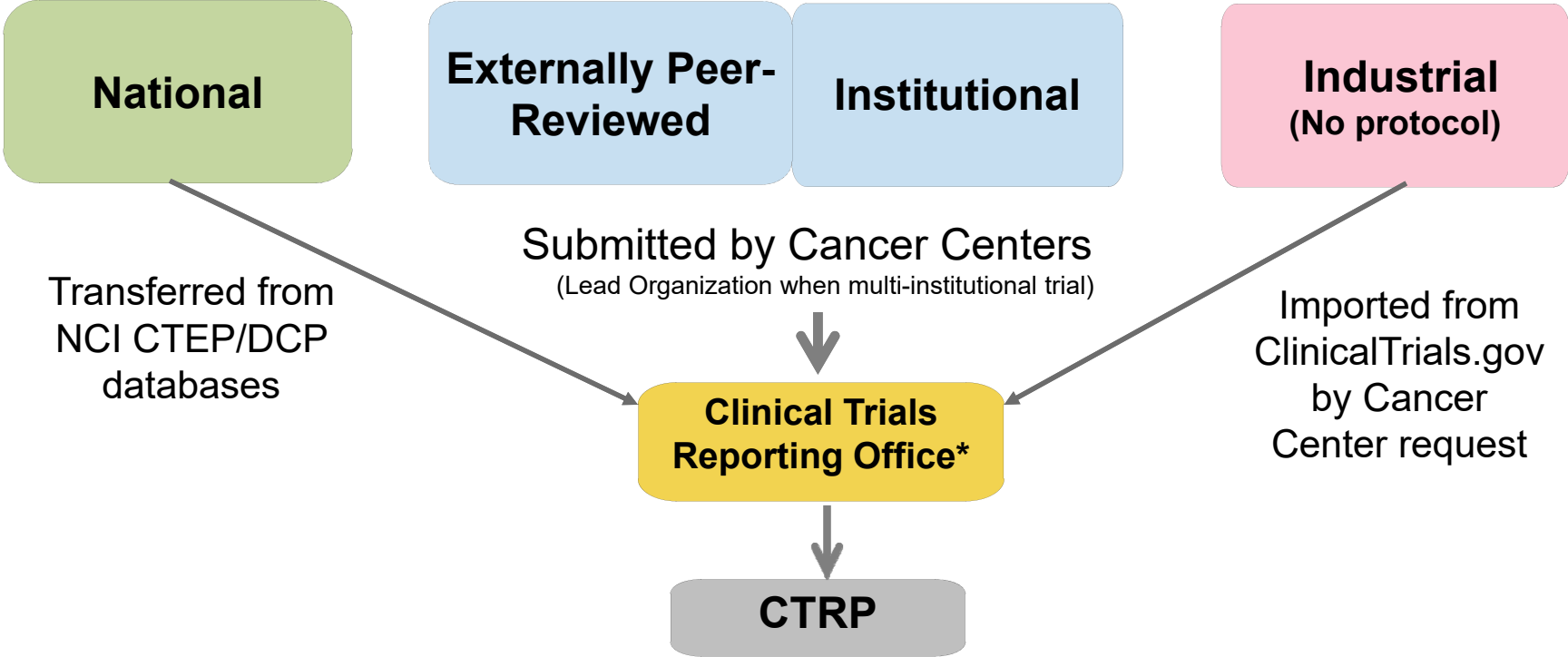
---

- NCI-supported interventional<sup>1</sup> clinical trials
  - Trials taking place in at least one NCI Designated Cancer Center, including *industrial* trials
  - Trials sponsored (per FDAAA) by NCI as well as trials sponsored by other entities
- Supports, but does not require, registration of non-interventional trials (e.g., observational, ancillary/correlative)
- Accrual data reported for all active trials, at least quarterly
  - Participant Level<sup>2</sup> (except for industrial trials)
  - Cumulative (accrual to date)

<sup>1</sup>Studies in human beings in which individuals are assigned by an investigator, based on a protocol, to receive specific interventions. Subjects may receive diagnostic, therapeutic, behavioral or other types of interventions. The assignment of the intervention may or may not be random. The individuals are followed and biomedical and/or health outcomes are assessed. (Source: <http://prsinfo.clinicaltrials.gov/definitions.html> and <http://cancercenters.cancer.gov/documents/CCSGDataGuide508C.pdf>)

<sup>2</sup>Participant Level Data: Protocol ID; Patient ID, Registering Institution Code, Patient Zip Code (if US), Country Code (if not US), Patient Birth (Mo/Year); Gender, Ethnicity; Race; Date of Entry on Study; Disease Code

# CTRP Workflow: Trial Registration, Amendments and Updates

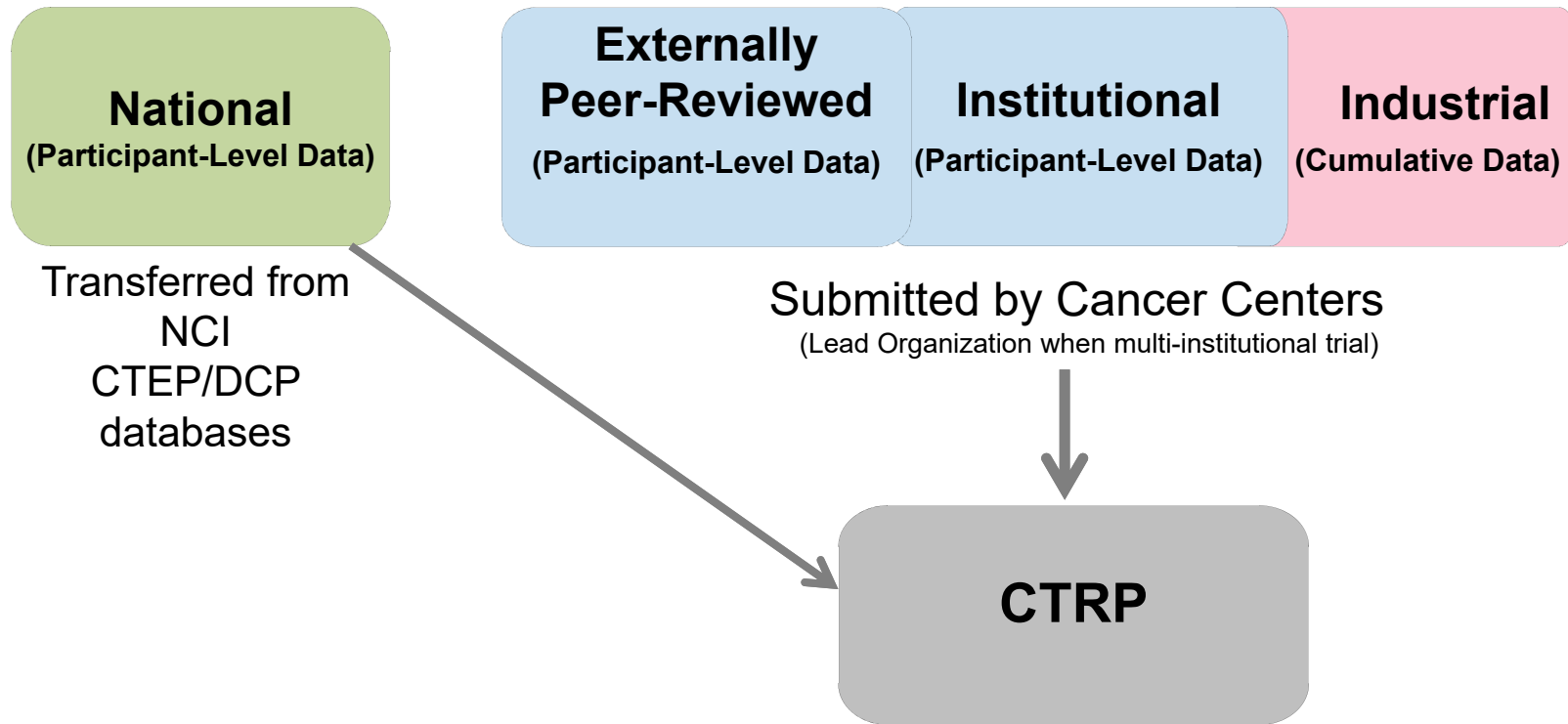


\*NCI staff who abstract, code and review data for entry in CTRP

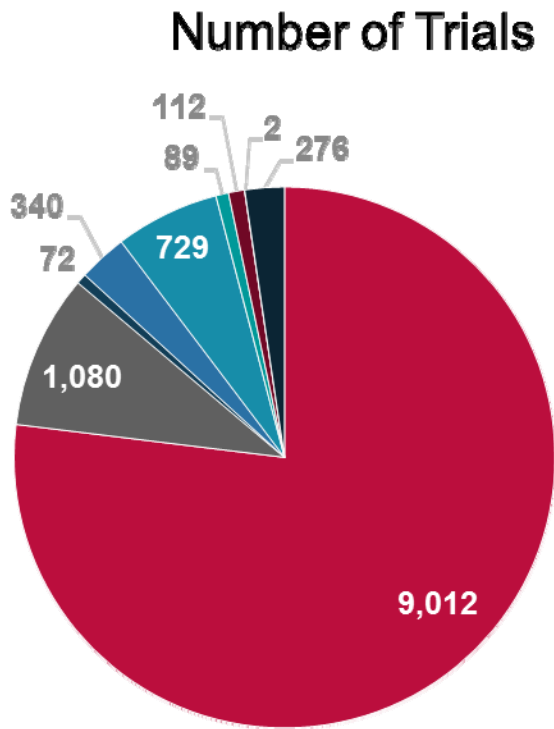


# CTRP Workflow: Accrual Data

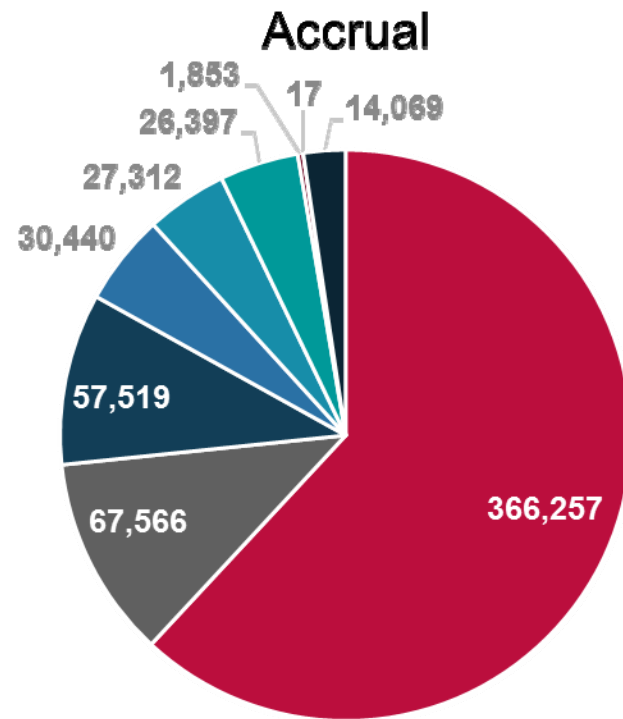
---



# CTRP: Interventional Clinical Trials as of September, 2017\*



N= 11,712 as of 09-2017



N= 591,430 as of 09-2017



# Data Table 4

*Henry Ciolino, Ph.D.*

*Director, Office of Cancer Centers*

## Data Table 4

---

- Data Table 4 is submitted as part of a Cancer Center Support Grant (CCSG) application
- Summarizes the Cancer Center's clinical research activity
  - Interventional, observational and ancillary-correlative studies open during the reporting period
  - Accrual during the reporting period
- Required:
  - Non-competing renewals
  - Competitive applications

# Data Table 4: Example

## Data Table 4 Study Source Definitions:

**National:** NCI National Clinical Trials Network (NCTN) and other NIH-supported National Trial Networks

**Externally Peer-Reviewed:** R01s, SPORES, U01s, U10s, P01s, CTEP, or any other clinical research study mechanism supported by the NIH or organizations on this list: Organizations with Peer Review Funding System

**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:** A pharmaceutical company controls the design and implementation of these clinical research studies

INSTITUTIONAL											Total Targeted Accrual		Cancer Center: Primary Accrual Institution		Other Accrual Institution(s)	
Specific Funding Source	Anatomic Site	Protocol ID	PI	Prog Code	Date Opened	Date Closed	Phase	Primary Purpose	Official Title	Multi-Inst study?	Entire Study	Your Center	12 Months	To Date	12 Months	To Date
NYU	Multiple	NCT998112	Berry J	8	5/1/2015		N/A	OTH	Risk factors for childhood cancer and hematological disorders by case-control studies	Yes	4000	1500	125	499	86	600
NYU, NIH	Multiple Myeloma	NCT889111	Smith S	6	1/1/2010	4/7/2011	N/A	OTH	Treatment Decision Making in Older Adults Newly Diagnosed with MM	No		20	6	18		

<https://cancercenters.cancer.gov/Documents/CCSGDataGuide508C.pdf>

## Rationale for CTRP-Generated Data Table 4

---

- Eliminates duplicate reporting by Cancer Centers
- Assures consistency
  - CTRP includes the NCT ID and a consistent title for each clinical trial
  - More uniform application of trial characteristics (e.g., primary purpose, phase)
- Improves accuracy
  - Only one registration record exists in CTRP for each trial or study
  - Each accrual is uniquely represented, supporting more accurate accrual reporting across trials
- Supports portfolio analysis across Cancer Centers

## CTRP-Generated Data Table 4 for Interventional Trials

---

- CCSG Data Table 4 (DT4) reports reconciled with CTRP-generated DT4 reports (completed 2017)
  - Trial status
  - Participating site status
  - Protocol IDs
  - Number of open trials
  - Accrual (particularly accrual to multi-institutional trials)
- Implementing CTRP enhancements to facilitate data submission
- Centers now running CTRP-generated DT4 reports independently



# NCI Clinical Trials Informatics Working Group

***Louis Weiner, M.D.***

*Director, Georgetown-Lombardi Comprehensive  
Cancer Center*

***Warren Kibbe, Ph.D.***

*Professor, Biostatistics and Bioinformatics  
Division Chief, Translational Biomedical Informatics  
Chief Data Officer, Duke Cancer Institute*



## Clinical Trials Informatics Working Group Purpose

---

- Provide expertise and advice on implementation of NCI clinical trials informatics initiatives
- Goals:
  - Improve value of cancer clinical trial data
  - Increase usability and accessibility of clinical trial information for physicians, patients, and the public
  - Minimize burden of cancer clinical trial data management
  - Streamline clinical trial initiation, conduct, data analysis and reporting
- Focus to date: NCI's Clinical Trials Reporting Program

# Clinical Trials Informatics Working Group Members

---

**Co-Chairs**    **Warren Kibbe, Ph.D.**, Duke University  
                  **Louis Weiner, M.D.**, Georgetown University

**Members**     **Rhoda Azoomanian, R.N., M.S.M.**, Yale University  
                  **Walter Curran, Jr, M.D.**, Emory University  
                  **Stanton Gerson, M.D.**, Case Comprehensive Cancer Center  
                  **Michael LeBlanc, Ph.D.**, Fred Hutchinson Cancer Research Center  
                  **Mia Levy, M.D., Ph.D.**, Vanderbilt University  
                  **Lynn Matrisian, Ph.D., M.B.A.**, Pancreatic Cancer Action Network  
                  **Robert Miller, M.D., F.A.C.P., F.A.S.C.O.**, American Society of Clinical Oncology  
                  **Sorena Nadaf, M.S., M.M.I.**, City of Hope  
                  **George Sledge, Jr, M.D.**, Stanford University  
                  **Richard Zellars, M.D.**, Indiana University

**Exec. Sec.**    **Gisele Sarosy, M.D.**, National Cancer Institute

## Clinical Trials Informatics Working Group: NCI Liaisons

---

- **Jeffrey Abrams, M.D.**, Associate Director, Cancer Therapy Evaluation Program
- **Henry Ciolino, Ph.D.**, Director, Office of Cancer Centers
- **Andrea M. Denicoff, MS, RN, ANP**, Head, NCTN Clinical Trials Operations; Cancer Therapy Evaluation Program
- **Peter Garrett**, Director, Office of Communications and Public Liaison
- **James Gulley, M.D., Ph.D., F.A.C.P.**, Director, Medical Oncology Service, Office of the Clinical Director, CCR
- **Bradford W. Hesse, Ph.D.**, Chief, Health Communication & Informatics Research Branch, DCCPS
- **Anthony R. Kerlavage, Ph.D.**, Chief, Cancer Informatics Branch, Center for Biomedical Informatics and Information Technology
- **Lori Minasian, M.D., F.A.C.P.**, Deputy Director, Division of Cancer Prevention
- **Sheila Prindiville, M.D., M.P.H.**, Director, Coordinating Center for Clinical Trials

# Clinical Trials Informatics Working Group - Process

---

- Convened two subgroups which met independently
  - Subgroup 1 – Improving clinical trials search tool on NCI’s Cancer.gov website, which draws on CTRP data.
  - Subgroup 2
    - Resolving inconsistencies and ambiguities in existing CTRP data
    - Potential expansions of CTRP scope
- Full CTIWG met via face to face meetings and webinars over 2 years
  - Discussed and ratified recommendations of the two subgroups
  - Addressed the following topics:
    - Envisioning CTRP data analyses that would provide value to the extramural community
    - Facilitating access to CTRP information
    - Transitioning to a CTRP-generated CCSG Data Table 4 for interventional trials
    - Improving communication concerning the rationale and value of CTRP



## Highlights of CTIWG Recommendations

*Improving Access to CTRP Data*

## Current Status of CTRP Data Access

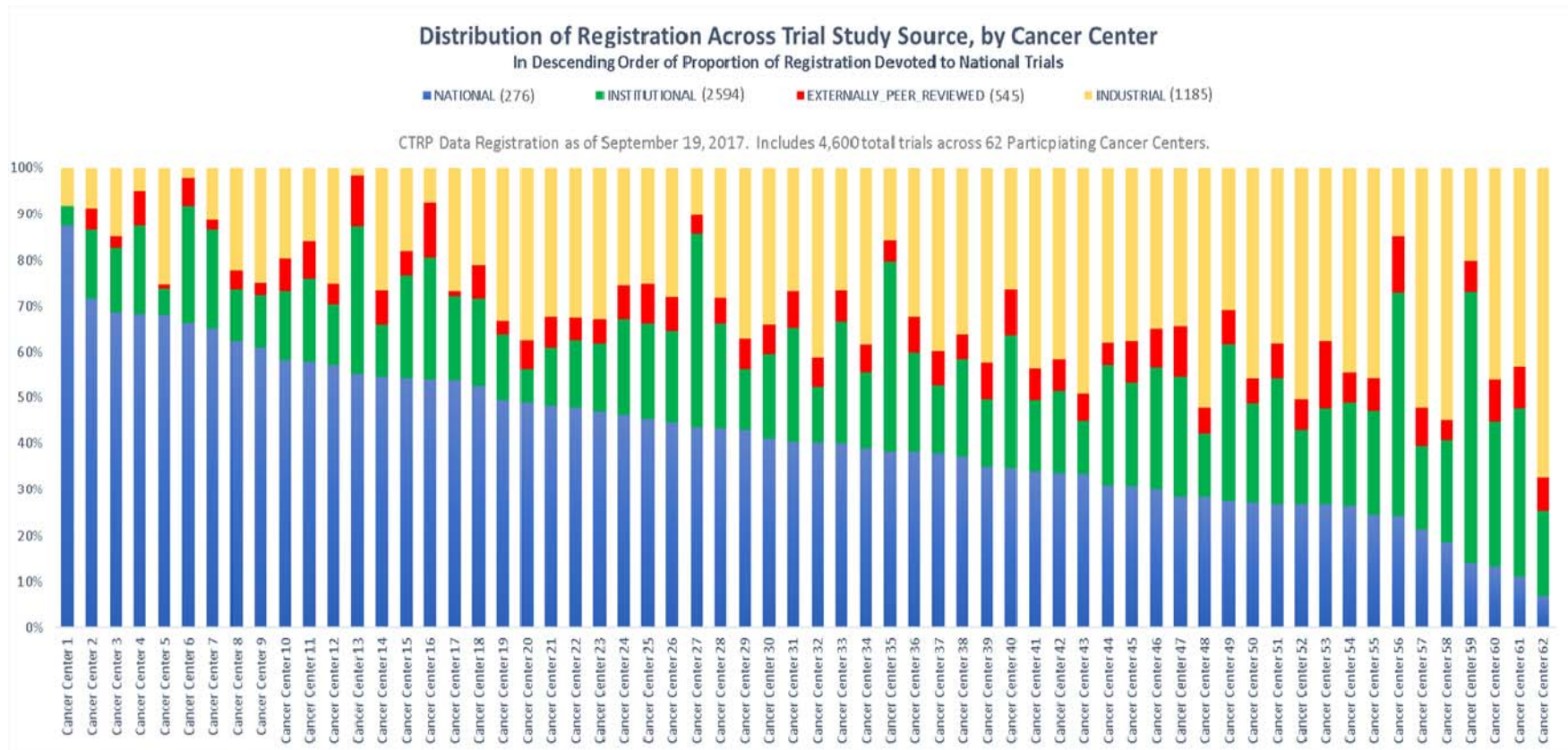
---

- CTRP data for all trials are public, with the following **exceptions**:
  - **Data Table 4 Study Source** (national, externally-peer reviewed, institutional and industrial)
  - **Biomarkers that are not inclusion/exclusion eligibility criteria**
  - **Accrual data** (accrued subjects per trial and associated participant-level demographic data)
- NCI Clinical Trials Search API\* provides public access to CTRP data
  - Source of Cancer.gov information for clinical trials searching
  - Available to extramural parties for applications development
  - Requires computer programming expertise to retrieve data in a useful format

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

# Recommendation: Data Table 4 Study Source should be public

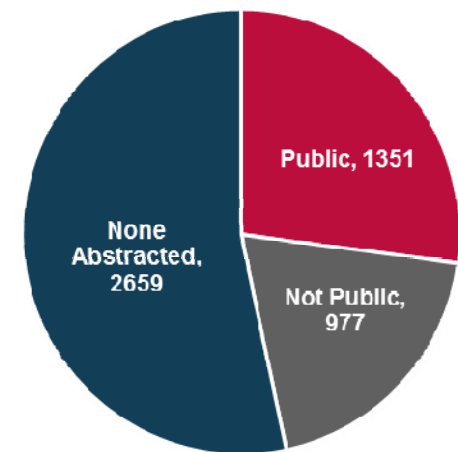
*Enables analyses of trials by Study Source*



## Recommendation: All CTRP information on biomarkers should be public

- Biomarker information in eligibility criteria currently public
- Biomarker information not currently public include biomarkers for
  - Treatment assignment
  - Response assessment
  - Stratification of trial results
- Expansion of public biomarker data enables comprehensive analysis of biomarker involvement in NCI supported trials

Number of Trials with Biomarkers





## Recommendations on Accrual - Overview

---

- Participant-level accrual
- Aggregate accrual – overall count
- Aggregate accrual – demographic data

## Recommendation: Participant-level accrual data should not be public

---

- Releasing participant-level accrual data could violate informed consent agreements
- Even if de-identified, participant-level data includes demographic elements which could result in identification of individuals in certain circumstances
- Subsets of participant-level data might be made available by NCI to researchers for approved research purposes

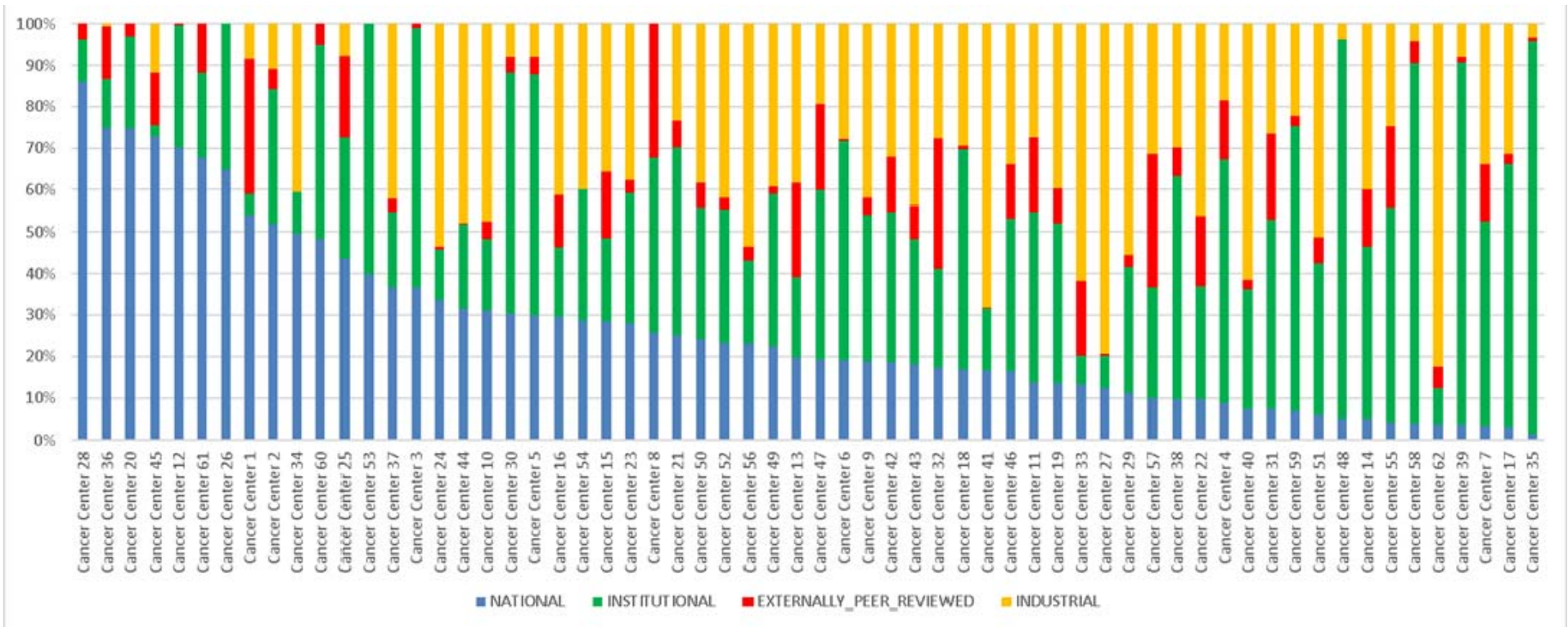
## Recommendation:

### Aggregate accrual data should be public under certain conditions

---

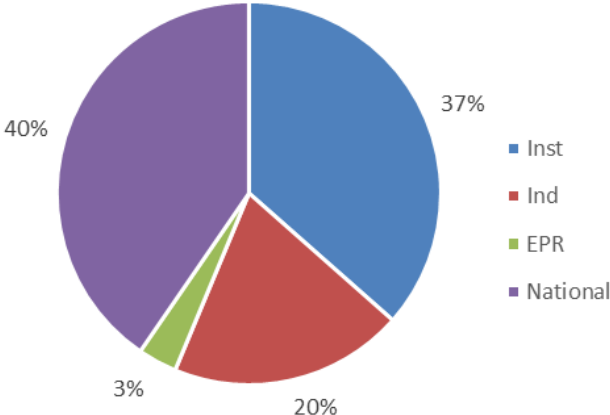
- Availability enables accrual analyses by disease, trial phase, primary purpose, Study Source, Cancer Center, etc.
- Conditions for public availability of aggregate data:
  - Actively accruing and closed national, externally peer-reviewed and institutional trials
  - Industrial trials only after study closure and results are posted on ClinicalTrials.gov
  - Lead investigators for externally peer-reviewed and institutional trials may, due to contractual requirements, request that aggregate accrual data be available only after study closure and when trial results are posted on ClinicalTrials.gov

## Distribution of Aggregate Accrual Across DT4 Study Source, by Cancer Center In Descending Order of Proportion of Accrual Devoted to National Trials



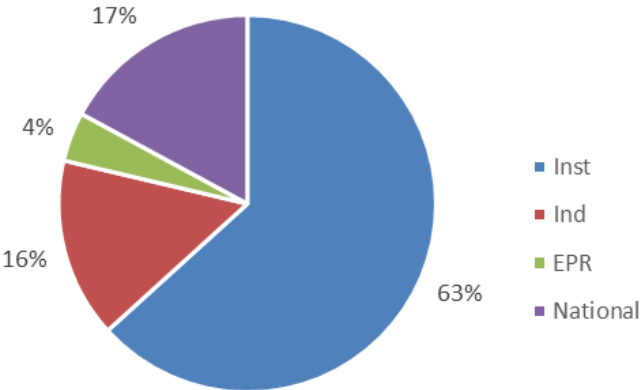
# Trials and Accrual for a Single Center by Study Source

Trial by Study Source - 334 Total



Data Collected - 07/24/17  
Date Range: Jan 1, 2016 - Dec 31, 2016

Accruals\* by Study Source - 3721 Total



Data Collected - 07/24/17  
Date Range: Jan 1, 2016 - Dec 31, 2016 \*Center to date accruals used

## Recommendation: Aggregate accrual data by demography should be public for trials closed to accrual

---

- Enables accrual analyses by gender, age, race, ethnicity and geography for individual trials and for specific diseases
- Enables identification of eligibility criteria and/or other trial characteristics that influence the demographic distribution of accrual
- Essential to implement measures to limit the risk that demographic annotation of aggregate accrual could identify specific individuals (i.e., instances where a small number of individuals have a particular set of demographic characteristics)



## Highlights of CTIWG Recommendations

*Expanding CTRP Data*

## Recommendations on Expansion of CTRP Data - Overview

---

- CTRP **should** collect:
  - Minimal information on observational studies
- CTRP **should not** collect:
  - Information on ancillary/correlative studies at the present time
  - Toxicity and adverse event data
  - Outcomes data



## Recommendation: Observational studies should be reported to CTRP

---

- Supports reporting of observational studies in Cancer Center Support Grant Data Table 4 submissions
- Enhances comprehensiveness of portfolio analyses based on CTRP data
- Promotes awareness of observational studies among investigators and the public
- Reporting requirements should be minimal to limit reporting burden
  - Registration: Data required for DT4 reporting
  - Accrual: Annual accrual count

## Recommendation:

### Ancillary/correlative studies should not be reported to CTRP at this time

---

- Reporting to CTRP would support Data Table 4 submissions
- Working Group raised questions regarding ancillary/correlative studies:
  - Definition of accrual (e.g., participants, specimens, data)
  - Who should report (e.g., Cancer Center conducting study, Cancer Centers contributing data/specimens)
  - Only a subset of ancillary/correlative study activity at a Center is reported, i.e., only those with separate protocol documents
  - Value of ancillary-correlative studies for NCI Cancer Center program staff and reviewers
- CTRP reporting judged premature until these topics are examined

## Recommendation:

### Toxicity/adverse event data should not be reported to CTRP

---

- No centralized NCI collection of real-time serious adverse events (SAEs) for NCI-supported trials, with the exception of those under an NCI IND
- SAEs reported to ClinicalTrials.gov for completed trials
- Disadvantages of CTRP real-time SAE reporting include:
  - Substantially increases CTRP reporting burden for Cancer Centers
  - Creates responsibility for analyzing real-time SAE data for emerging issues

## Recommendation: Outcome data should not be reported to CTRP

---

- CTRP reporting of summary outcome data would duplicate ClinicalTrials.gov outcome reporting
- CTRP reporting of de-identified participant-level outcome data\* would impose too high a burden to justify benefits
- Outcomes data could be requested directly from the investigator per NIH policies on availability of research data and dissemination of NIH-funded clinical trial information

\*De-identified participant-level outcome data for Phase III NCTN and NCORP trials with published results will be reported to the NCTN/NCORP Data Archive



# Highlights of CTIWG Recommendations

*Improving Clinical Trial Search*

## Recommendation: Structure eligibility criteria as feasible

---

- Currently structured eligibility criteria
  - Age
  - Gender
  - Biomarkers
- Prioritize structuring of additional eligibility criteria to enable more precise identification of clinical trials for participants
  - **Clinical Significance:** What is the clinical importance of the attribute or metric captured in the criterion?
  - **Structuring Ease:** How easy is it to structure the criterion across trials?
  - **Frequency:** How many trials list the criterion?
  - **Practicality:** How easy is it for the typical physician or clinical research staff member to determine whether the criterion is met?
  - **Durability:** Is the criterion unlikely to change over time?



## Highlights of CTIWG Recommendations

### *Accruals to Precision Medicine Trials*

## Recommendation: Record screening accruals for precision medicine trials separately from accruals to intervention arms

---

- Screening subjects for a precision medicine trial requires sufficient effort to warrant capturing as a separate accrual in CTRP
- Essential to distinguish between accrual to the screening intervention and accruals to a treatment intervention to avoid double counting participants
- Screening for conformance with general trial eligibility criteria or routine screening for standard of care markers should not be separately reported





## Highlights of CTIWG Recommendations

*Implementation of CTRP-  
Generated DT4 for  
Interventional Trials*

## Recommendation: Implement a phased transition to a CTRP generated DT4 for interventional clinical trials

---

- The CTIWG recommended transition to CTRP for DT4 for:
  - Non-competing CCSG renewal submissions beginning in FY18
  - Competing review submissions beginning in FY19
- Phased implementation provides additional time to:
  - Address 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)
  - Improve the completeness and accuracy of CTRP reporting by Cancer Centers



## Discussion

Questions on any other aspect of the  
Working Group Report?

Motion for Approval of the Report?



**NATIONAL  
CANCER  
INSTITUTE**

[www.cancer.gov](http://www.cancer.gov)

[www.cancer.gov/espanol](http://www.cancer.gov/espanol)