ClinicalTrials.gov Modernization and How to Provide Your Input

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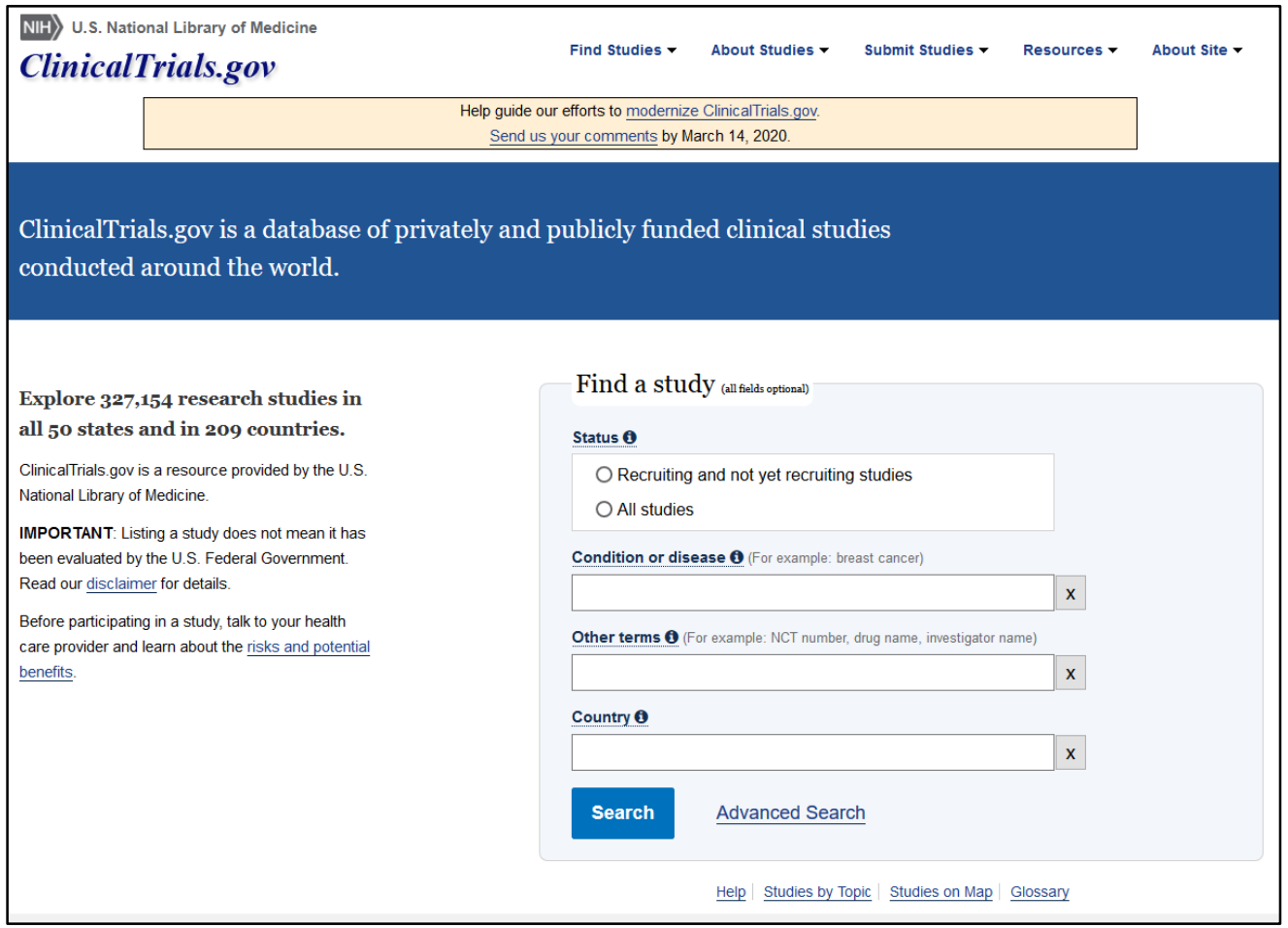
January 22, 2020

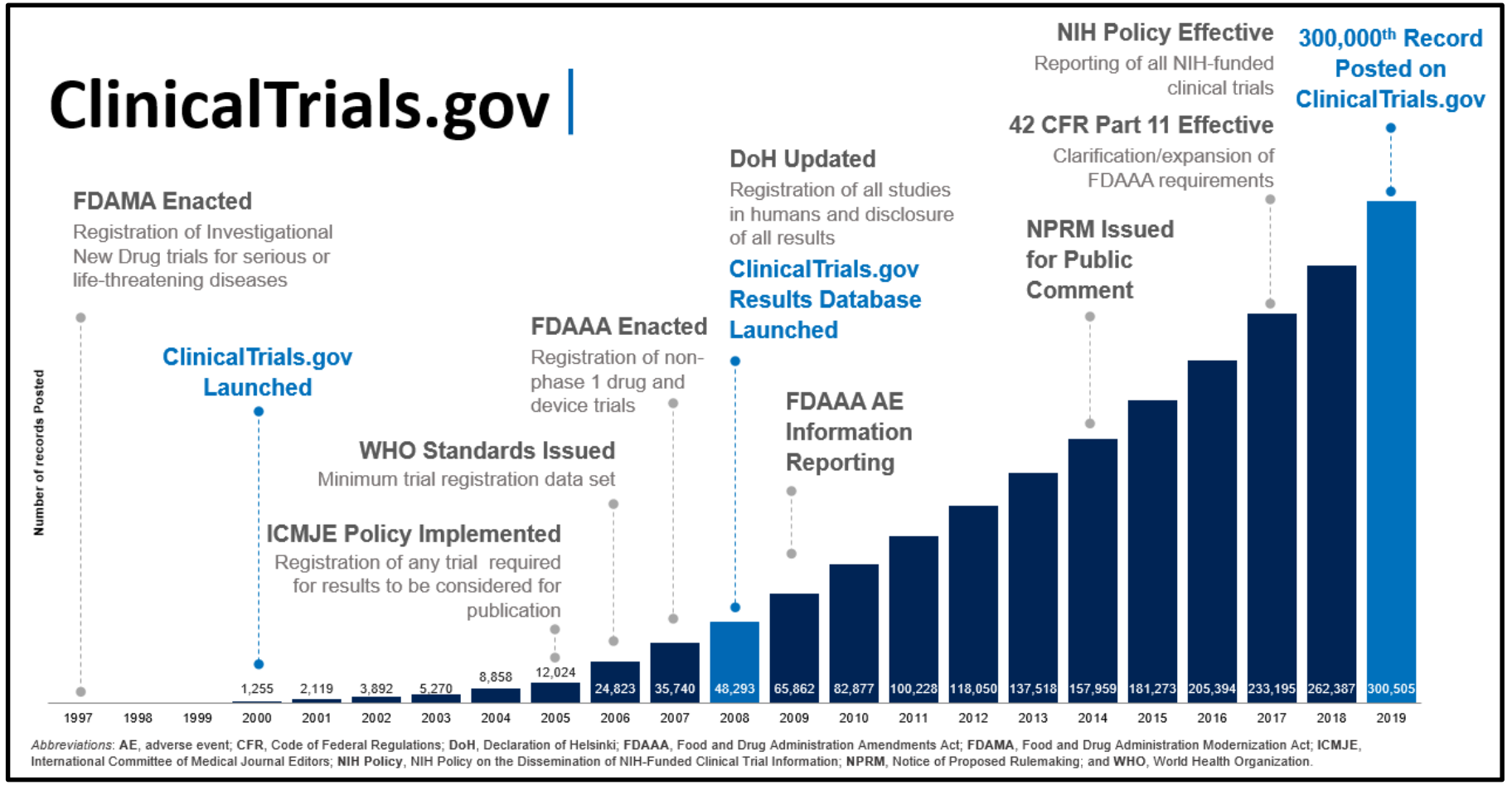
Agenda

- ClinicalTrials.gov Background
- Modernization Overview
- Request for Information (RFI)
- Provide Your Input



Overview

- 320,000+ registrations
- 40,000+ posted results
- 145,000 unique visitors daily
- 215 million page views per month



Benefits of Comprehensive Registration and Results Reporting

All contribute to increased public trust in clinical research

- Honor commitment to participants that their contributions will advance science; support enrollment
- Mitigate publication bias
- Advance stewardship and accountability
  - Identify unmet research needs
  - Facilitate complete reporting
  - Avoid unnecessary study duplication
  - Evaluate research integrity
- Support evidence-based medicine

ClinicalTrials.gov Modernization

Ensure ClinicalTrials.gov continues to be a trusted and valued premier public health resource that provides maximum value to the public and serves its mission well into the future.

Aim 1: Collect complete and informative information about clinical studies

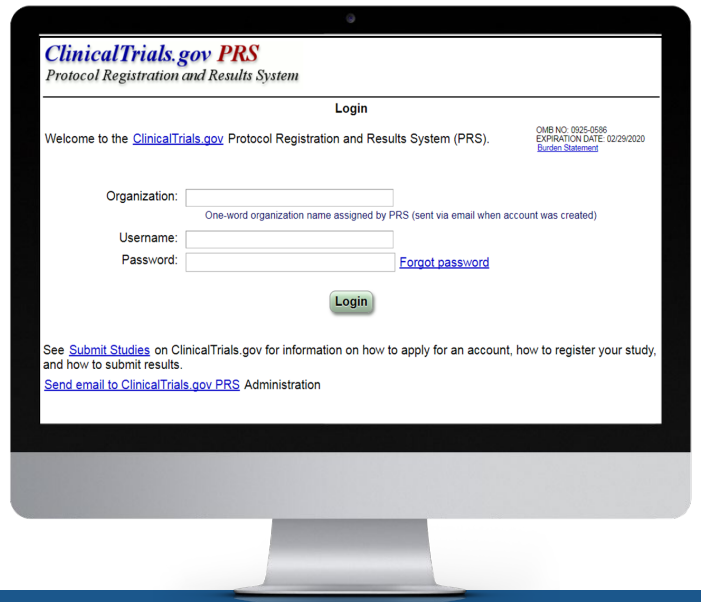
Create new study record

Submit study record

Backend Processing (NCT Number Assigned)

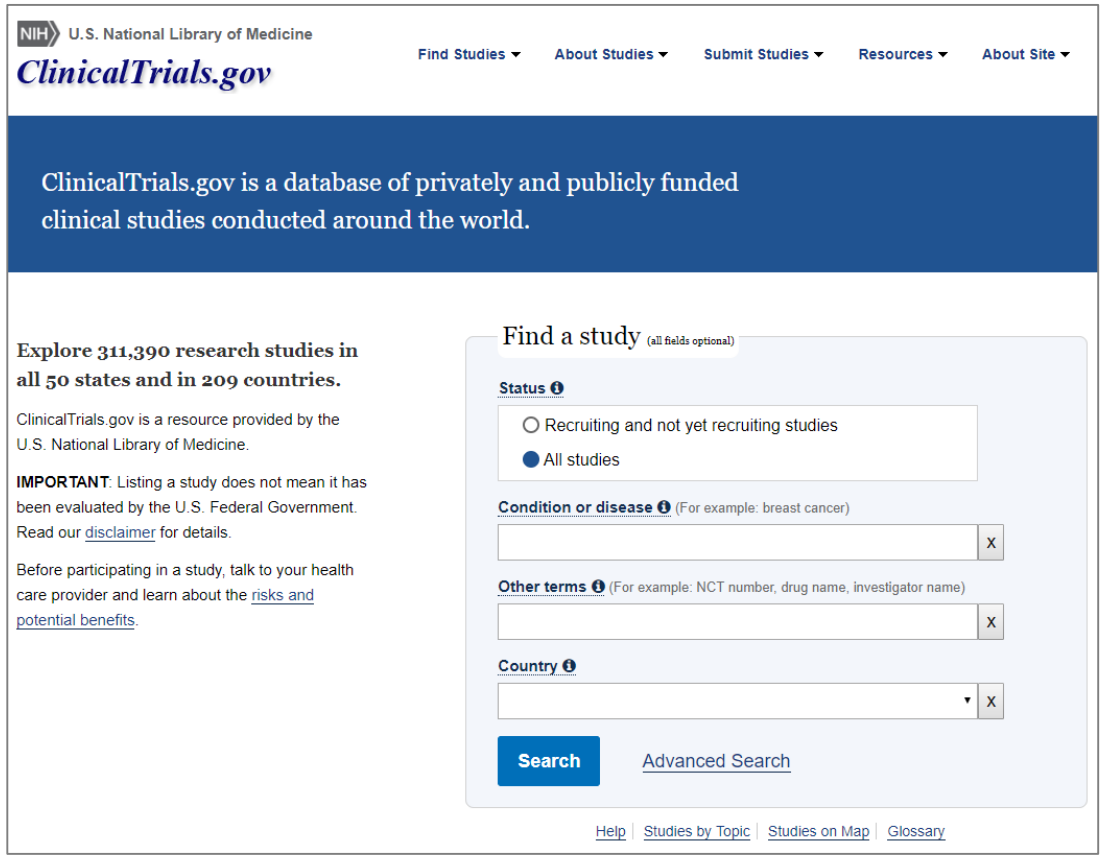
1 **Sponsor Account** → 2 Registration Information → 3 **Manual Validation – Quality Control Review** → 4 **Public Posting**

Automated Validation



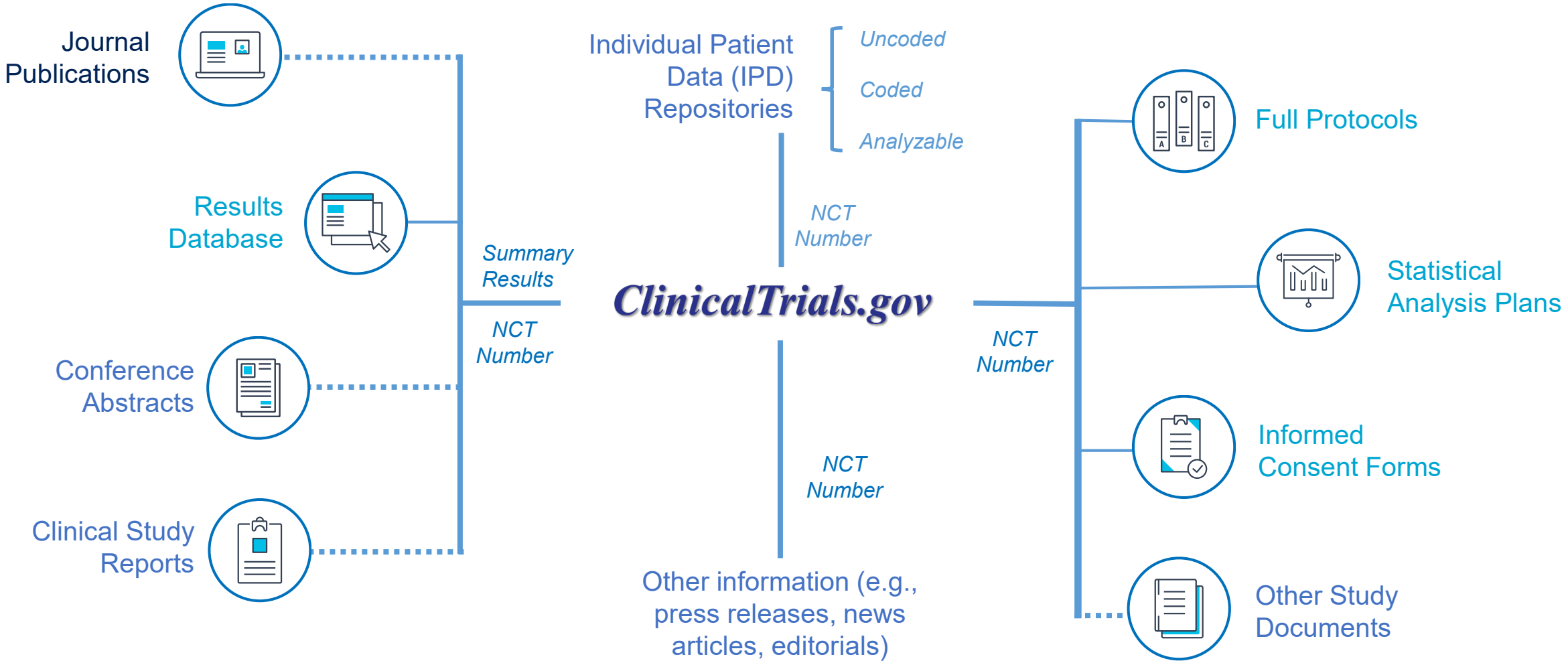
ClinicalTrials.gov

Aim 2: Facilitate use of information to help the public and researchers find studies of interest



ClinicalTrials.gov API

ClinicalTrials.gov: Information Scaffold

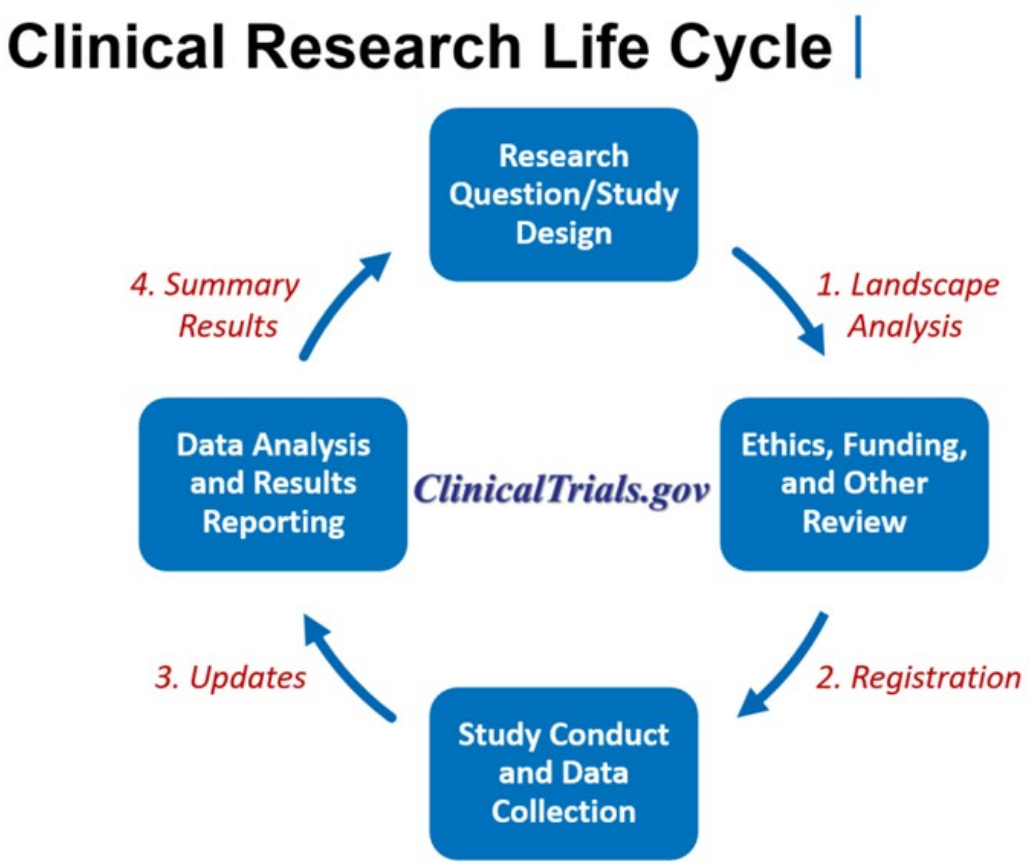


ClinicalTrials.gov Key Roles and Principles

- Sponsor or investigator
  - Submits study information directly to ClinicalTrials.gov; keeps up-to-date
  - Responsible for safety and validity of study and following applicable laws and regulations
- NLM conducts a limited quality control (QC) review
  - Identifying apparent errors, deficiencies, or inconsistencies
  - Listing does not mean study itself has been evaluated by U.S. government
- Site lists information for many uses, including research participation
  - Participation is an important personal decision; encourage learning about all options and consulting with health care provider and other trusted advisors

Source: Disclaimer https://clinicaltrials.gov/ct2/about-site/disclaimer

ClinicalTrials.gov Modernization Overview



Current year: Engagement

- Engage with stakeholders to determine and validate approach and specifications
  - Request for Information (RFI) and Public Meeting
- Develop modernization roadmap
- Enhance internal business processes

Future (years 2 – 5): Implementation

- Implement modernization roadmap
  - User testing/evaluation and continue engagement
  - Improvements to support compatibility across clinical trial lifecycle (seamless end-to-end process)
  - Upgrade system infrastructure components

Request for Information (RFI): ClinicalTrials.gov Modernization

Notice Number:
NOT-LM-20-003

Key Dates

Release Date:
December 30, 2019

Response Date:
March 14, 2020

Related Announcements

None

Issued by

National Library of Medicine (NLM)

Purpose

Introduction

The purpose of this Request for Information is to solicit public input to guide the National Library of Medicine (NLM) in planning infrastructure enhancements aimed at users and submitters of ClinicalTrials.gov as part of a multi-year modernization initiative.

Request for Information (RFI)

- *"… we aim to gather information to help maximize the value of ClinicalTrials.gov to its many users, while continuing to provide essential services to support existing legal and policy requirements."*

- **March 14 – responses due**

https://grants.nih.gov/grants/guide/notice-files/NOT-LM-20-003.html

We Request Your Input on These Topics

1. Website functionality
2. Information submission
3. Data standards

<u>Note</u>: RFI not intended to modify existing legal and policy requirements for clinical trial registration and results submission

1. Provide Your Input: Website Functionality

a. Uses that are not currently supported and examples of other good models
b. Resources that should be linked from ClinicalTrials.gov and explanation of why such resources are useful
c. Examples of how you currently use site, what features work well, and what could be improved
d. Describe whether uses are dependent on wide range of studies or more limited and explain any limiting criteria that are useful to you

ClinicalTrials.gov Users by Role

42% Patients and Caregivers, including:

- 24% Patient
- 8% Family/friend of patient
- 5% Healthcare provider
- 5% Healthy person

9% Not Categorized ("Other")

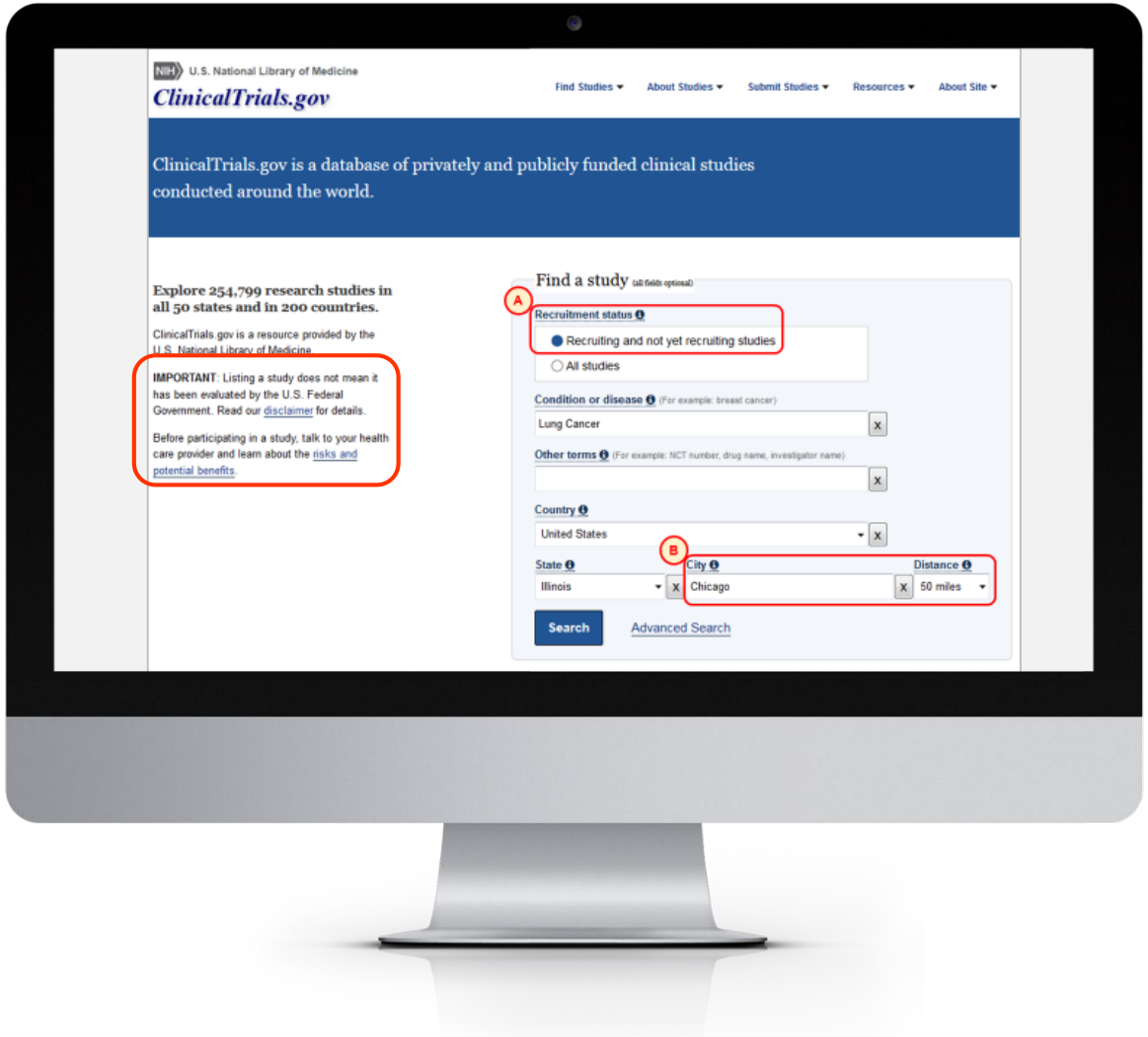
49% Researchers and Others, including:

- 26% Scientist/researcher
- 8% Clinical research support (e.g., regulatory affairs)
- 6% Clinical trials staff
- 5% Student/educator
- 3% Medical communications
- 2% Librarian or information professional
- <1% IRB or ethics committee member

Source: ClinicalTrials.gov Qualtrics Survey Data: 1 July 2019 – 31 December 2019 (n=3,399)

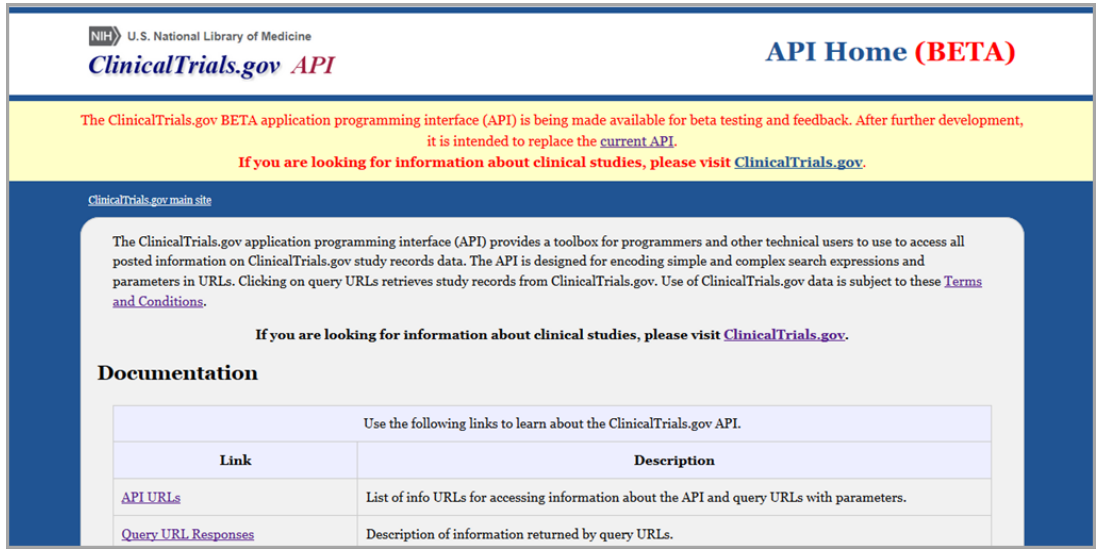
Recent Website Updates

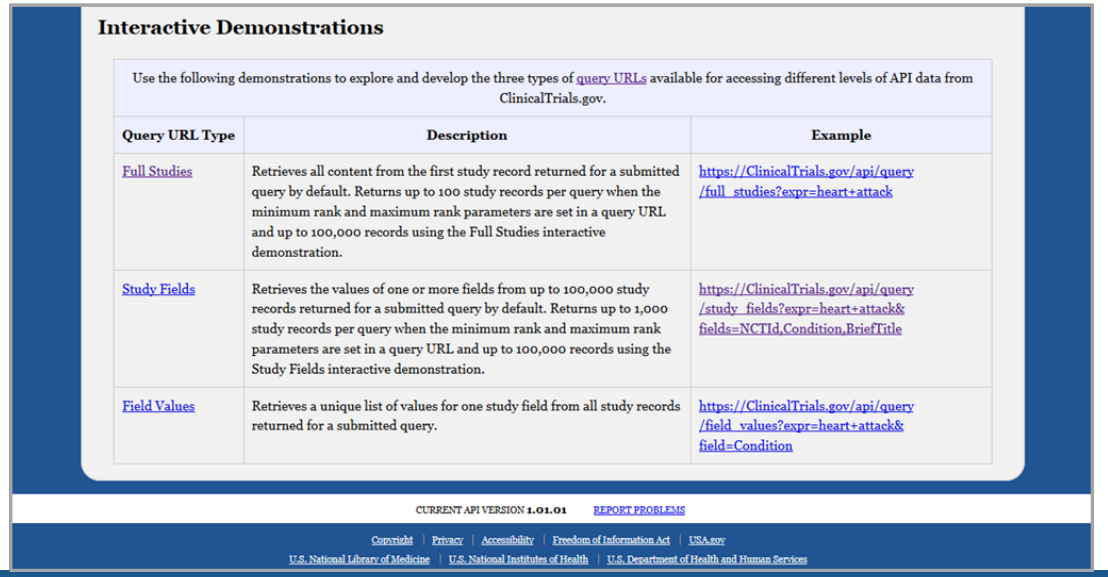
- Options to improve first search precision
  - A. Recruitment status
  - B. Location
- Research participation resources and disclaimer
  - Help people learn what ClinicalTrials.gov listing does and doesn't mean
- Search results options; filters and custom display



Beta API (Application Programming Interface)

- Supports 3rd party electronic use of ClinicalTrials.gov content
- Over 300 search fields available (current API has 24 key fields)
- Formats: XML, JSON, SVI, tree
- Query and Info URLs
- Documentation and interactive training demos
- https://clinicaltrials.gov/api/gui



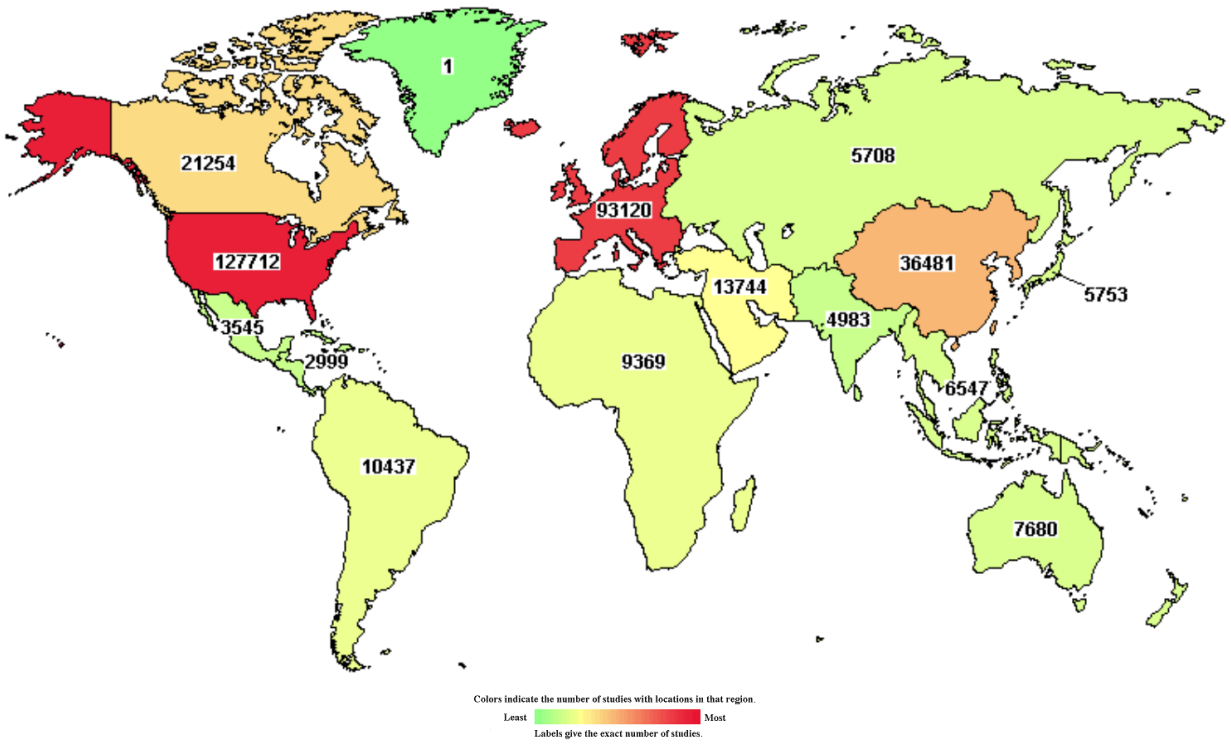


Content of ClinicalTrials.gov (as of Jan 10, 2020)

Study and Intervention Type		Number Registered Studies (% Total)	No. Studies with Posted Results (% Total) ***
Total Records		**326,612**	**40,841**
Interventional Studies		**257,482 (79%)**	**38,361 (94%)**
Type of Intervention*	Drug or biologic	144,503	29,807
	Behavioral, other	83,013	7,279
	Surgical procedure	27,089	2,068
	Device**	32,977	5,063
Observational Studies		**67,671 (21%)**	**2,480 (6%)**
Expanded Access		**603**	**N/A**

*A study may include more than one type of intervention, meaning that a single study may be counted more than once.
**A total of 856 applicable device clinical trials have been submitted as "delayed posting" under FDAAA/Part 11 (i.e., in “lockbox”) and are not included in the counts of trials.
***Results are required to be submitted only for certain studies.
Source: ClinicalTrials.gov Trends, Charts, Maps (Jan 10, 2020) https://clinicaltrials.gov/ct2/resources/trends

Location of Registered Studies (as of Jan 10, 2020)



Location of Study Sites	Number Registered Studies (% Total)
United States (U.S.) only	110,661 (34%)
Both U.S. and non-U.S.	17,051 (5%)
Non-U.S. Only	160,085 (49%)
Not provided	38,815 (12%)
Total	326,612 (100%)

Source: ClinicalTrials.gov Trends, Charts, Maps (Jan 10, 2020) https://clinicaltrials.gov/ct2/resources/trends

2. Provide Your Input: Information Submission

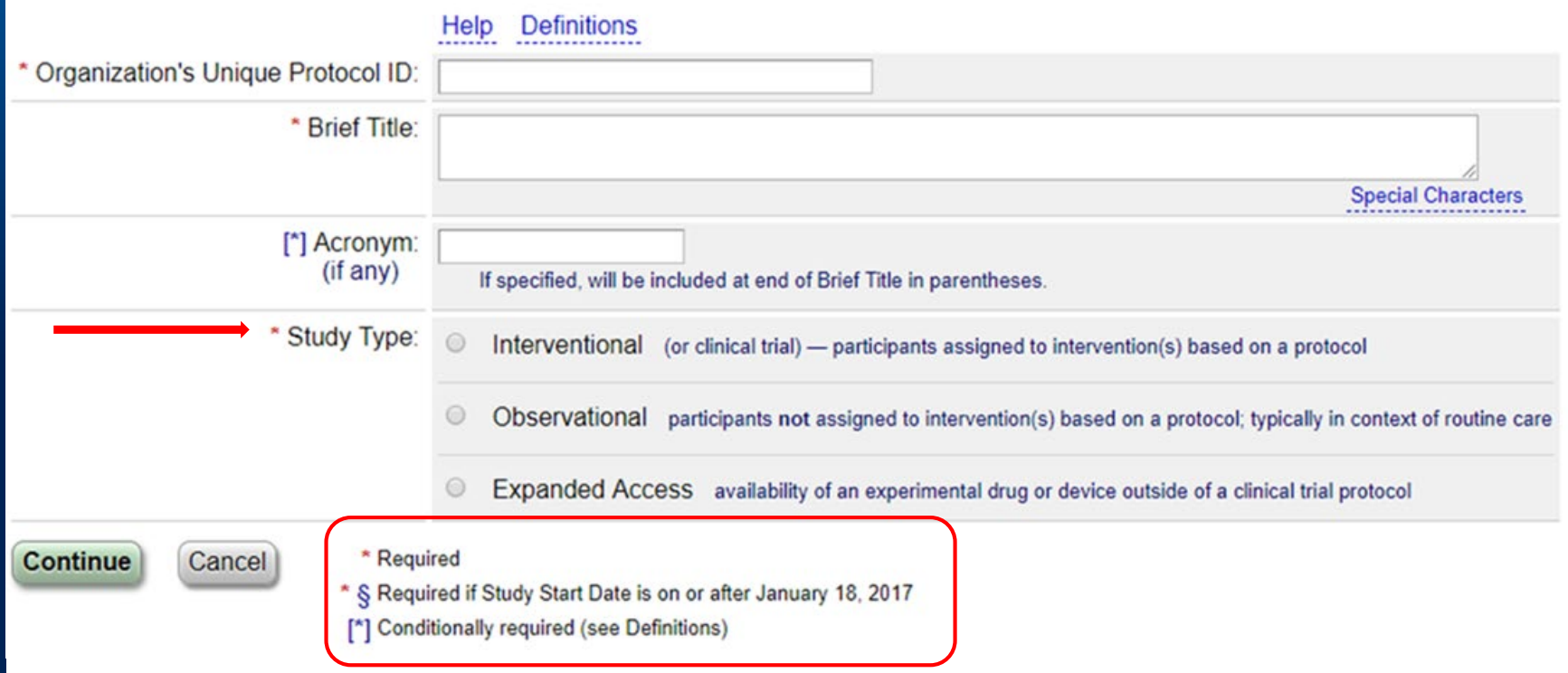
a. Steps in submission process that would most benefit from improvements
b. Opportunities for alignment with organization processes, such as interoperability with clinical trial management software or tools
c. Novel or emerging methods for enhancing quality and submitted content and displayed on ClinicalTrials.gov
d. Informational materials that would make process easier
e. Ways to credit, incentivize, or recognize efforts of individuals and organizations submitting complete, accurate, and timely information

Basics of Registration Information Submission

ClinicalTrials.gov PRS

Protocol Registration and Results System

- Interactive data entry or automated upload
- Anyone can enter data, but "responsible party" must submit
- Content reflects:
  - Legal requirements
  - International standards
  - Good reporting practices
- NIH grant application aligns with subset of content

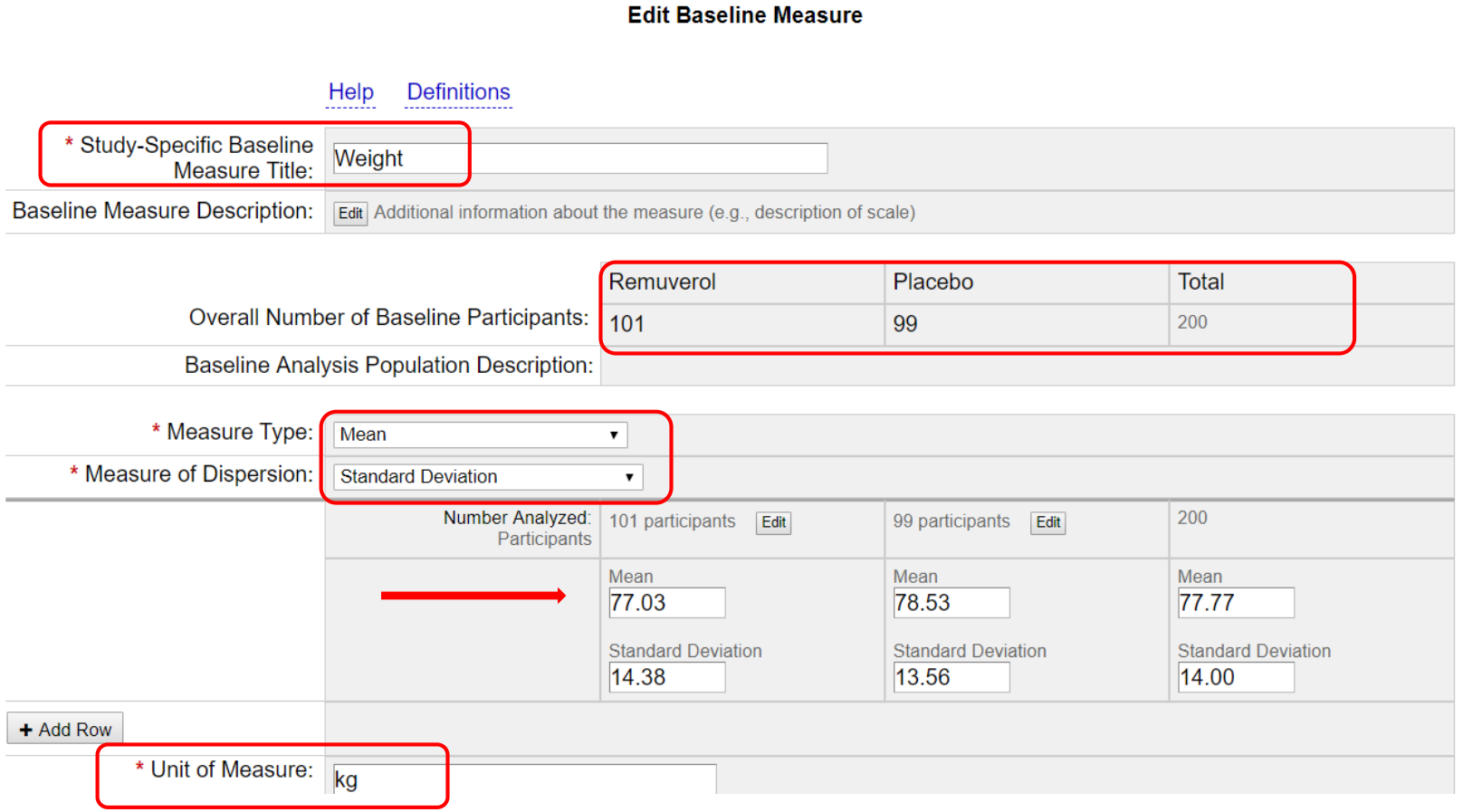


Basics of Results Information Submission

ClinicalTrials.gov PRS

Protocol Registration and Results System

- Structure supports:
  - Complete reporting
  - Efficient quality review
  - Consistent data display
  - Detailed search and integration of other NLM resources
- Aligns with good reporting practices (CONSORT)



Quality Control Review Process and Volume

- Quality control review focused on identifying apparent errors, deficiencies, or inconsistencies
- Review all registration study records < 5 days
  - ~1,200 new registration records per week (includes new records and previously reviewed records that did not meet QC review criteria)
  - ~6,600 updated registration records per week
- Review all results study records < 25 days
  - ~280 new results records per week (includes new records and previously reviewed records that did not meet QC review criteria)
  - ~140 updated results records per week

Quality Control Review Example

Baseline Measures – Example

	Drug X
GOG Performance Status [units: participants]	
0	48
1	27
2	4

Baseline Measures – Example Corrected

	Drug X
Gynecological Oncology Group (GOG) Performance Status [units: participants]	
0 – Fully Active	48
1 – Restricted Strenuous Activity, Ambulatory	27
2 – Ambulatory, Difficulty Walking	4
3 – Limited Self-Care, Partly Confined to Bed	0
4 – Completely Disabled, No Self-Care	0

5-point, ordinal scale specifying patient's ability to perform activities from 0 (fully active) to 4 (completely disabled, no self-care)

Results Submission "Success:" Industry and Non-Industry Orgs

Sample: initial results submitted ≥ 1 May 2017 and QC reviewed ≤ 30 Sept 2018

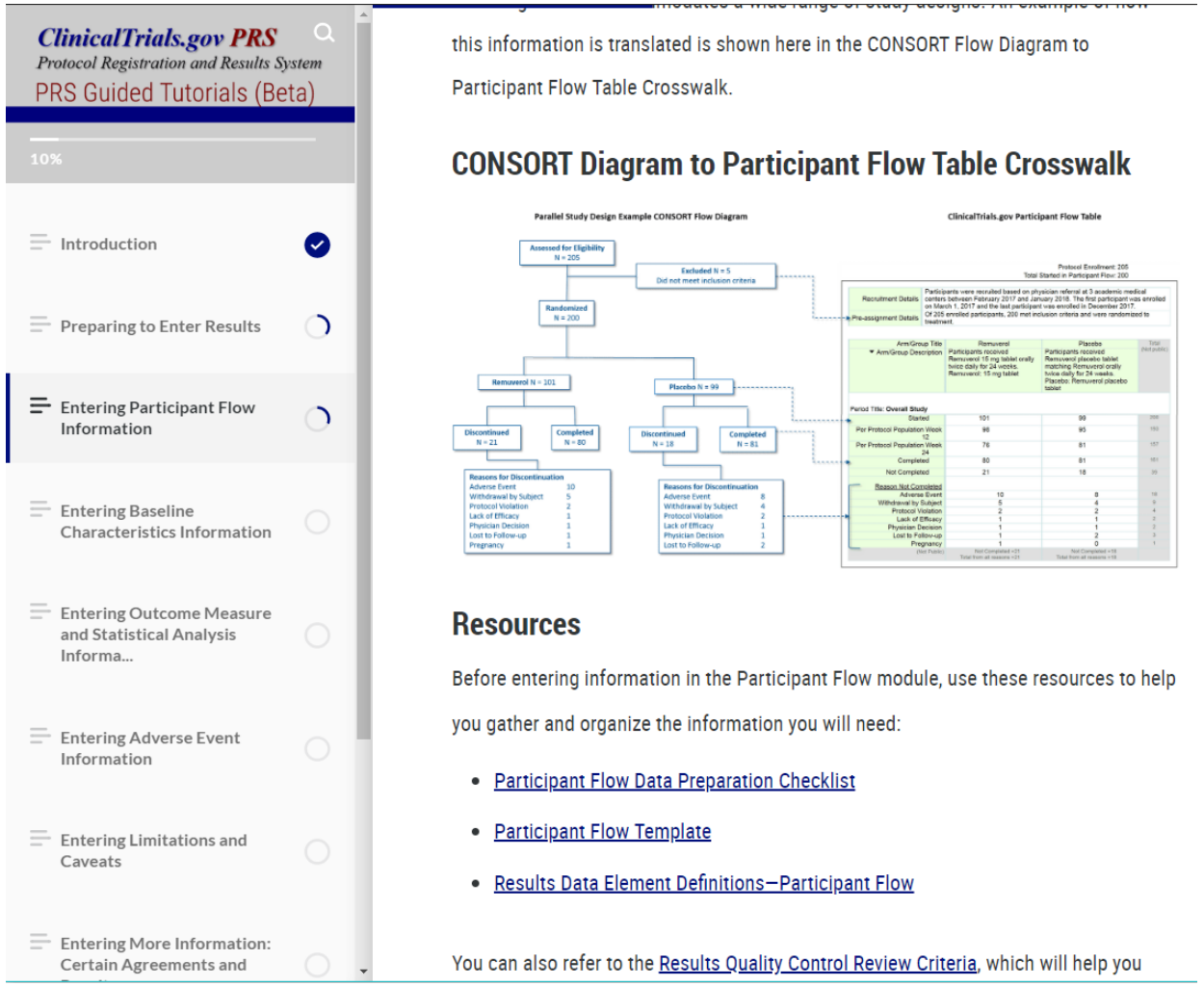
		Cycle 1		Cycle 2	
Org Type	**# Orgs**	**#Records**	**% Success**	**#Records**	**% Success**
Industry	572	2780	31	2140	77
Non-Industry	777	3486	17	2359	63
All	1349	6266	23	4499	70

Source: N Engl J Med 2019; 381:1966-74. DOI: 10.1056/NEJMsr1907644

$$\%Success = 100\% \times \frac{\#\ Records\ with\ no\ Major\ Issues}{\#\ Total\ Record\ Submissions}$$

PRS Guided Tutorials

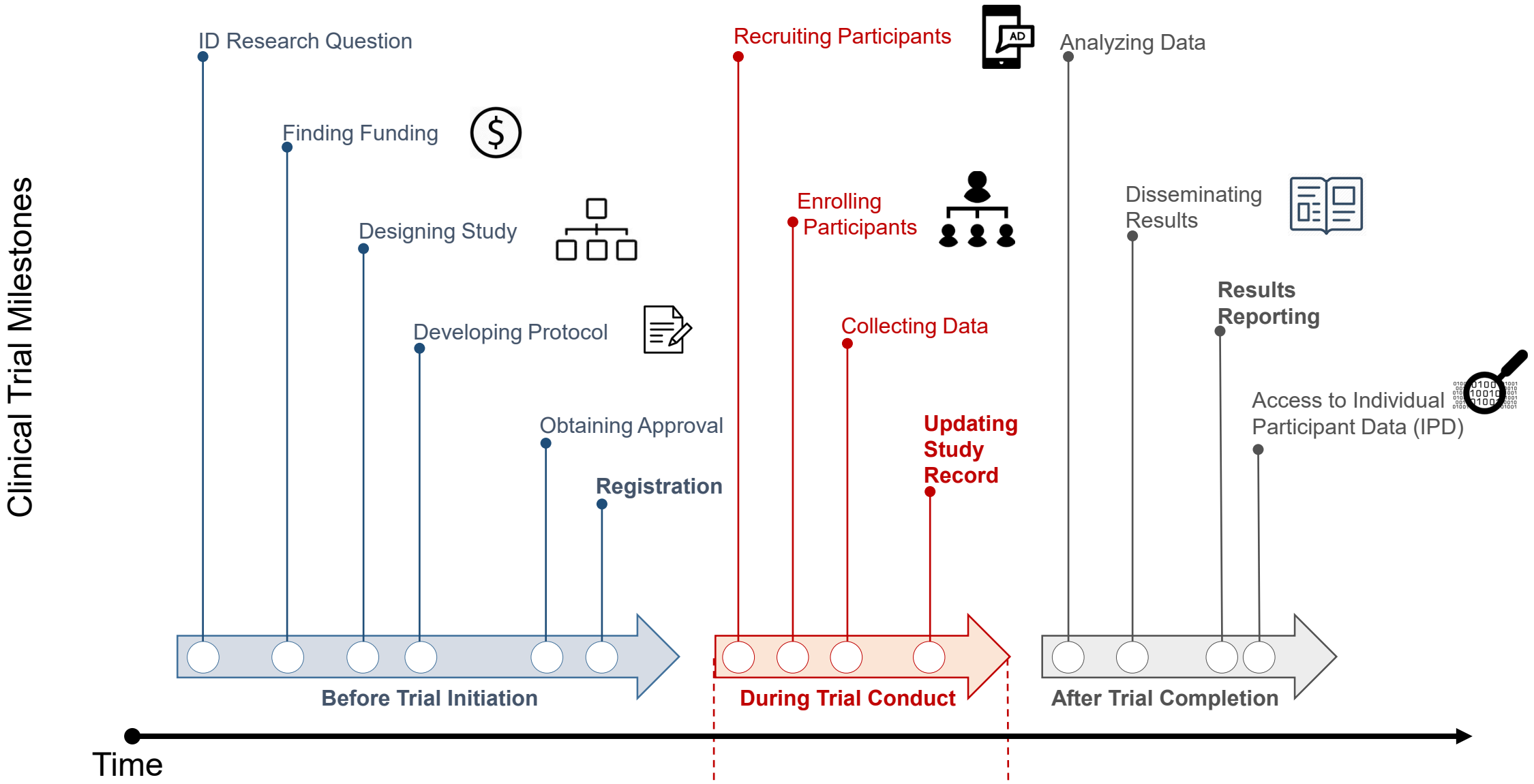
- Launched August 2019
- Access on ClinicalTrials.gov or PRS
- Results submission content first
  - Registration content expected in early 2020
- Collecting feedback via survey
  - https://bit.ly/2N1mMHV
  - Further evaluation planned



3. Provide Your Input: Data Standards

a. Input on ways to balance use of standards while also retaining flexibility to accurately reflect content of study protocol and statistical analysis plan
b. Name specific standards and explain how they may be useful in improving data quality, enabling reuse of data to reduce reporting burden, or improving consistency and management of data on ClinicalTrials.gov

Clinical Trial Lifecycle Opportunities



Submitting Feedback

- “The Insider’s Guide to Effective Commenting on NIH Policies” (from the NIH Office of Science Policy)
  - Be specific
  - Provide data
  - Answer the questions
  - Include new ideas
  - Emphasize what matters most
- Reference: https://osp.od.nih.gov/2018/06/08/insides-guide-effective-commenting-nih-policies/

Submitting Feedback - Reminders

- **March 14, 2020** is the deadline for submitting feedback using web-based form accessible from the RFI:
  - https://grants.nih.gov/grants/guide/notice-files/NOT-LM-20-003.html
- Submitted responses will be posted publicly without change after the close of the comment period.
  - Do not include proprietary, classified, confidential, or sensitive information
  - Do not include personally identifiable information you do not wish to be made public
- RFI not intended to modify existing legal and policy requirements for clinical trial registration and results submission

Public Meeting – April 30, 2020

- We will share a summary of the RFI responses and initial interpretation of themes and priorities
- Opportunity for further discussion and clarification of topics
- More details on how to register will be available soon
  - Hosted at the NIH in Bethesda, MD and also available by Webcast

Stay up to date with *Hot Off the PRS!*

- E-mail bulletin
- Provides timely updates for PRS users on new information about the PRS and ClinicalTrials.gov
- Sign up: https://bit.ly/33qcZBb

Having trouble viewing this email? View it as a Web page.

SHARE

What's New?

Welcome to *Hot Off the PRS!*

We are excited to share the first *Hot Off the PRS!* bulletin. We are planning to use the bulletin to provide timely announcements about the Protocol Registration and Results System (PRS), including updates on new features planned for the PRS, 42 CFR Part 11 implementation, and resources for PRS users. We will still continue to post announcements of new features and resources when they are available in the What's New on ClinicalTrials.gov and in the PRS. We hope you find *Hot Off the PRS!* to be a valuable resource for staying informed.

Note: This bulletin replaced the NIH FDAAA Update listserv on Aug. 1, 2019.

Resources

Parallel Study Design Example Has Been Updated

The Example Studies for Results Data Entry are example study records and study papers that are useful for understanding key concepts for results data entry in the PRS. The Parallel Study Design example has been updated for consistency with the data elements and content in the Final Rule for Clinical Trials Registration and Results Information Submission (42 CFR Part 11). The example also now reflects

Thank You

Questions? Submit to the ClinicalTrials.gov Information Team
National Library of Medicine
register@clinicaltrials.gov

ClinicalTrials.gov Modernization Information

https://clinicaltrials.gov/ct2/about-site/modernization

A recording of this presentation will be posted within 7 days.