ClinicalTrials.gov Modernization Update

Webinar Moderator - Anna M. Fine, PharmD, MS
Assistant Director, ClinicalTrials.gov

The webinar is being recorded and the recording will be made available with the slides.

Submit questions through the Q&A box and we'll try to answer them at the end of presentation.

ClinicalTrials.gov Modernization Update

Rebecca J. Williams, PharmD, MPH, Acting Director ClinicalTrials.gov

Webinar

February 18, 2021

National Library of Medicine

Webinar Goals

- Provide brief program updates
- Reflect on modernization progress to-date
- Provide insights into less visible modernization-related activities
- Share general expectations for what is ahead

Audience Warm-up Poll

What time zone are you joining from today?

- ET (Eastern Time)
- CT (Central Time)
- MT (Mountain Time)
- PT (Pacific Time)
- GMT (Greenwich Mean Time)
- CET (Central European Time)
- Other

Program Updates

ClinicalTrials.gov and COVID-19 Information

- Serves as centralized resource for COVID-19 clinical research
  - Over **4,750 COVID-19–related study records** on ClinicalTrials.gov as of Feb. 12, 2021
  - Plus **3,600 COVID-19–related studies** from World Health Organization (WHO) portal
- Provides rapid dissemination of COVID-19 studies and results information
  - Registration information processed within 2 business days
  - Expedited results review, within 7 days, and one-on-one assistance available
- Added COVID-19 research "views" by location, funder, and vaccine/drug
  - Beta: https://clinicaltrials.gov/ct2/covid_view
- Posted "Responses to Top Questions from Responsible Parties Related to Coronavirus (COVID-19)" in April 2020
  - See: https://prsinfo.clinicaltrials.gov/TopQuestionsFromResponsibleParties-Covid19.pdf

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

NIH Director's Statement
November 10, 2020

NIH calls on clinical researchers to swiftly share COVID-19 results

NIH is taking an all-hands-on-deck approach to speeding life-saving research for vaccines, treatments, and diagnostic tests to end the COVID-19 pandemic. Through the establishment of major public-private initiatives such as the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) and the Rapid Acceleration of Diagostics (RADx) initiatives, NIH and its partners have launched dozens of COVID-19 vaccine and treatment clinical trials and funded dozens of new and innovative testing technologies at an unprecedented rate.

To maintain this record pace, it will be crucial for clinical researchers involved in COVID-19 and SARS-CoV-2 clinical trials to share their results as swiftly as possible. Toward this end, I strongly encourage the clinical research community to register their clinical trials and submit summary results information for COVID-19 and SARS-CoV-2 trials as quickly as possible and ahead of regulatory and policy deadline requirements to ClinicalTrials.gov, the publicly accessible database operated by NIH's National Library of Medicine.

To ensure such information is accessible as quickly as possible, NIH is prioritizing the processing of COVID-19 submissions to ClinicalTrials.gov to make the information rapidly available in a matter of days, not weeks. We are also providing one-on-one support to researchers during the process of submitting results information to ClinicalTrials.gov to address questions and optimize reporting.

NIH National Library of Medicine

ClinicalTrials.gov

"I strongly encourage the clinical research community to register their clinical trials and submit summary results information for COVID-19 and SARS-CoV-2 trials as quickly as possible and ahead of regulatory and policy deadline requirements to ClinicalTrials.gov, …

- Francis S. Collins, MD, PhD

Audience Question

Have you used ClinicalTrials.gov to look for COVID-19–related information?

- Yes
- No
- I don’t remember

Recent Resources for Data Providers

See ClinicalTrials.gov What's New: https://clinicaltrials.gov/ct2/about-site/new

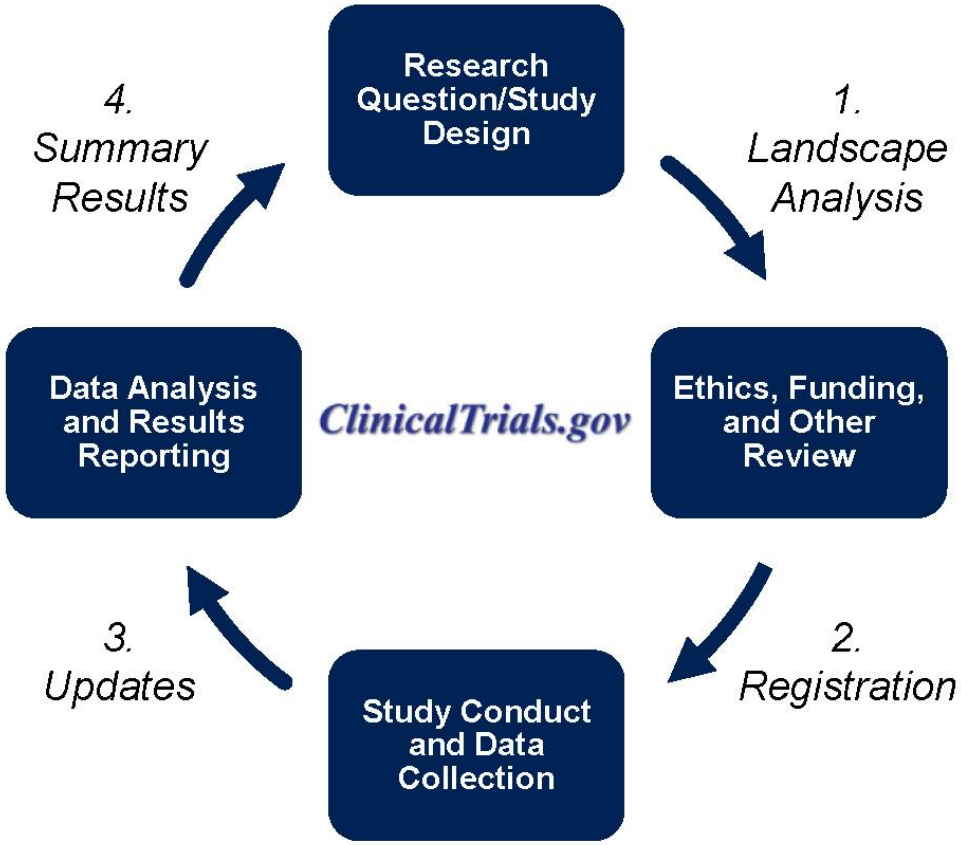
- **New Study Design Examples** – Added fictional study records and manuscripts to illustrate key concepts for reporting behavioral and social science research studies
  - Developed with the NIH Office of Behavioral and Social Sciences Research (OBSSR)
  - Study Types: Cluster Randomized; Fractional Factorial; Micro-Randomized; and Sequential, Multiple Assignment, Randomized Trial
- **42 CFR Part 11 FAQs and Updates**
  - Clarified the deadline for submitting certifications to delay submission of results information (January 2021)
  - Results information submission requirements for applicable clinical trials following the Federal court decision in *Seife et al. v. HHS et al*. (July 2020)
- **BESH Webinar** – Summarized findings and issues to consider from an analysis of challenges in registering and reporting results information for basic experimental studies with humans (BESH) on ClinicalTrials.gov

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.

National Library of Medicine

ClinicalTrials.gov Modernization Overview



Year 1: Engagement

- Engage stakeholders to determine and validate approach and specifications
- Enhance internal business processes
- Develop modernization roadmap

Years 2 – 5: Implementation

- Implement modernization roadmap
  - Conduct user testing/evaluation
  - Continue engaging stakeholders
  - Improve support for compatibility across clinical trial lifecycle
  - Upgrade system infrastructure

ClinicalTrials.gov Modernization: Year 1

Enhanced Infrastructure

- Moved platform to NCBI infrastructure (lift and shift)
- Established agile teams and user-centered design approach
- Completed Google Cloud Platform (GCP) pilot projects
- Initiated build of cloud-based public website

Engaged Stakeholders

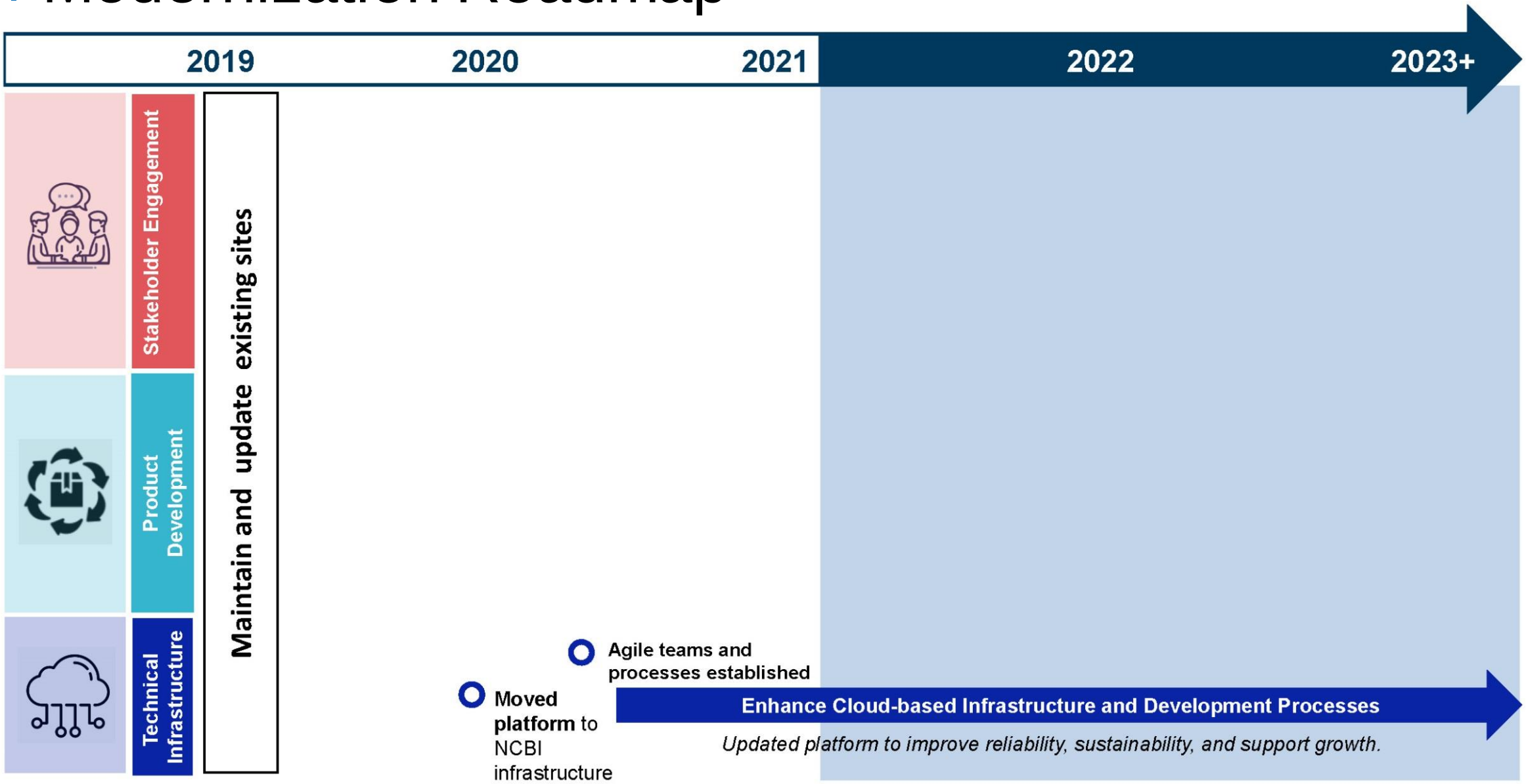
- Held 12 listening sessions with 20 NIH ICs
- Established NLM BOR Working Group – hosted 7 meetings
- Issued RFI, analyzed 268 responses, issued summary report, completed internal report
- Hosted interactive virtual meeting with ~400 attendees

Planned Roadmap

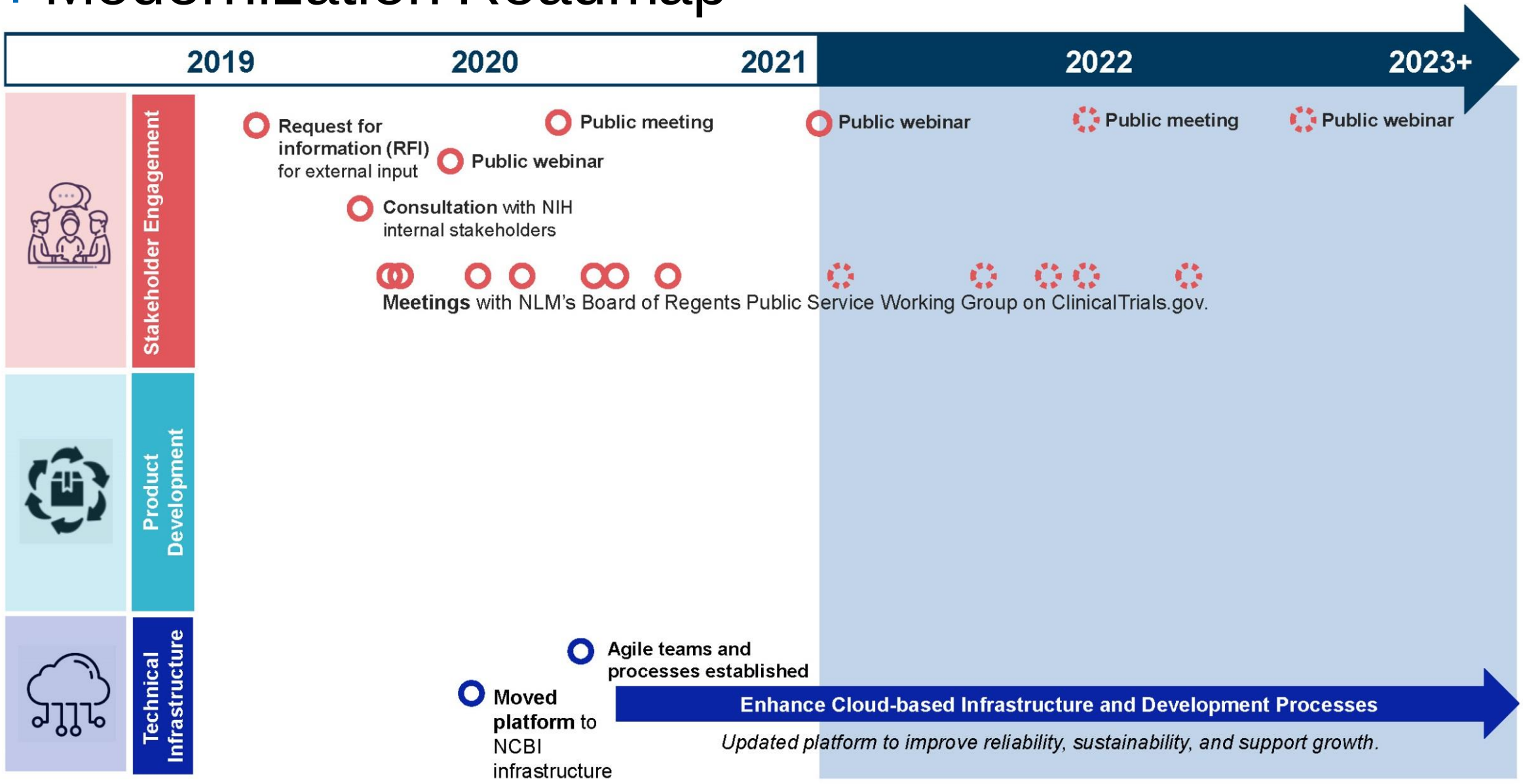
- Organized and synthesized stakeholder comments
- Gathered input from BOR Working Group during facilitated session
- Developed modernization roadmap

Accomplished Year 1 Goals

Modernization Roadmap



Modernization Roadmap



Request for Information (RFI) Topic Areas

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

1. **Website functionality** of ClinicalTrials.gov website and application programming interface (API)
2. **Information submission** using the ClinicalTrials.gov Protocol Registration and Results System (PRS)
3. **Data standards** that may support submission, management, or use of information content

Audience Question

What is your primary use of ClinicalTrials.gov?

- Search for clinical trial information using the ClinicalTrials.gov website (or the API)
- Submit or manage clinical trial information using the PRS
- Both search using the ClinicalTrials.gov website and submit clinical trial information using the PRS
- None of the options

Public Site

Key RFI Response Themes

Search Options and Managing Search Results

Make search more user friendly

Add more options to search

Improve tools for managing search results

Study Record Format and Content

Standardize more content

More prominently display certain content; make more content available

Add features to make using content easier

Plain Language Information

General health information and learning about study participation

Resources for using site features

Study record content

PRS

Key RFI Response Themes

Data Structure and Format

Additional standardization for some data elements

More flexibility for data elements and record structure

Structural support for a variety of study designs

Data Entry, Submission, and Quality Control (QC) Review

More tools to simplify data entry

Additional streamlining of QC review process

Workflow Management

More customizable features to manage workload

Data Standards

Key RFI Response Themes

Balance Between Standards and Flexibility

Apply data standards (e.g., FHIR, CDISC) to facilitate data entry, sharing, reuse, and harmonization across systems

Adhere to FAIR (Findable, Accessible, Interoperable, Reusable) data principles

Retain reporting flexibility for studies using a wide range of designs across research domains and their results

Application of Enabling Technologies

Explore approaches (e.g., natural language processing, machine learning) to improve data quality and reduce reporting burden (e.g., automated mapping to controlled vocabularies)

FHIR = Fast Healthcare Interoperability Resources
CDISC = Clinical Data Interchange Standards Consortium

Virtual Public Meeting

April 30, 2020
9:30 a.m.–12:30 p.m. ET

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- Approximately 400 meeting attendees:
  - 48% Researchers and Related
  - 6% Patients and Caregivers
  - 17% Other
  - 29% Unknown
- RFI response trends and topics summarized by ClinicalTrials.gov staff members
- Members of BOR Working Group presented their perspectives during two panels:
  1. Information Submission to ClinicalTrials.gov
  2. ClinicalTrials.gov Website Functionality
- Over a dozen interactive electronic polling questions to obtain real-time input

NLM Board of Regents Public Service Working Group on ClinicalTrials.gov Modernization

Board of Regents and NIH Members

- Chair: Carlos R. Jaén, MD, PhD, University of Texas Health Science Center at San Antonio
- Executive Secretary: Rebecca (Becky) J. Williams, PharmD, MPH, National Library of Medicine, NIH
- Lourdes Baezconde-Garbanati, PhD, MPH, University of Southern California
- Kent J. DeZee, MD, MPH, FACP, COL, MC, U.S. Army Office of the Surgeon General
- Jennifer (Jennie) S. Lucca, MSW, The Children's Inn at NIH
- *Ex Officio* NIH Members:
  - Lyric A. Jorgenson, PhD, Office of Science Policy
  - Pamela Reed Kearney, MD, Office of Extramural Research

External Members

- Carrie Dykes, PhD, University of Rochester Medical Center
- Alissa Gentile, MSN, RN, Dana-Farber Cancer Institute
- Sally A. Gore, MS, MS LIS, University of Massachusetts Medical School
- Barbara Kress, BSN, RN, Merck
- Seth A. Morgan, MD, National Multiple Sclerosis Society
- Stephen J. Rosenfeld, MD, MBA, Freeport Research Systems, LLC and North Star Review Board
- Joseph S. Ross, MD, MHS, Yale School of Medicine
- Steven Woloshin, MD, The Dartmouth Institute

Summary of Working Group Charge

The NLM Board of Regents Public Service Working Group is charged to explore topics related to ClinicalTrials.gov modernization such as, but not limited to, ways NLM can:

Maintain the *integrity* of ClinicalTrials.gov as a trusted resource

Maximize the *utility* of the growing corpus of information

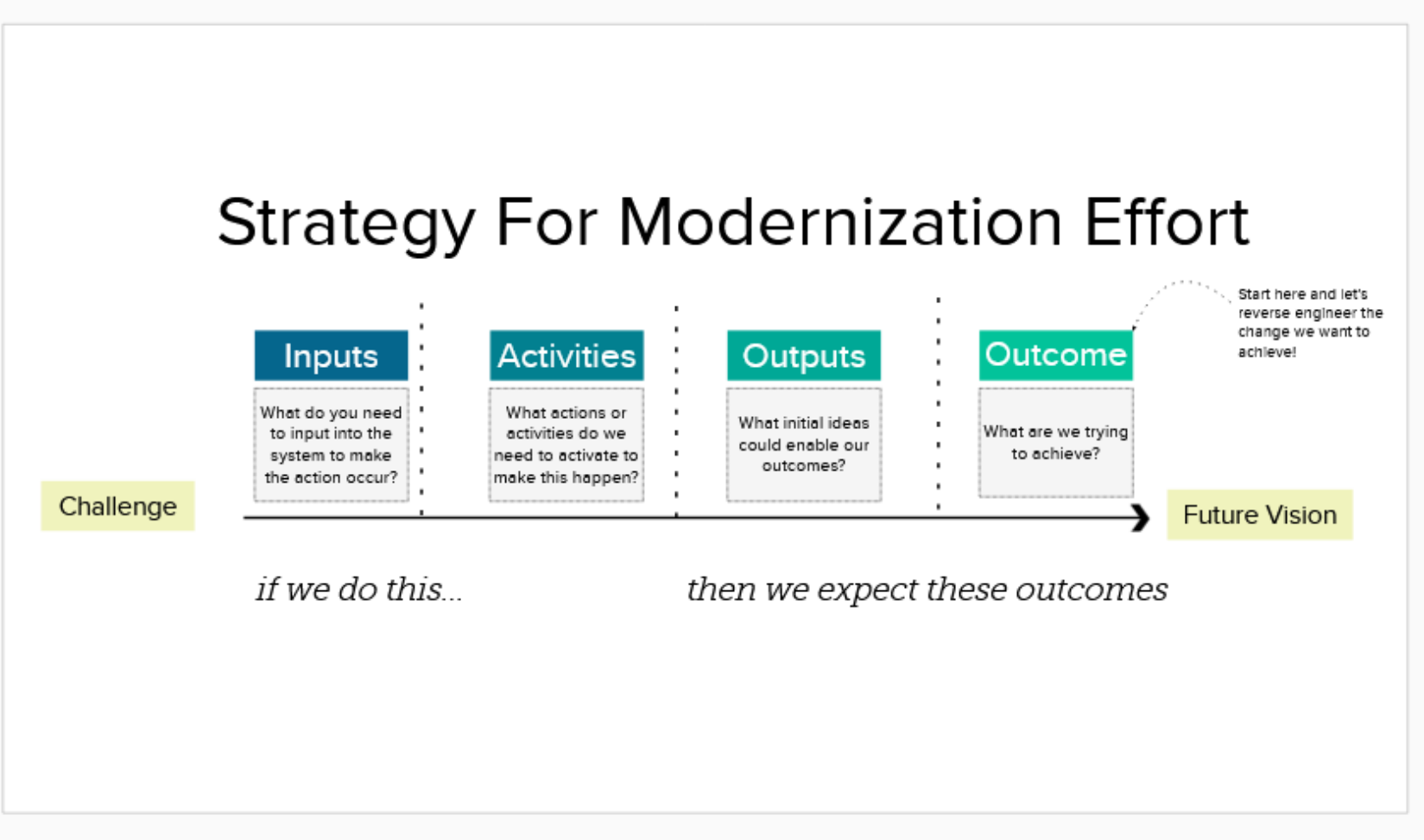
Connect with stakeholders through *engagement* to ensure evolving needs are understood and considered

- Established at Sept. 2019 NLM Board of Regents Meeting
- Kick-off Dec. 2019
- Seven meetings to-date
- Reports in open session to the NLM Board of Regents

Participatory Design Sessions

NLM Board of Regents Working Group

- Sept. - focused on Vision & Outcomes
- Dec. - focused on public site challenges
- Next - focusing on PRS challenges



Key Areas of Discussion

- Importance of NLM's role as a central "data aggregator"
- Clarifying areas where NLM can directly vs. indirectly serve users

Vision and Strategic Goals

Vision

ClinicalTrials.gov serves as an essential, integral, and trusted part of the research ecosystem to advance medical knowledge.

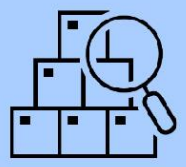
Strategic Goals

1

Clinical trial information is current, complete, and reliable.

2

Anyone can easily find and use information about clinical trials.



3

Trial information, resources, and tools provide value to the research ecosystem.

Vision – Who do we want to impact?

External Stakeholders

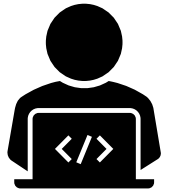
Patients and Advocates

Data Providers

Data Researchers

Internal Stakeholders

Policy and Oversight



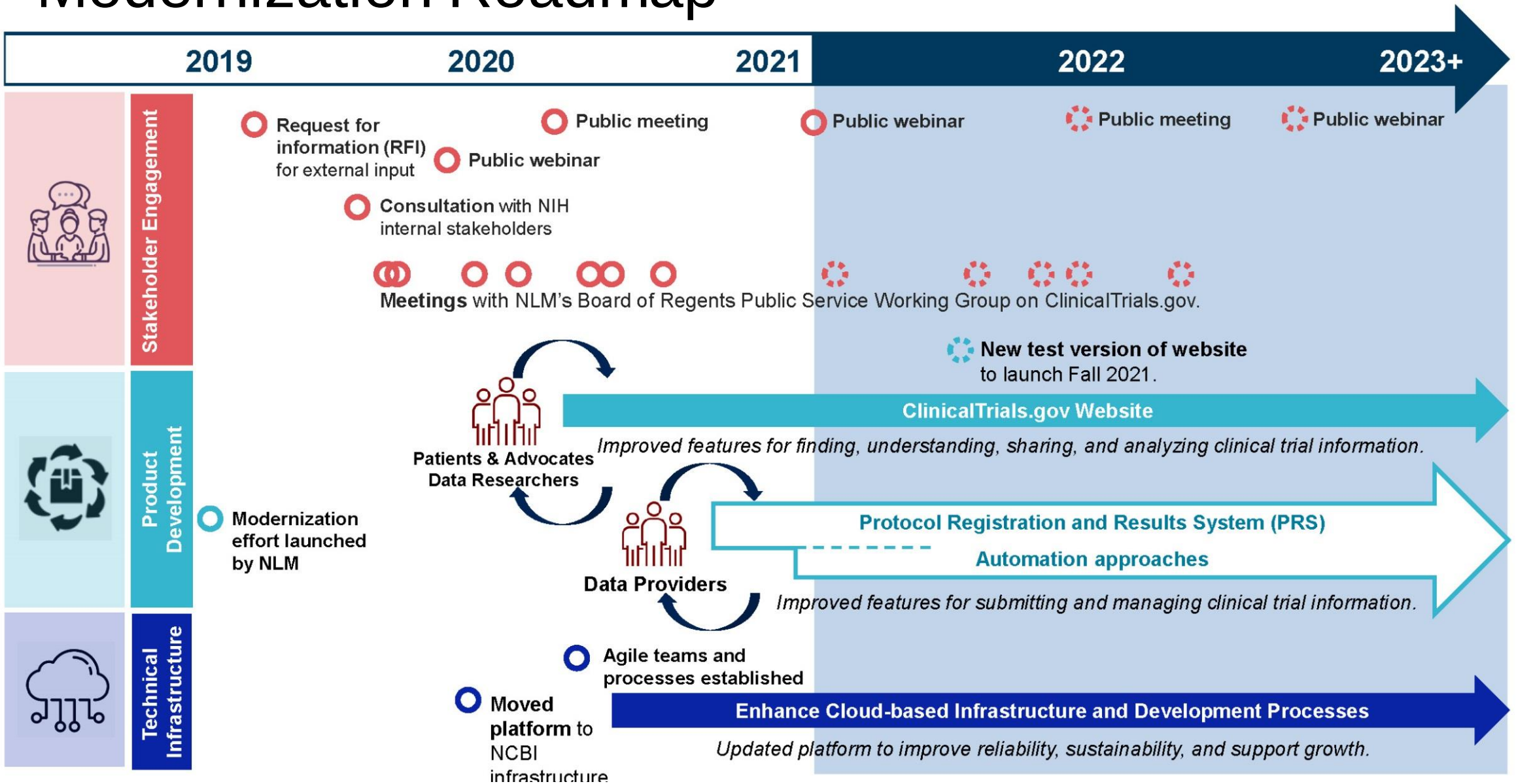
Information Specialists, Reviewers, and Developers

Audience Question

Which user group best describes you?

- Patients and advocates (including health care providers)
- Data providers (PRS Administrators, investigators, sponsors, 3rd party support services)
- Data researchers and journal editors (including systematic reviewers, IRBs)
- None of the above

Modernization Roadmap



User Feedback and Modernization

Why We Are Engaging Users

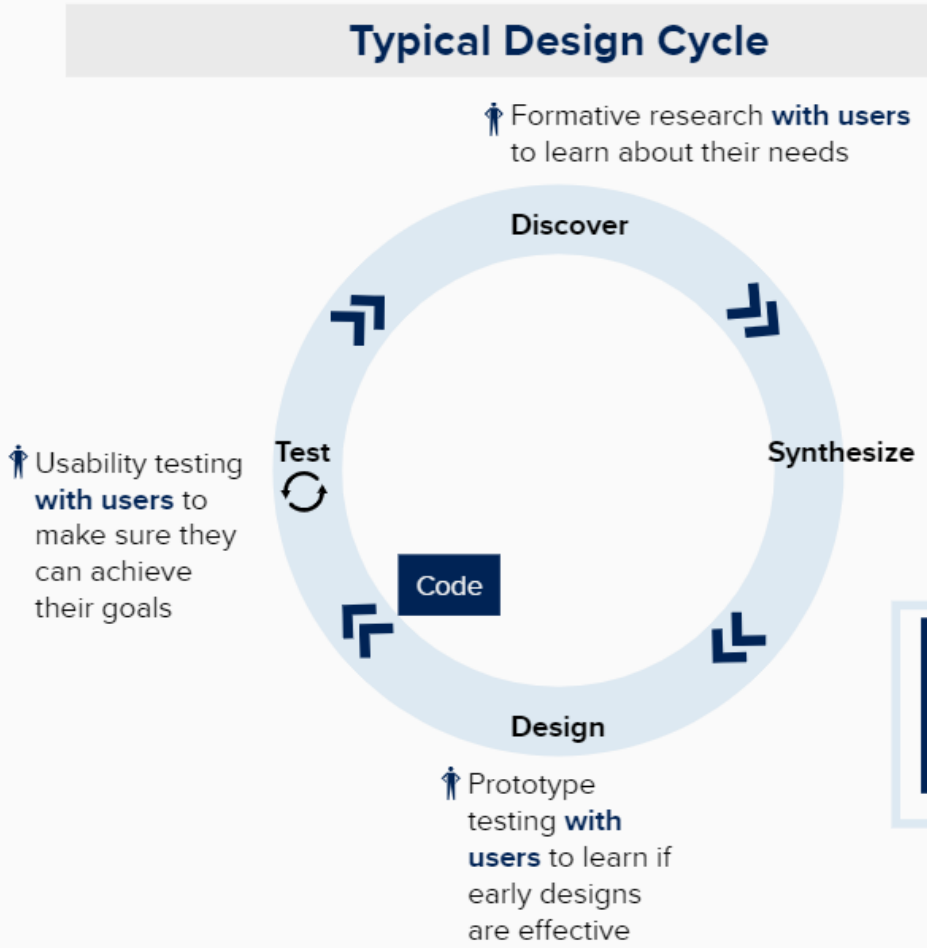
- People with different backgrounds and experience levels use the site for a variety of reasons.
- Designing and developing with real users is critical for better addressing user needs.

How We Are Engaging Users

- Modernization teams are designing and developing content in increments, or sprints.
- Teams will seek feedback from people from specific user groups to try out new features and prototypes during a sprint.
- Teams will use this feedback immediately to build better prototypes.

ClinicalTrials.gov: How User Feedback Fits In

Typical Design Cycle



Agile Design Sprints

The user-centered design cycle is completed in agile sprints.

- Translate user needs into small tasks
- Choose tasks that can be completed in a 2-week sprint
- Start Sprint

Types of User Feedback Sessions

User Interviews

- To understand overall journeys of users and interaction with ClinicalTrials.gov/PRS
- One-on-one interviews, up to 60 minutes
- Users answer questions about goals, motivations, and how they navigate the process

Moderated Usability Testing

- To assess efficacy of preliminary prototypes for ClinicalTrials.gov/PRS
- One-on-one moderated testing sessions, up to 60 minutes
- Users review web prototypes, answer questions, and complete tasks
- Users share computer screen and express comments and concerns while completing tasks (“think aloud”)

Unmoderated Usability Testing

- To gather insights into information architecture, menu structure, and website navigation paths for ClinicalTrials.gov/PRS
- Self-directed testing sessions, up to 60 minutes
- Users review web, tablet, and mobile prototypes

Sign-up to Participate in User Feedback Sessions

Please sign up here:
https://loom.ly/r6DRE50

Identify your interest in participating in the feedback process

Share with your friends and colleagues. Your input is valuable in helping to inform modernization.

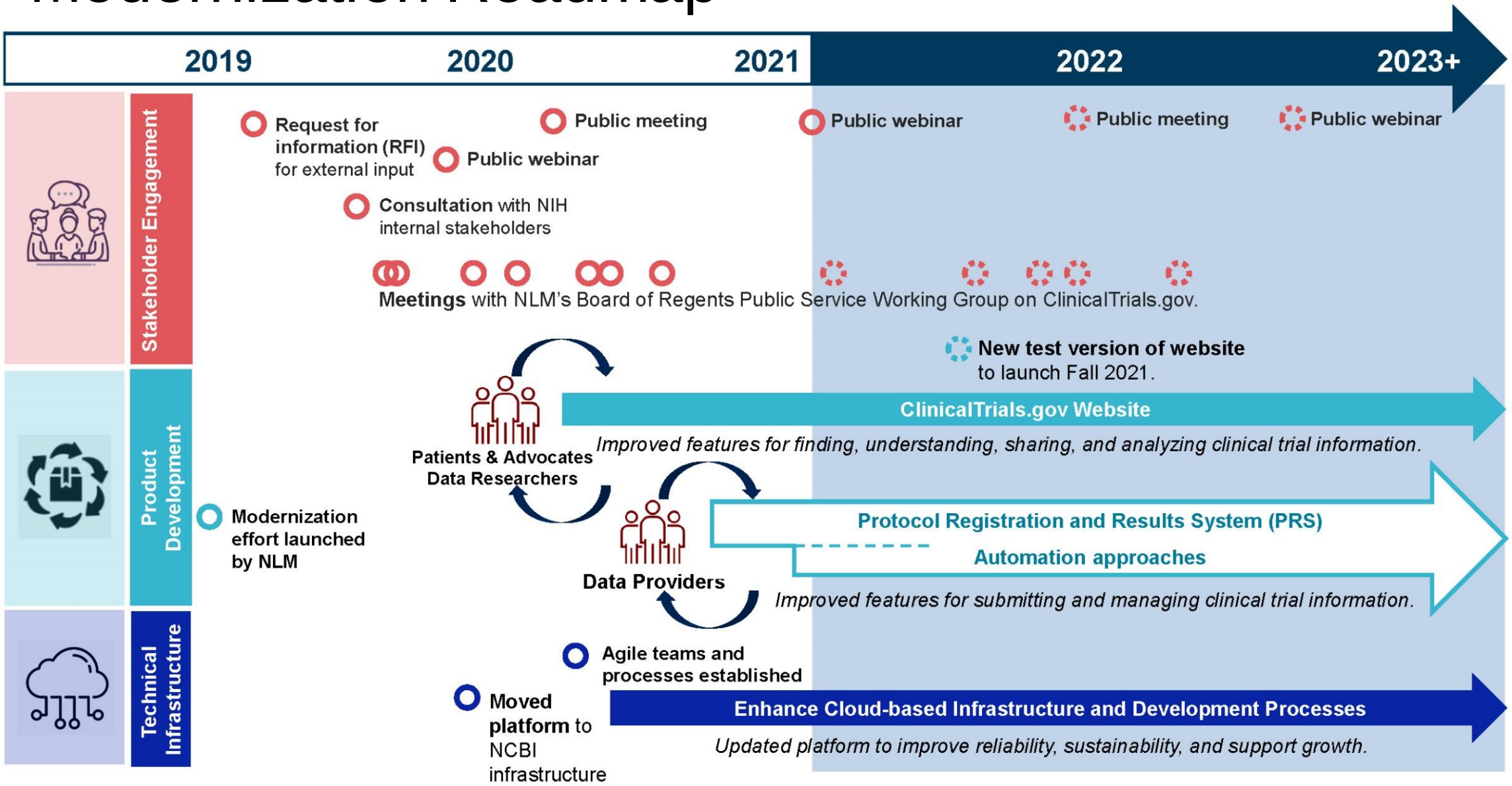
We will contact people over the next year

It may take some time for us to reach out to you. We cannot guarantee that everyone who signs up will be contacted.

If you don't sign up, you can still provide input

Later stages of modernization will include releases of "test versions" for wider testing and input.

Modernization Roadmap



Summary

- Aim to deliver an improved user experience to further advance the goals of comprehensive registration and results reporting.
- RFI feedback combined with user feedback loops are driving the modernization effort; coordinated with infrastructure upgrades.
- Approach will allow adequate time for users to try test versions of new systems and allow for improvements before implementation.
  - ClinicalTrials.gov website – test version planned for Fall 2021
  - Protocol Registration and Results System (PRS) – in early stages of planning and development
- We will continue to keep stakeholders well-informed.

Audience Question

How often would you like updates on the ClinicalTrials.gov modernization effort?

- Annually
- Bi-annually
- More frequently than just annually or bi-annually
- Only when there is something new that impact users
- I don’t need updates

Latest Blog: *Progress Towards a Modernized ClinicalTrials.gov*

February 10, 2021 blogpost:

https://nlmdirector.nlm.nih.gov/2021/02/10/progress-towards-a-modernized-clinicaltrials-gov/

- Highlights **user-centered design** approach, using **user feedback loops** and **prototypes,** to obtain user input on new features.
- Emphasizes core principle of **minimizing user disruption** during modernization effort.
- Shares that NLM will continue to provide stakeholders with more detailed **updates and timelines** as they become available.

Stay Up to Date with *Hot Off the PRS!*

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

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SHARE

What's New?

Progress Towards a Modernized ClinicalTrials.gov

ClinicalTrials.gov acting director Rebecca Williams, PharmD, MPH, has authored a guest post on the National Library of Medicine Musings from the Mezzanine blog. Read the post to learn more about the progress to modernize ClinicalTrials.gov.

Meetings + Conferences

Webinar on ClinicalTrials.gov Modernization

Reminder to mark your calendars for an update on the ClinicalTrials.gov modernization effort on February 18, 2021 from 3 to 4 p.m. ET. Please register via the ClinicalTrials.gov webinar registration page to attend the live event. A recording and the presentation slides will be posted after the webinar.

Moderator

Stand by - we will answer questions that were submitted through the Q&A box.

Thank You!

National Library of Medicine

Webinar

Recording and slides will be made available on the modernization webpage.

About Modernization

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

Participate

https://loom.ly/r6DRE50