Report on the ClinicalTrials.gov Modernization Effort

Summary of Progress: 2021–22

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NIH National Library of Medicine

ClinicalTrials.gov

Contents

1. Introduction

Overview of ClinicalTrials.gov and the Modernization Effort

ClinicalTrials.gov, the world's largest public clinical research registry and results database, provides patients, families, health care providers, researchers, and others with access to information on a wide range of clinical studies. Operated by the National Library of Medicine (NLM), a component of the National Institutes of Health (NIH), this web–based resource lists records for over 425,000 clinical trials, observational studies, and expanded access programs. More than 200,000 visitors use the website daily to find and learn about clinical studies. Launched in 2000, ClinicalTrials.gov has grown considerably, in terms of both the number of records and the scope of information that it contains, in conjunction with key policy and regulatory events (figure 1).

Figure 1. Total number of study records posted per year on ClinicalTrials.gov and timeline of related major events, from 1997 to 2022
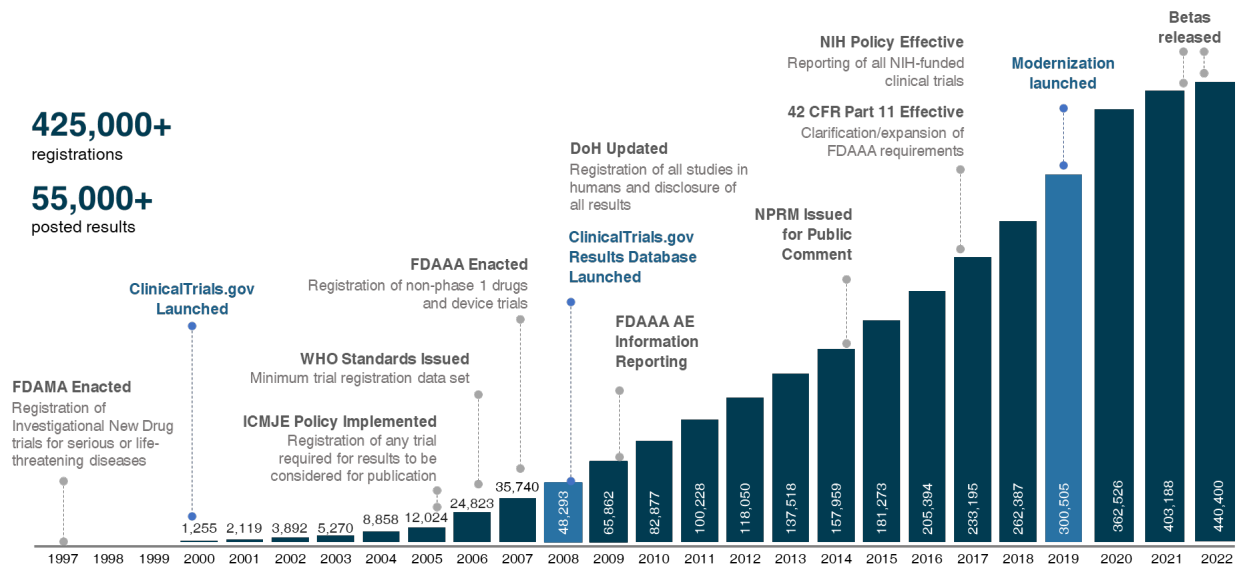
Abbreviations: AE = adverse event, CFR = Code of Federal Regulations, DoH = Declaration of Helsinki, FDAAA = Food and Drug Administration Amendments Act, FDAMA = Food and Drug Administration Modernization Act, ICMJE = International Committee of Medical Journal Editors, NIH Policy = NIH Policy on the Dissemination of NIH–Funded Clinical Trial Information, NPRM = Notice of Proposed Rulemaking, WHO = World Health Organization

In August 2019 NLM initiated a modernization effort for the ClinicalTrials.gov website and components of the Protocol Registration and Results System (PRS) to ensure that ClinicalTrials.gov continues to be a trusted premier public health resource that provides maximum value to the public well into the future. The approach to modernization involves three key activities: stakeholder engagement, product development, and technical infrastructure enhancements. The multiyear effort aims to deliver an improved user experience on an updated platform that will accommodate growth and enhance efficiency.

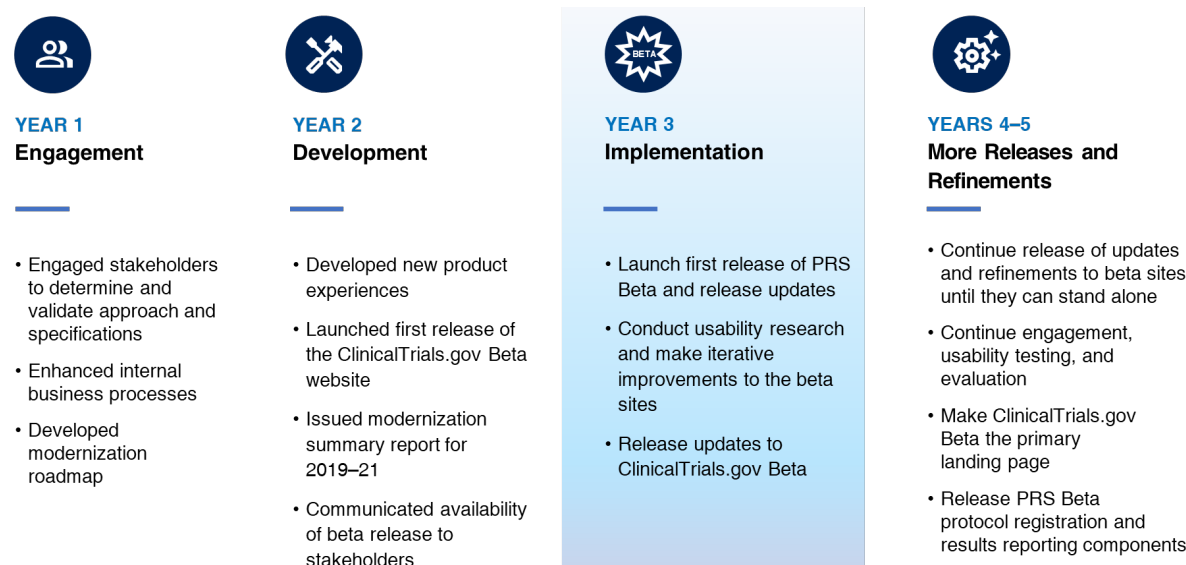## Overview of the 2021–22 Modernization Summary Report

This report provides a summary of the ClinicalTrials.gov modernization effort from September 2021 to September 2022. It presents an update on the ClinicalTrials.gov Beta website and PRS Beta, progress made on the modernization strategic goals, the stakeholder input received during the period, the modernization communication strategy, research undertaken to support the modernization effort, and future modernization activities.

During this reporting period, the NLM Board of Regents (BOR) Public Service Working Group on ClinicalTrials.gov Modernization (Working Group) continued to be an important source of input on modernization; the group's charge, roster, and member biographies are provided in appendix A, and the group's meeting schedule for the period is provided in appendix B. The Working Group supported the adoption of three strategic goals that organize the desired outcomes, or effects, of the modernization effort: (1) Clinical trial information is current, complete, and reliable; (2) Anyone can easily find and use information about clinical trials; and (3) Trial information, resources, and tools provide value to the research ecosystem. These goals help structure the efforts of the ClinicalTrials.gov team members involved in modernization, who are listed in appendix C. The abbreviations used in this report are listed in appendix D. More detailed information about the history of ClinicalTrials.gov and the first two years of the modernization effort can be found in the previous modernization summary report.

Current Phase of the Modernization Effort

The modernization effort encompasses a five-year period that began in 2019 and will continue through 2024 (figure 2).

Figure 2. ClinicalTrials.gov modernization overview, by year

YEAR 1
Engagement

- Engaged stakeholders to determine and validate approach and specifications
- Enhanced internal business processes
- Developed modernization roadmap

YEAR 2
Development

- Developed new product experiences
- Launched first release of the ClinicalTrials.gov Beta website
- Issued modernization summary report for 2019–21
- Communicated availability of beta release to stakeholders

YEAR 3
Implementation

- Launch first release of PRS Beta and release updates
- Conduct usability research and make iterative improvements to the beta sites
- Release updates to ClinicalTrials.gov Beta

YEARS 4–5
More Releases and Refinements

- Continue release of updates and refinements to beta sites until they can stand alone
- Continue engagement, usability testing, and evaluation
- Make ClinicalTrials.gov Beta the primary landing page
- Release PRS Beta protocol registration and results reporting components

In years 1 and 2 of the modernization effort, NLM prioritized engagement and development, conducting broad stakeholder engagement activities and focused usability research; assembling Agile, cross-functional modernization teams; and establishing the foundation for an updated technical infrastructure. The first release of ClinicalTrials.gov Beta was launched at the end of year 2. In year 3 we focused on implementation of the beta site experiences, while continuing to conduct stakeholder engagement and usability research activities and to update the technical infrastructure. As noted above, in year 3 the Working Group continued to provide input, validate our approach, and support our public communications about modernization. The main achievements of year 3 were three releases of updates to ClinicalTrials.gov Beta and the first release of PRS Beta (see section 2). Subsequent updates included additional features and refinements in response to stakeholder and user feedback and usability research. Years 4 and 5 will focus on more releases and refinements, further usability testing and stakeholder engagement, and the shift to the beta products as the primary systems.

Modernization work for this reporting period through 2024 is being guided by a strategic roadmap that groups tasks and events by the modernization approach's three key activity categories (stakeholder engagement, product development, and technical infrastructure) (figure 3).

Figure 3. 2021–24 strategic roadmap for ClinicalTrials.gov modernization
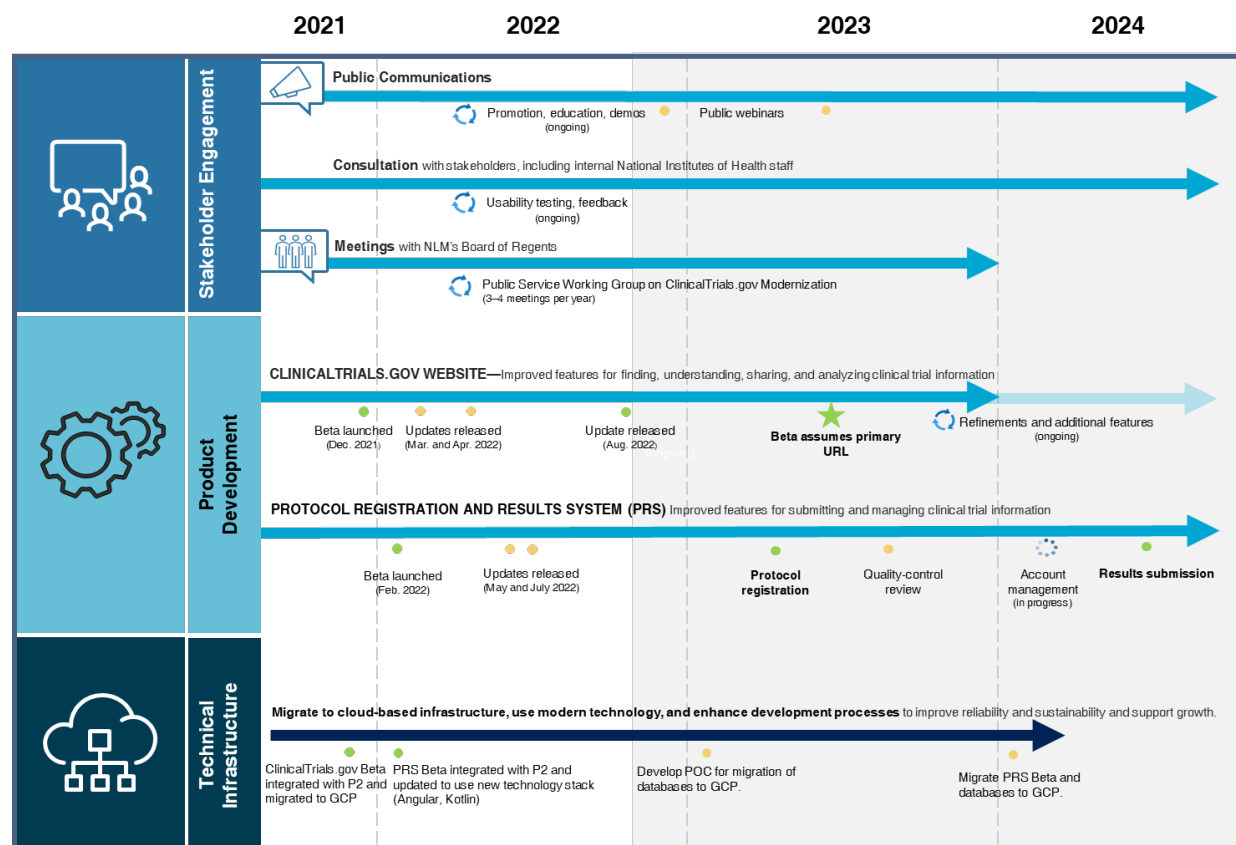
Key: GCP = Google Cloud Platform   P2 = NCBI's DevOps Platform v.2   POC = Proof of concept

As demonstrated throughout this report, users have been and remain central to the ClinicalTrials.gov team's approach to modernization. How users see changes to the beta sites and how their feedback helps inform further improvements are key considerations (figure 4).

Figure 4. How users see change
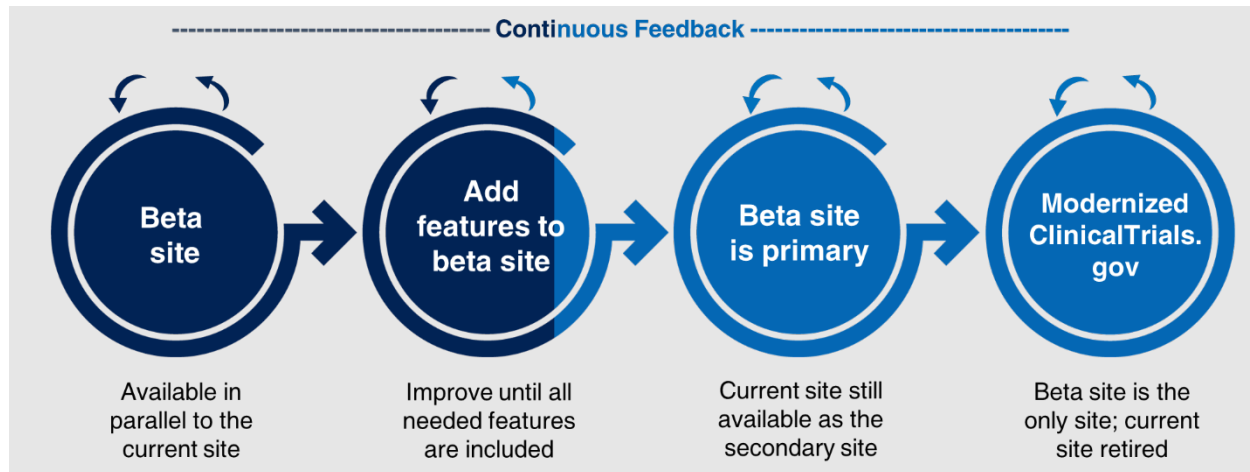
Activities and Achievements

NLM BOR Working Group Meetings

The Working Group met three times during the September 2021–September 2022 reporting period (see appendix B). Highlights from the meetings are detailed in section 4 of this report.

Webinars and Prerecorded Demonstrations

As part of continuing stakeholder engagement activities, NLM conducted two public webinars and released a prerecorded demonstration of the updated Record List in PRS Beta. Recordings of the webinars and the presentation slides (in PDF) are available on the ClinicalTrials.gov Modernization webpage.
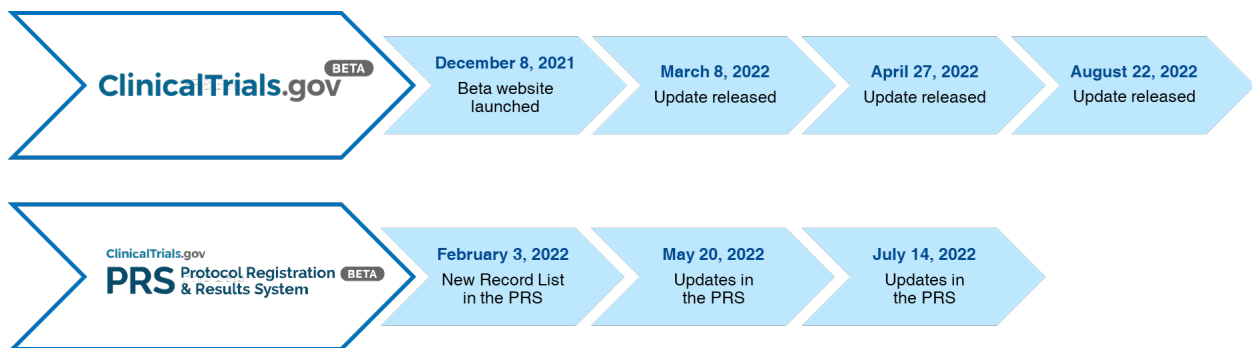
During the ClinicalTrials.gov Modernization Beta Preview public webinar held on October 7, 2021, NLM provided background on the ClinicalTrials.gov modernization effort, shared information on how users will be able to view and explore upcoming changes to ClinicalTrials.gov Beta and PRS Beta, communicated next steps, and answered questions from among the more than 450 attendees. A second public webinar was held on December 10 and attracted more than 300 attendees. During this ClinicalTrials.gov Modernization Update and Beta Website Demonstration, NLM provided an update on the modernization effort, shared an overview and demonstration of the new ClinicalTrials.gov Beta website, highlighting the changes that users will see, communicated next steps, and answered questions. Through an interactive poll, attendees could provide feedback on the features they would like to see in future ClinicalTrials.gov Beta releases. The overwhelming majority selected an advanced search feature, followed by the ability to download search results in more formats.

On December 8 NLM released the ClinicalTrials.gov Protocol Registration and Results System (PRS) Beta Preview, a prerecorded preview and demonstration of the updated Record List in PRS Beta. As of September 30, 2022, the video has been viewed 772 times.

Beta Releases

The most significant accomplishments during year 3 were the launch of the initial beta version of the PRS and the subsequent updates made to both ClinicalTrials.gov Beta and PRS Beta (figure 5). ClinicalTrials.gov Beta launched on December 8, 2021, and PRS Beta launched on the production site on February 3, 2022. Further information about the beta releases is provided in section 2 of this report, and the details of each release are summarized on the ClinicalTrials.gov Beta Release Notes and PRS Beta Release Notes webpages.

Figure 5. Chronology of the beta releases

ClinicalTrials.gov BETA

| December 8, 2021 | March 8, 2022 | April 27, 2022 | August 22, 2022 |
| Beta website launched | Update released | Update released | Update released |

ClinicalTrials.gov PRS Protocol Registration BETA & Results System

| February 3, 2022 | May 20, 2022 | July 14, 2022 |
| New Record List in the PRS | Updates in the PRS | Updates in the PRS |

2. Beta Product Releases
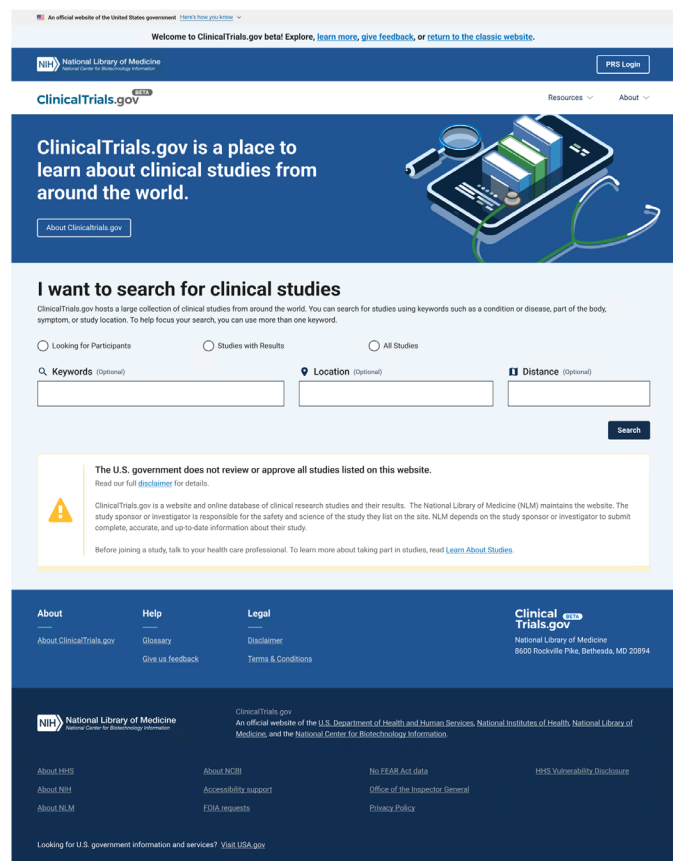
ClinicalTrials.gov Beta

2021–22 Releases

The ClinicalTrials.gov Beta website was launched on December 8, 2021, with basic features that correspond to the overall goals for improving the ClinicalTrials.gov user experience (figure 6). This first beta release introduced a new, modern look and feel with a responsive design to better support users on mobile devices and provided content in plain language and contextual educational information. Features of this release included the following:

- A new home page with a welcome message
- A simple search, located on the home page, which uses a cloud-based infrastructure with elastic search for lightning-fast response times
- Study cards that highlight key information such as study and recruitment status, study locations relevant to the user's search, and related terms within the study record
- A redesigned study record page with easy navigation, collapsible sections, interactive study results tables for data researchers, and an integrated Google Maps application programming interface (API) for viewing study locations
- Updated background information about ClinicalTrials.gov and educational information about clinical research, presented in plain language

Figure 6. ClinicalTrials.gov Beta home page (as of December 2021)

The March 8, 2022, release focused on the study record page to provide a more complete search experience for data researchers. The main features and improvements included the following:

- Availability of study documents when they are part of the study record
- Addition of information about the individual participant data plan
- Improved navigation among groups of publications
- Updated study results tables for better mobile viewing

As part of this release, a Release Notes page was also added to the ClinicalTrials.gov Beta website to keep users and the broader public informed about the beta releases. This page provides the details of what is included in each release, by release date.

The April 27, 2022, release focused on expanding the file formats available for downloading search results so that the various ClinicalTrials.gov user groups are able to select the file format that is most useful to them. Features and improvements included the following:

- Addition of Medical Subject Headings (MeSH) terms, U.S. Food and Drug Administration drug and device information, and violations of Section 801 of the Food and Drug Administration Amendments Act (FDAAA 801) to the study record page
- Addition of information to the Study Results tab that explains why study results may not be visible
- Expansion of the file format options for downloading search results to include comma-separated values (CSV) format

The August 22, 2022, release focused on the advanced search feature, providing a new search experience that combines the features of the basic search for clinical studies with the ability to narrow a search using additional criteria. Other updates and improvements included the following:

- Home page
  - Replacing the separate basic and advanced searches with a single, fully customizable combined search available on the home page
  - Making the text larger and easier to read and adding the ability to enlarge images in the documents found under "Resources" and "About"
- Search results page
  - Adding a tabular view of search results
  - Adding an action bar for selecting and downloading studies
  - Updating the filters to match the search options available in the new, enhanced search
  - Improving the age range filter to allow users to either select or manually enter age ranges
  - Adding a button to make it easier to navigate to the top of the page
- Study record page
  - Adding a navigation bar at the top of the page for viewing the previous or next study in the search results list
  - Adding an action bar with options for downloading and viewing study records
  - Adding the option to download a single study record in CSV or JavaScript Object Notation (JSON) format
  - Providing a pilot download of single study record in Fast Healthcare Interoperability Resources (FHIR) JSON format
  - Adding a bar to the Study Overview section for navigating directly to NLM resource links
- Bug fixes that corrected misaligned elements, overlapping titles, style element issues, and typos; improved the navigation to related publications and between study records and search results; and improved the overall spacing

In conjunction with this release, the banner on the classic ClinicalTrials.gov home page was updated to promote the beta website and draw more users (figure 7). The updated banner resulted in roughly three times as many daily visitors to the beta website and almost three times as many daily page views. In just one week, the banner link to the beta site received 10,221 clicks, nearly as many clicks as in an entire month previously.

Plans to further increase the number of visitors to ClinicalTrials.gov Beta are summarized in figure 8.

Figure 7. Classic ClinicalTrials.gov home page with updated banner
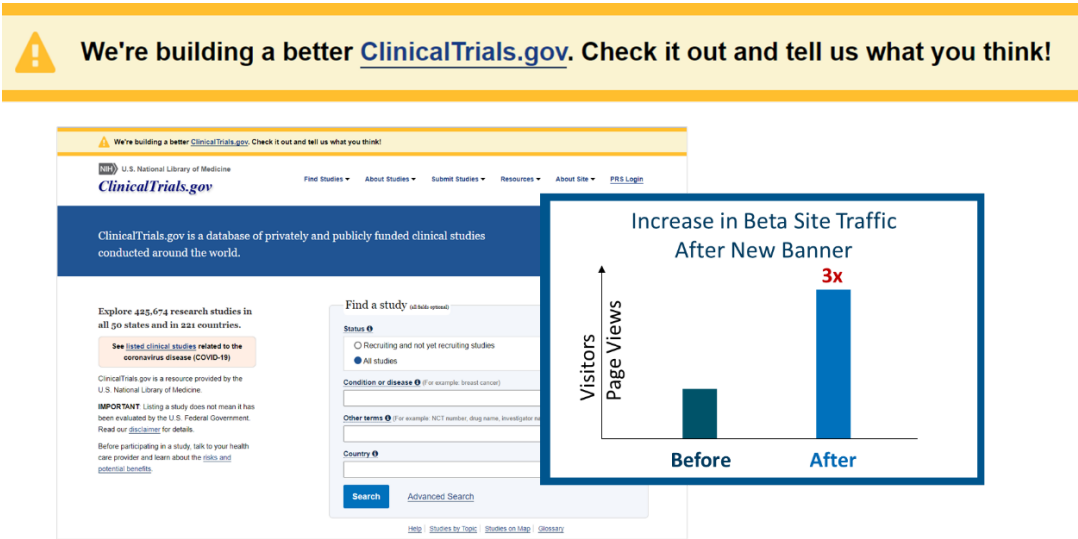
Figure 8. Plans to increase ClinicalTrials.gov Beta site traffic

2022	**Update classic site banner**
	Add more pathways from classic site to beta site
2023	Add pop-up to classic site
	Make experience persistent
	Make beta primary
	Allow web crawlers

Metrics and Evaluation, Including Feedback from Users

Since the launch of ClinicalTrials.gov Beta, the modernization team has continued to solicit user feedback through the site's **Give feedback** button, surveys, and several rounds of usability testing. The feedback received has been integrated into the design and development process to help shape each subsequent release.

The majority of early user feedback related to the search feature (figure 9), and these comments directly informed the August release. In response to user input, the team prioritized this feature and included the new search in an earlier release than originally planned.

Figure 9. ClinicalTrials.gov Beta feedback
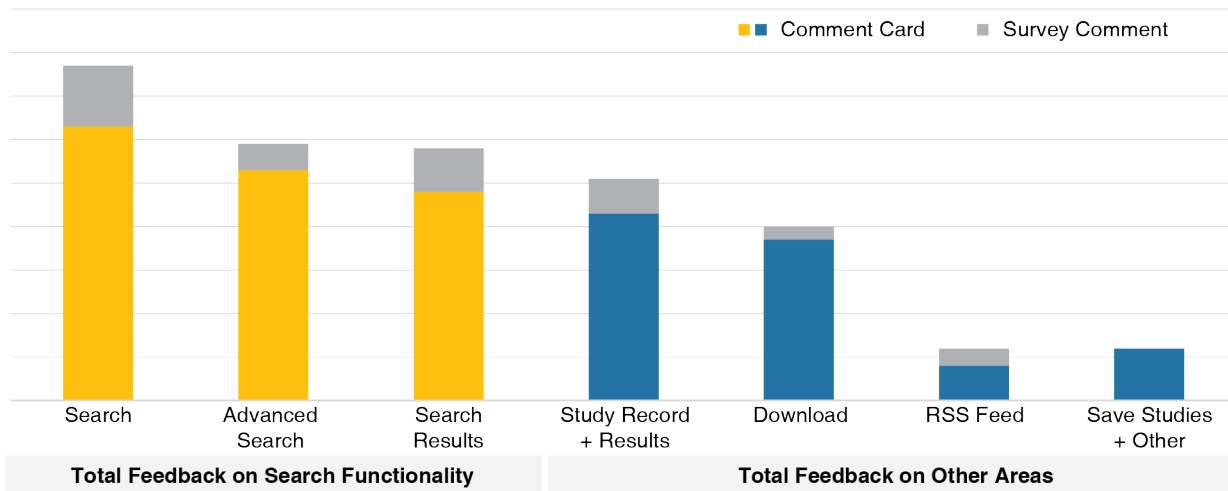
Source: Beta website comments, 12/8/2021–3/1/2022

The new, enhanced search (figure 10) was created after several usability sessions were conducted, which allowed time to connect with users and understand their specific search needs, and after users were provided the opportunity to test multiple prototypes. Refinement of the search feature on ClinicalTrials.gov Beta will continue, based on user feedback on the new search.

Figure 10. Enhanced search
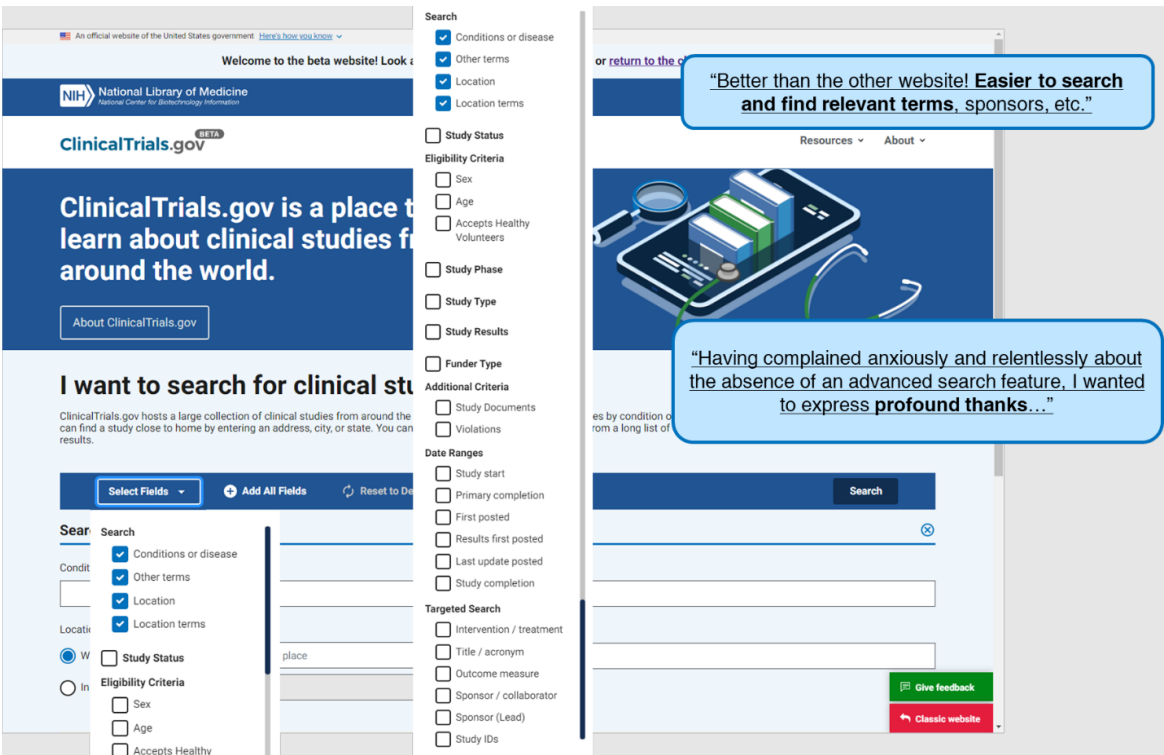
Upcoming Releases and Features

Upcoming releases and features under development for ClinicalTrials.gov Beta include a tabular view of study content and an improved study record history. Available, in-progress, and planned features for ClinicalTrials.gov Beta are summarized in figure 11.

Figure 11. ClinicalTrials.gov Beta features

	Search Experience	Study Record Experience	Easy-to-Find and Easy-to-Use Content
AVAILABLE	Expanded download formats Enhanced search* Improved ability to refine search results* Tabular view of search results*	Expanded study record data Fast Healthcare Interoperability Resources (FHIR) API pilot*	Learn About Studies About ClinicalTrials.gov Learn About FHIR*
IN PROGRESS		Tabular view of study records Improved study record history	Content migration and information architecture Support materials for using search
FUTURE	Beta application programming interface (API) access Download to XML	Connections to trusted health information Next steps to join a study	Onboarding users

* Features released on August 22, 2022

PRS Beta

2022 Releases

The initial release of PRS Beta on the production site occurred on February 3, 2022, with a modern and intuitive design and the introduction of the new Record List (figure 12). Features of this release included the following:

- The ability to email study staff directly from the Record List
- A customizable display that includes the ability to reorder, add, and hide columns and apply multicolumn filters
- Additional content, including more study dates with date type (actual or anticipated)
- The ability to choose to export only the displayed columns or all columns in the Record List to Microsoft Excel or CSV format

Figure 12. PRS Beta Record List

The May 20, 2022, release improved the appearance and functionality of the Record List, including addressing bugs, and added features from the classic PRS. Specific updates and improvements included the following:

- Adjustments to the filter display so that when one column is filtered, all the filter options for the other columns can also be seen
- Addition of the ability to select multiple filter options for one column

- A column that shows which study documents, if any, have been added to a study record
- An About menu that includes links to the About PRS Beta page and the Release Notes page
- Tool tips for each column heading in the Customize Columns menu that explain the information found in that column
- Updates to the filtering for columns, with names to make searching easier

The July 14, 2022, release included the addition of the Planning View and Public Site View to help administrators manage their organization's study records. Other feature of this release included the following:

- The ability to customize, filter, sort, and export the Planning View and Public Site View, just like the Default View
- Addition of a Group column to the Default View for users with PRS Administrator access
- Improved accessibility (i.e., compliance with Section 508 of the Rehabilitation Act of 1973) across the site

Metrics and Evaluation, Including Feedback from Users

The modernization team has been documenting user comments about PRS Beta received via the site's **Feedback** button (figure 13) as well as in emails sent directly to ClinicalTrials.gov. Members of the Clinical Trials Registration and Results Reporting Taskforce and the Clinical Trial Disclosure group of the Drug Information Association (DIA) have also provided helpful input. The team reviews all feedback received, prioritizes items for implementation, and determines how to specifically respond. For example, the team recently incorporated user feedback and usability testing results into the design process for the PRS data–entry screens.

Figure 13. Positive feedback about PRS Beta

"**I like the new format**, especially the ability to click on any name/title (e.g., Record Owner)."

"I like the layout. **Easily accessible.**"

"Thank you VERY MUCH for the group column."

"**I like the sort feature**; that will be helpful."

"You are rock stars, I appreciate the: 1) Search boxes for each field. It allows for more complex searching. 2) Awesome! Keep up the good work! Looking forward to seeing the planning report!"

"Love the new layout. It's **simple, straightforward, and easy to navigate.**"

Source: Give Feedback Comment Card, 2/22/2022–7/19/2022

Upcoming Releases and Features

Future changes to PRS Beta include further updates and other adjustments to the Record List to address user feedback and resolve bugs. A new design for the registration portion of the PRS, the Protocol Section, will be implemented at a later time.

3. Progress on the Modernization Strategic Goals

Features included in the ClinicalTrials.gov Beta and PRS Beta releases, or planned for 2021–22, that align with ClinicalTrials.gov modernization priorities established by the Working Group are described in the sections that follow, grouped by strategic goal.

Goal 1: Clinical Trial Information Is Current, Complete, and Reliable

Efforts that align with modernization priorities related to strategic goal 1 include the following:

- Enhancing features of the PRS (e.g., automated notifications, alerts, support materials) to help data submitters more easily identify trials that are subject to reporting requirements and with approaching deadlines
- Improving PRS functionality that supports intuitive use
- Enhancing submission and record-management workflows in the PRS to make them more flexible and customizable
- Improving automated just-in-time PRS support and resources to limit the need for one-on-one assistance, particularly with the quality-control (QC) review process
- Providing sufficient advance notice of planned PRS changes to give organizations ample time to update their standard operating procedures, templates, and training and educational materials

Goal 2: Anyone Can Easily Find and Use Information about Clinical Trials

Efforts that align with modernization priorities related to strategic goal 2 include the following:

- Improving the ClinicalTrials.gov search experience—The new search experience combines the features of the basic search for clinical studies with the ability to narrow a search using additional criteria, and new features help users better manage their search results; for example, a tabular view allows easy navigation and comparisons of results. Other features include improved filtering functionality, the ability to compare trials, the ability to save searches (including complex queries) for future use, alerts when there are updates to saved searches, visualizations of search results, and contextual information to help users better understand what the search included (e.g., synonyms).
- Enhancing resources for ClinicalTrials.gov users—These enhancements will help users learn about website functions specific to their user group and include a glossary of common site terms, information about study participation, and background information about the ClinicalTrials.gov website. A Learn About Studies page on ClinicalTrials.gov Beta, for example, provides information on study participation for individuals who are considering joining a study. A health literacy review of the site's glossary terms is also in progress.

- Adding plain language content to ClinicalTrials.gov and improving accessibility—This effort will provide an accessible and inclusive website experience by using plain language to support all users and ensuring that the site can be easily used on all devices and by anyone with a physical disability. For example, the information on ClinicalTrials.gov Beta's Learn About Studies and About ClinicalTrials.gov pages has undergone a plain language review, and the ClinicalTrials.gov Beta website is being developed with an adaptive design that supports accessibility.

- Providing contextual support for ClinicalTrials.gov users—This effort focuses on connecting users to other sources of trusted, high-quality information, including general health information about conditions; information about specific study interventions; information that situates evidence in its broader context (e.g., systematic reviews, results publication); and, potentially, third-party trial navigation resources.

- Improving the standardization of unstructured text in ClinicalTrials.gov study records—This effort involves evaluating opportunities to improve standardization for data fields that collect key study information such as conditions, interventions, eligibility criteria, and outcome measures. It is especially important in relation to the search experience.

  For example, the current capabilities of ClinicalTrials.gov's advanced search feature rely on querying the structured information in the eligibility criteria, thereby limiting the advanced search to age, sex, and whether the study accepts healthy volunteers. However, many more characteristics of the target population for a clinical trial can be provided in the Eligibility Criteria data element's free-text field. The Automation Support team explored the feasibility of applying advanced computational techniques to automatically index body mass index (BMI) from inclusion and exclusion statements in the Eligibility Criteria field. BMI was selected because it is one of the more common numerical characteristics described in the Eligibility Criteria; because it is derived from height and weight, which is information individuals typically know about themselves; and because there are multiple categories of BMI that can divide the search space. Indexing BMI involved determining four pieces of information: statements associated with BMI, whether those statements were in the inclusion or exclusion criteria, the thresholds reported in the Eligibility Criteria free-text field, and the units of the reported threshold values. Determining this information was not always straightforward because the Eligibility Criteria for some studies are complete and thorough, but those for other studies are not. In certain cases, the Eligibility Criteria may refer to sources of criteria that are external to the record or may assume prior knowledge of the criteria (e.g., "usual exclusion criteria for MRI"). Even when statements are complete, they can be complex and can include parentheticals or conditionals that are more difficult for a machine to parse (e.g., "Inclusion: BMI > 35 or BMI > 30 with comorbidity," statements that appear after the phrase "one or more of the following apply"). Ensuring that the criteria for all groups included in a study were accounted for was an additional factor to consider. Despite these complexities, a classifier was developed that proved to be accurate and faster than manual annotation. This research confirmed the feasibility of indexing a

numerical characteristic described in free text, and the methodology holds promise for enhancing the discovery of relevant studies using the search feature.

The Automation Support team is also exploring the application of advanced computational techniques to normalize and drive high-quality data. Specifically, there is considerable variability in the way in which information is entered in free-text fields (e.g., the same Unit of Measure may be written in more than one way as a result of the use of symbols or abbreviations, or because of typos). The team is developing an approach to predicting relevant Units of Measure, based on information available in the Outcome Measure Title and Outcome Measure Description data elements, that could provide tailored suggestions for the Unit of Measure, thereby encouraging high-quality entries.

- Increasing the visibility of the ClinicalTrials.gov website and sharing the website's resources through educational campaigns, search engine optimization, and journal publications and other outreach to the research community—Journal articles report findings and demonstrate to researchers different ways of using ClinicalTrials.gov for analysis of the clinical research enterprise (CRE). Journal articles prepared by ClinicalTrials.gov staff have shown research use cases with information from ClinicalTrials.gov such as informed consent forms, master protocol research programs, and the results database.

Goal 3: Trial Information, Resources, and Tools Provide Value to the Research Ecosystem

Efforts that align with modernization priorities related to strategic goal 3 include the following:

- Evaluating opportunities to standardize unstructured text in key fields (e.g., condition, intervention, eligibility criteria) that limits ease of reuse—Currently, the PRS can detect certain problematic data entries automatically using regular expressions and rule-based methods. This automated validation safeguards the quality of the data by notifying data submitters of missing information for required data elements and logical inconsistencies between data elements during the data-entry process. Once the record has been submitted, QC reviewers manually review entries for any apparent errors, deficiencies, or inconsistencies that cannot be detected by the automated validation. This manual QC review can be time consuming and is asynchronous, which may delay public access to new or modified information about a clinical trial.

Advanced computational techniques, such as natural language processing and machine learning, offer the potential to improve aspects of the QC review workflow by learning associations in the data without being explicitly programmed. Use of these advanced techniques can augment the efforts of QC reviewers to ensure high-quality data and reduce the delay in providing feedback to data submitters and information to the public.

In the past year, the Automation Support team has made considerable progress applying advanced computational techniques to support QC review of protocol registration information. Two common major issues identified by the QC review team are the Multiple Measures major issue and the Vague Time Frame major issue. The Multiple Measures

major issue is identified when multiple assessments with different Units of Measure are described in a single outcome measure. Because outcome measure data tables can accommodate only a single Unit of Measure, multiple measures with different units must be separated into different outcomes or clarifying information must be provided to explain how the measures will be combined to report a single measure. Outcome Measure Time Frames should indicate the specific time points or duration during which the outcome measure was assessed, expressed from the participant's perspective. An Outcome Measure Time Frame of "2 m" would be considered vague because it is not clear whether the outcome measure was assessed at two minutes or two months.

The team analyzed various approaches to creating a natural language–processing, machine–learning algorithm to detect both the Multiple Measures and Vague Time Frame major issues. This research demonstrated that a fine–tuned, transformer–based model can correctly classify these major issues with a high level of accuracy. It also confirmed the feasibility of detecting major issues in outcome measures and therefore holds promise for developing a useful tool for QC review staff.

- Advancing common data formats that support the interoperability of clinical trial information submission with data sources such as protocol templates and clinical trial management systems—FHIR is a data exchange standard developed by Health Level Seven International that is widely used for electronic health records in the United States to allow interoperability between systems. FHIR reduces waste and redundancy created by reentering data and makes the data findable, accessible, interoperable, and reusable. FHIR is important for clinical trial data exchange because clinical trial data in FHIR are more easily translated into clinical decision support and other health care applications. As applications develop ClinicalTrials.gov data in FHIR, the data-interchange format JSON may be used to find relevant trials for individual patients, find patients matching trial eligibility criteria, extract results data for meta-analyses, and extract study characteristics for evidence synthesis.

  To date, mappings and converter tools have been developed that allow the transformation of data between the ClinicalTrials.gov JSON and FHIR JSON structures. Mappings and converter tools have also been developed that allow the transformation of data between the ClinicalTrials.gov Beta JSON and FHIR JSON structures. An API is being developed to allow users to convert a ClinicalTrials.gov Beta JSON record to FHIR JSON and then download the record in FHIR JSON.

  A pilot was conducted from August to September 2022 to measure use of the API and obtain feedback from users via a link on the beta website. (A demonstration stress test was conducted before the pilot began.) A Learn About HL7® FHIR® Standard page was added to ClinicalTrials.gov Beta, and additional educational materials on the utility of the FHIR API as well as customer support will be provided to expand the pilot, if successful, to further facilitate ClinicalTrials.gov modernization.

- Proposing a metadata model for standardizing citation formats for ClinicalTrials.gov records—As part of ClinicalTrials.gov modernization, NLM intends to develop a standardized format for citing ClinicalTrials.gov records. This effort seeks to better support investigators by providing

clear recognition of their work to prepare, curate, and share their research data with other researchers and the public. It could also provide a foundation for establishing a mechanism that would allow researchers to conveniently download ClinicalTrials.gov record citation information into citation management software to better support research activities such as systematic reviews.

Creating a standardized citation format for ClinicalTrials.gov records involves three main challenges. The first is record version control. Data submitters can edit records at any time via the PRS. Because ClinicalTrials.gov records are dynamic, the citation format needs contextual metadata to allow researchers to determine which version of the record the citation refers to. The second challenge is the lack of an established definition of an "author" in the context of clinical trials. Authors are included as part of citations, and authorship is clearly defined for other research products such as peer-reviewed publications. In the case of clinical trials, however, there are typically investigators, sponsors, and organizations attached to a record, and who is considered the "author" of the trial has not been agreed on. The third challenge is the dynamic nature of the study status of clinical trials, specifically, the fact that studies typically progress from a recruiting status to a completed status, with various stages in between.

To support this effort, user experience research and informational interviews were conducted. A questionnaire was sent to representatives of the academic data submitter user group, and interviews were conducted with eight medical librarians. Ultimately, a format was developed that leverages existing ClinicalTrials.gov fields. ClinicalTrials.gov staff shared this format with NLM colleagues who are evaluating how the format might be incorporated into *Citing Medicine: The NLM Style Guide for Authors, Editors, and Publishers*.

- Creating robust download and API services that support data reuse by third parties, including patient-oriented organizations that provide clinical trial navigation services and researchers who conduct analyses of the CRE or the clinical research landscape or who create customized dashboards—One example of a beneficiary of this effort is the Reagan-Udall Foundation's Expanded Access Navigator resource, which uses API calls to help users find ClinicalTrials.gov records describing expanded access to investigational drug products made available by pharmaceutical manufacturers listed in the foundation's company directory.

- Providing resources that allow users to find important contextual information such as related health information, results publications, systematic reviews, and data sets

- Supporting best practices for data reporting, including important participant demographics such as sex, gender, race, and ethnicity, to better support data reuse—The 2016 Final Rule for Clinical Trials Registration and Results Information Submission (42 CFR Part 11) requires disclosure during registration of whether participant eligibility is based on a person's self-representation of gender identity and, if so, requires a brief, free-text description of those gender-based criteria. (The Gender Eligibility Description data element was not structured because of the lack of reporting standards for gender identity.) The Final Rule also requires the submission of participant demographics for age, sex/gender, and race and ethnicity, by study arm or group, in the Baseline Characteristics module during results reporting. As part of

the modernization effort, ClinicalTrials.gov team members are conducting two projects to characterize how participant demographic data elements have been used by trial sponsors and investigators during the past five years, which will allow us to assess ways to improve the standard reporting of participant demographics to ClinicalTrials.gov.

4. Working Group Input on Modernization

Working Group

The NLM Board of Regents Public Service Working Group on ClinicalTrials.gov Modernization was formed in September 2019 to provide oversight of and input on the modernization effort. The Working Group includes individuals that represent the three key external stakeholder groups: (1) data submitters, (2) patients and their advocates, and (3) data researchers. Working Group members were initially asked to serve for 1–2 years; of the 15 current members, 12 have participated since the initial 2019–20 period. During the current reporting period, two new members were added; one of these new members has a background in machine learning and artificial intelligence (AI), contributing relevant experience and expertise corresponding to the activities of the Automation Support team. The other new member has a background in effectively connecting health care providers and patients to biomedical information, facilitating access to knowledge for public and professional use.

During this reporting period, the Working Group met three times. Following each meeting, Working Group Chair Lourdes Baezconde-Garbanati reported on the group's activities during the corresponding NLM BOR meeting.

Highlights from the three Working Group meetings from this period, as well as the two August 2021 meetings, are provided below. (Although the August 2021 meetings were mentioned in the 2019–21 modernization summary report, the meeting summaries were not available before that report was released.)

August 20, 2021, Working Group Meeting

This meeting provided a brief overview of the Report on the ClinicalTrials.gov Modernization Effort, Summary of Progress: 2019–21, including the report's goals, sources of information, authors, and next steps. That report summarized ClinicalTrials.gov modernization activities and the input and feedback received from the Working Group, stakeholders, users, and the public from 2019 to 2021; presented information about the implementation of that input; and served as a guide for future modernization activities.

During the meeting, the ClinicalTrials.gov team also presented background information on the modernization effort, referenced the key themes and overall design goals guiding the effort, described the basic goals and main components of the first beta release, and noted some of the other modernization initiatives underway at that time. Feedback and evaluation mechanisms were also described.

Attendees discussed the stakeholder communications timeline; points to emphasize in communications to the public (e.g., the beta releases do not yet meet the needs of all users, some additional user needs will be addressed directly by ClinicalTrials.gov modernization while other needs can be supported only indirectly by modernization); the importance of foreshadowing coming features and managing expectations; and, specifically regarding PRS

Beta, the need for early and clear communication about timelines to allow organizations to easily transition to the new PRS and to improve the workflow without disrupting it.

August 30, 2021, Working Group Meeting

During this meeting, attendees discussed the Working Group's feedback to the Report on the ClinicalTrials.gov Modernization Effort, Summary of Progress: 2019–21, high-level themes and issues, and next steps. The Working Group confirmed the completeness of the list of modernization outcomes in section 3 of that report and confirmed that the characterizations of user challenges as able to be either directly or indirectly supported by modernization (in section 4 of that report) were correct.

The Working Group continued to reinforce the importance of ClinicalTrials.gov and NLM as central aggregators of information. They agreed that the best way for ClinicalTrials.gov to provide value to the research ecosystem is by focusing on how to maximize that value in the role of a central data aggregator and on where it would be best to invest time and effort.

Attendees discussed communications about the PRS and the need for clarity regarding what is being prioritized and why, and what will not happen and why, especially in relation to the detailed features of the system. It was noted that these issues are important to address because ClinicalTrials.gov cannot change the data submission requirements, which are grounded in regulations and the law; instead, the goal is to make using the PRS, and the processes for data submission overall, as intuitive as possible and to provide better features for managing study record portfolios. Regarding communications, two levels of information were identified: high-level information (e.g., the data elements will not be changing) and detailed information about what has changed and what has not for each release.

Attendees also discussed possible Working Group priorities for 2022, including automation that supports data submission and QC review processes; plain language information that supports patients, the public, and individuals who must meet regulatory and policy requirements and expectations; and the reporting of certain study types such as basic experimental studies involving humans.

All but one of the 13 Working Group members confirmed their willingness to continue participating during calendar year 2022.

Key findings from the modernization summary report and the next steps for the Working Group were reported to the full NLM BOR during the September 14, 2021, meeting.

January 28, 2022, Working Group Meeting

Two new Working Group members were welcomed during this meeting, Lauren Maggio of the Uniformed Services University of the Health Sciences and Omolola (Lola) Ogunyemi of Charles R. Drew University of Medicine and Science.

The meeting highlighted the first beta releases of the ClinicalTrials.gov public website and the PRS as well as other research being conducted to support modernization, based on stakeholder feedback. It was emphasized that modernization was always intended to be a

multiyear process, and it was noted that year 3, the first year of the implementation phase, had begun.

The following modernization priorities discussed during the last meeting were revisited: (1) metrics and evaluation, (2) data standards and data normalization, (3) automation to support submission and QC review processes, including support using technologies such as natural-language processing, machine learning, and AI, and (4) advancing interoperability with FHIR-based API exchange formats.

ClinicalTrials.gov staff described the work of the Automation Support team, which is exploring the possible applications of AI technologies to ClinicalTrials.gov data. The team's vision is that users will experience advanced automated processes that will help improve the quality of their data submissions to the PRS and refine their search experiences on the ClinicalTrials.gov public website. The computational techniques being considered allow the interpretation of a wide variety of syntactic and semantic patterns in free text and therefore could be leveraged to identify data quality issues earlier in the submission process, provide guidance for reporting high-quality data, and create structure from free text. The team is piloting advanced computational techniques to address comments received from users of the PRS and the public website related to the asynchrony of the feedback provided by ClinicalTrials.gov staff regarding data entry as well as comments about challenges related to unstructured free text.

An overview of the initial beta releases, metrics and methods for evaluating the success of modernization so far, areas needing improvement, and plans for future releases and associated communications were reported to the full NLM BOR during the February 8, 2022, meeting.

April 29, 2022, Working Group Meeting

During this meeting, the overall timeline for the launch of and updates to the beta sites was reviewed. ClinicalTrials.gov staff provided details about PRS Beta, summarized feedback received after its launch, and described future updates that are planned. Based on the initial feedback, users were most interested in better use of the screen space, the addition of columns or menus from the classic PRS, and improvements to features and functionality. Comments also indicated that users were excited about the changes made so far and were looking forward to further improvements.

ClinicalTrials.gov staff also provided details about ClinicalTrials.gov Beta, summarizing the usage of the initial version of the beta website and feedback collected via the site's **Give feedback** button, the pop-up survey, usability testing, interactions with NIH Institutes and Centers, DIA monthly meetings, Clinical Trials Registration and Results Reporting Taskforce monthly meetings, emails sent directly to ClinicalTrials.gov staff, and public webinars. The areas of most interest to users were the search, advanced search, and search results. In addition, a high-level overview of planned features for ClinicalTrials.gov Beta, grouped in three general areas (search experience, study record experience, and easy-to-find and

easy-to-understand content) was displayed, and it was noted that changes to the prioritization of features had been made based on user feedback.

Staff then discussed how users will see change. In the current stage of the overall workflow for the beta site, features and functionality are being added, and the beta site will continue to be improved until all needed features are included. The beta website will not become the primary website until everything that users need to accomplish their goals has been incorporated. Along with this general information, highlights of the March 8 and April 27 releases and the various methods used to communicate those updates (see section 5) were provided. The Working Group emphasized the importance of increasing traffic to the beta website.

Inputs for consideration in presenting content on ClinicalTrials.gov Beta were also presented to the Working Group. During this portion of the meeting, the user research team conducted a user preference activity involving placement of the updated disclaimer on the website. The group strongly preferred the option involving a pop-up message requiring acknowledgment, which corroborated the results of a similar activity conducted with users. Staff hope to implement the recommended update to the disclaimer design in 2023.

ClinicalTrials.gov staff then discussed the data elements targeted for plain language in the PRS.

A chronology of the beta releases; updates on ClinicalTrials.gov Beta and PRS Beta, including initial feedback and next steps; and navigating usability in a regulated environment, including a demonstration of the preference testing activity, were reported to the full NLM BOR during the May 10, 2022, meeting.

September 2, 2022

This meeting featured lightning talks on the topic of plain language summaries from Working Group members Barbara Kress of Merck and Sally Gore of the University of Massachusetts Medical School. Ms. Kress reviewed the importance of health literacy for both patients and caregivers and for health organizations and presented the plain language summary process from the perspective of a pharmaceutical study sponsor. Ms. Gore noted the need for trustworthy resources that are accessible to the lay public and presented several ideas for improving ClinicalTrials.gov to better support the lay public, such as providing guidance in plain language on interpreting a study record, improving the utilization of links to NLM-vetted resources and study sponsor-provided information, and embedding relevant plain language resources directly in the study record.

The PRS Beta team has adopted the Working Group recommendation to add a plain language checklist designed to promote the use of plain language by data submitters when drafting the registration protocol Brief Summary. ClinicalTrials.gov is considering the current landscape in determining how to best support data submitters in preparing all data elements required to be written in language for the lay public by FDAAA 801 and the Final Rule and may revisit this effort after modernization.

ClinicalTrials.gov staff noted that the modernization effort was nearing the end of its third year, with, most recently, the successful release of a ClinicalTrials.gov Beta update on August 22. Staff described recently released and upcoming PRS Beta features such as the updated Record List, as well as progress made on the prototype designs for the protocol registration section. Staff also described recently released ClinicalTrials.gov Beta features, such as the enhanced search, as well as upcoming features that are planned. A tabular view of the study record and of the study record history are under development.

Research focused on potential applications of AI, specifically machine learning, to help streamline the QC review process was described. Working Group members discussed additional approaches to reducing errors before and during QC review, including applying machine learning during data entry to provide real-time feedback to data submitters.

Working Group members confirmed that the key features that the team plans to develop are ones that Working Group members would like included in future releases of the ClinicalTrials.gov Beta website, namely, links to trusted health resources, guidance on next steps for joining a study, an XML download option, API access, and more educational resources about clinical trials.

The next PRS Beta release, which will include protocol registration submission tools, is anticipated for early 2023. It is anticipated that ClinicalTrials.gov Beta will become the primary public website by mid-2023. Stakeholder engagement through public webinars is anticipated for fall 2022 and spring 2023, alongside an ongoing social media campaign.

Discussions and decision from this Working Group meeting were reported to the full NLM BOR during the September 13, 2022, meeting.

5. Public Communications Related to Modernization and the Beta Releases

The ClinicalTrials.gov team has taken an informational and educational approach to public communications about modernization. The team has focused on ensuring that stakeholders, including data submitters, patients and their advocates, and data researchers (including journal editors), have the basic information they need about the modernization effort to date while also generating excitement about what is to come by showcasing the ClinicalTrials.gov Beta and PRS Beta features that have already been released and sharing information about future plans. The team uses a variety of external engagement strategies, such as the following:

- Disseminating communications through various channels (e.g., posting on NLM and National Center for Biotechnology Information (NCBI) social media channels)
- Briefing stakeholders and conducting targeted outreach to stakeholder groups, including reporting to the full NLM BOR during regularly scheduled meetings
- Hosting public webinars and demonstrations
- Attending and presenting at industry meetings, conferences, and other events

When there is new information about the overall modernization effort or about specific beta releases, an announcement is shared via the following:

- Hot Off the PRS! e-bulletin (with 8,000+ subscribers)
- What's New and ClinicalTrials.gov Modernization pages of the classic ClinicalTrials.gov website
- Release Notes pages of ClinicalTrials.gov Beta and PRS Beta (where summaries all releases are publicly accessible)

When appropriate, longer-form communications have been employed, such as a December 8, 2021, Musings from the Mezzanine blog post and a December 2021 *NLM Technical Bulletin* article. Communications have also been disseminated via the NIH Extramural Nexus. Public webinars and demonstrations held in October and December 2021 have been useful ways to share the latest modernization news with a wide audience and engage the community in question-and-answer sessions. Possible communication activities planned for the coming year include more public webinars and prerecorded demonstrations and continued stakeholder and social media outreach.

In addition to our own communication activities, information about the modernization effort has been disseminated via mentions in the literature. For example, in August 2022 *Applied Clinical Trials* published an article on the modernization effort that noted, "We are hopeful that the currently ongoing redesign of the ClinicalTrials.gov website will improve the user experience. We acknowledge significant improvements in useability of their beta website and look forward to the final product."

6. Research in Support of the Modernization Effort

ClinicalTrials.gov staff have undertaken a variety of research activities in support of the modernization effort, and findings that are considered of interest to a broader audience are published to both inform and engage the research community as well as to demonstrate how ClinicalTrials.gov information can be used as a resource. Projects highlighted in this report address several areas of interest, including emerging trends and issues across the CRE and trial reporting systems as well as gaps in reporting or unaddressed needs to be considered during modernization planning and implementation.

Recent ClinicalTrials.gov Research Projects

The research projects described below are based on stakeholder feedback and priorities discussed during the August 30, 2021, January 28, 2022, April 29, 2022, and September 2, 2022, Working Group meetings.

- Plain language and health literacy—The ClinicalTrials.gov Brief Title and Brief Summary protocol registration data elements, which are prepared by data submitters, are required to convey key study information and objectives in language written for the lay public. A checklist based on plain language principles and regulatory guidelines and a template to assist data submitters in drafting the Brief Summary data element will be added to the PRS.

  During the April 2022 Working Group meeting, members suggested ways to support the use of plain, accessible language by data submitters, including identifying common keywords in user searches and incorporating them into the Brief Summary data element.

  As part of her lightning talk during the September 2022 Working Group meeting, Ms. Gore suggested additional ways to incorporate plain language into ClinicalTrials.gov, including rewriting in plain language the How to Read a Study Record webpage, better utilizing links to NLM-vetted resources and study sponsor–provided information, and embedding relevant plain language resources directly in the study record.

- Automation to support information submission and QC review processes—The Automation Support team is exploring possible applications of AI to support ClinicialTrials.gov data quality efforts. The team conducted a pilot analysis using AI to automatically index BMI requirements described in the free-text field of the Eligibility Criteria data element. Following training, the automated approach successfully indexed free-text BMI information in more than 90% of the study records in a test sample. The team has begun applying similar AI approaches to other clinical trial information, such as outcome measures, and scaling up the process to increase the use of automation during QC reviews. Throughout the project, emphasis has been placed on the importance of tailoring the application of AI technology to different situations to mitigate data-entry errors and improve data quality, which are both goals of the modernization effort.

  During the January 2022 Working Group meeting, members discussed the promises and limitations associated with automated approaches to quality control, emphasizing the

importance of balancing the workload of data submitters (e.g., false-positive flags) and improved data quality. Members also noted the need to consider the potential interactions between AI-driven validations and third-party submission tools used by some organizations.

During the September 2022 Working Group meeting, members discussed designing the data-entry interface so that users are prompted to enter each outcome measure separately. Members also expressed support for using advanced computational techniques at the point of data entry, if this can be done accurately, to avoid major issues and create a more streamlined user experience. Finally, members advised minimizing false positives to ensure that users do not become desensitized to or overburdened by alerts when there are no issues.

7. Modernization Next Steps and Future Activities

Continued Testing and Evaluation

The ClinicalTrials.gov team has integrated a testing and evaluation process for ClinicalTrials.gov Beta and PRS Beta. This user-centered, collaborative approach employs various methodologies to gather insights from users to enhance the discoverability of information and improve navigation for all user groups.

In the past six months, the team has employed user experience workshops to determine a cadence, goals, and priorities for testing. The team has conducted 20 usability testing interviews to evaluate ClinicalTrials.gov Beta and to improve the search function. The team has also used other methods to evaluate the way that information is organized on ClinicalTrials.gov Beta, including a preference-testing activity to gather insights from more than 30 users on the placement of the disclaimer. All these activities have informed the design and development of various ClinicalTrials.gov Beta features.

In addition to these usability research activities, the team has developed a process for analyzing user feedback collected by the NCBI comment card monthly. As of August 2022, the team has analyzed more than 600 comments, received from both new and returning ClinicalTrials.gov Beta users, and provided recommendations to inform the design and development process. In addition, the team continues to use the more than 1,400 modernization request for information responses and feedback from the more than 70 interviews the team conducted in 2020 to support the modernization of both the ClinicalTrials.gov website and the PRS.

Working Group Contributions

Upcoming Activities

NLM plans to hold at least three Working Group meetings during the October 2022–September 2023 period. These meetings will occur prior to the NLM BOR meetings scheduled for February 7, May 9–10, and September 12–13, 2023.

Membership

Working Group members who served during this reporting period were given the option to continue their participation for another year. Input from the Working Group is crucial as the ClinicalTrials.gov team prepares for the ClinicalTrials.gov Beta website to assume the primary URL by the third quarter of 2023 and plans communications about this milestone to be shared with users, stakeholders, and the public.

More Information

The following resources provide additional information about the ClinicalTrials.gov modernization effort:

- Report on the ClinicalTrials.gov Modernization Effort, Summary of Progress: 2019–21
- Recordings and presentation slides of public webinars and demonstrations
- ClinicalTrials.gov Beta website
- ClinicalTrials.gov Beta Release Notes webpage
- ClinicalTrials.gov What's New webpage
- ClinicalTrials.gov Modernization webpage
- PRS Beta Release Notes webpage

Appendices

Appendix A: NLM Board of Regents Public Service Working Group on ClinicalTrials.gov Modernization: Charge, Roster, and Biographies

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

CHARGE

The NLM Board of Regents (BOR) Working Group on ClinicalTrials.gov Modernization is charged to explore topics such as, but not limited to, ways NIH can:

- Maintain the integrity of ClinicalTrials.gov as a trusted resource, particularly among an ever-expanding research enterprise
- Maximize the utility of the growing corpus of information, including through submission practices and user-focused technical functionalities
- Connect with stakeholders through engagement to ensure that their evolving needs are understood and considered in iterative design enhancements

The Working Group is expected to meet at least three times a year in conjunction with the BOR meeting and report regularly in open session to the full BOR on issues essential to the ClinicalTrials.gov modernization process, keeping pace with changes in the external environment and user expectations of key functionalities. All analyses and findings will take into consideration the existing legal and policy requirements.

ROSTER

Chair: Lourdes Baezconde-Garbanati, PhD, MPH, University of Southern California

Executive Secretary: Anna M. Fine, PharmD, MS, NLM, NIH

Board of Regents Members:

- Kent J. DeZee, MD, MPH, MACP, COL, MC, Defense Health Agency
- Jennifer (Jennie) S. Lucca, MSW, The Children's Inn at NIH
- Lauren A. Maggio, PhD, Uniformed Services University of the Health Sciences
- Omolola (Lola) Ogunyemi, PhD, FACMI, Charles R. Drew University of Medicine and Science

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 Clinical and Translational Science Institute
- Alissa T. 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, North Star Review Board and Freeport Research Systems
- Joseph S. Ross, MD, MHS, Yale School of Medicine
- Steven Woloshin, MD, The Dartmouth Institute for Health Policy and Clinical Practice

Former Members:

- Carlos R. Jaén, MD, PhD, University of Texas Health Science Center at San Antonio (former BOR member and Working Group chair)
- Gary A. Puckrein, PhD, National Minority Quality Forum
- Rebecca (Becky) J. Williams, PharmD, MPH, NLM, NIH (former Working Group executive secretary)

BIOGRAPHIES

Chair: Lourdes Baezconde-Garbanati

Lourdes Baezconde-Garbanati, PhD, MPH, is Associate Dean for Community Initiatives at the Keck School of Medicine and Associate Director for Community Outreach and Engagement at the Norris Comprehensive Cancer Center at the University of Southern California (USC). She is tenured Professor of Population and Public Health Sciences and Associate Director for the Center for Health Equity in the Americas.

Dr. Baezconde-Garbanati is an expert in researching cancer disparities in diverse populations, developing effective culturally specific cancer-prevention interventions, and engaging at-risk populations in community-based participatory research. She has been a key member of six NIH-funded research centers. Currently she is one of the key investigators at the Tobacco Center for Regulatory Sciences at USC.

Dr. Baezconde-Garbanati speaks multiple languages and holds five academic degrees. She has a PhD and an MPH in public health from the University of California, Los Angeles, where she focused on community health sciences and social epidemiology. She has a master's degree from the Université catholique de Louvain in Belgium and received dual degrees in industrial and clinical psychology from the Universidad Nacional Pedro Henríquez Ureña in the Dominican Republic.

Executive Secretary: Anna M. Fine

Anna M. Fine, PharmD, MS, is Acting Director of ClinicalTrials.gov, an international registry and results database of clinical research, at the National Center for Biotechnology Information, National Library of Medicine, NIH. As Acting Director, she is responsible for technical, scientific, policy, regulatory, and outreach activities related to the operation of ClinicalTrials.gov. Dr. Fine assumed this role in 2021, after having served as deputy director since 2018. Her previous experience includes over a decade of service in stakeholder engagement, adverse drug event reporting, and supervisory roles at the U.S. Food and Drug Administration. Prior to that, she was Chief of Pharmacy Services at Hanscom Air Force Base in Massachusetts.

Dr. Fine has a PharmD from Northeastern University and an MS in psychopharmacology from William James College. She completed a postgraduate year two drug information residency at Stanford Hospital.

Board of Regents Member: Kent J. DeZee

Kent J. DeZee, MD, MPH, MACP, COL, MC, is Director for Graduate Medical Education at the Defense Health Agency. He previously served as Director of the Army Medical Education Directorate for the Office of the Surgeon General Defense Health Headquarters.

Col. DeZee earned his medical degree from The Ohio State University College of Medicine. He completed his residency at the Tripler Army Medical Center and a fellowship in general medicine at the Uniformed Services University of the Health Sciences, where he earned an MPH.

Board of Regents Member: Jennifer S. Lucca

Jennifer (Jennie) S. Lucca, MSW, is Chief Executive Officer of The Children's Inn at NIH. A seasoned human service professional, Ms. Lucca has more than 20 years of experience in the nonprofit sector. She previously served as The Inn's Chief Program and Services Officer, overseeing the daily management of resident services, family programs, and facility operations.

Ms. Lucca's career began in Anchorage, Alaska, where she worked for The Arc of Anchorage, an organization dedicated to serving individuals with disabilities. Since that time, she has focused primarily on developing and managing family support programs in community and health care settings. Passionate about supporting families during times of significant stress, Ms. Lucca has been acknowledged for her compassion, dedication, and strategic leadership.

Ms. Lucca has a bachelor's degree in child psychology from the University of Minnesota and an MSW with a focus on policy, planning, and administration from The Catholic University of America.

Board of Regents Member: Lauren A. Maggio

Lauren A. Maggio, PhD, is Professor of Medicine at the Uniformed Services University of the Health Sciences (USU) and Associate Director of Scholarly Communications at USU's Center for Health Professions Education. In addition, she is Programs Scholar at the Association of Academic Health Centers. Dr. Maggio's research explores how to effectively connect physicians, learners, and patients with biomedical information through the design of educational interventions and technical solutions and by facilitating access to knowledge for public and professional use. Her research interests include evidence-based practice, meta-research and responsible conduct of research, knowledge syntheses, and scholarly communication. She is a coauthor of *Clinician's Guide to Evidence-Based Practices: Behavioral Health and Addictions* (2nd ed.).

Dr. Maggio has been an editor for *Perspectives on Medical Education* since 2017 and is currently Acting Editor-in-Chief. She is also a member of the editorial board for *Academic Medicine* and has served as Associate Editor for *BMC Medical Education* and as an editorial board member for the *Journal of the Medical Library Association* and for *Evidence Based Librarianship and Practice*.

Dr. Maggio has a PhD in medical education from the University of Utrecht/University of California, San Francisco, and an MS from Simmons Graduate School of Library and Information Science.

Board of Regents Member: Omolola Ogunyemi

Omolola (Lola) Ogunyemi, PhD, FACMI, is Director of the Center for Biomedical Informatics (CBI) and a professor in the Department of Preventive and Social Medicine at Charles R. Drew University of Medicine and Science. She is also a co-chair of the UCLA Clinical and Translational Science Institute's biomedical informatics program and adjunct Professor of Radiological Sciences at the David Geffen School of Medicine at UCLA, with the Medical and Imaging Informatics group. Her research at CBI focuses on novel biomedical informatics solutions for problems that affect medically underserved communities, and her research interests include computerized medical-decision support, reasoning under uncertainty, 3D graphics and visualization, and machine learning. Before becoming Director of CBI, Dr. Ogunyemi was a biomedical informatics faculty member in the Department of Radiology at Brigham and Women's Hospital and Harvard Medical School, among other teaching positions.

Dr. Ogunyemi is currently an editorial board member for the *Journal of Biomedical Informatics* and was an editorial board member for *Computers in Biology and Medicine* from 2007 to 2013. She served on the National Library of Medicine's (NLM) Biomedical Library and Informatics Review Committee study section from 2003 to 2007 and on NLM's Literature Selection and Technical Review Committee from 2010 to 2014, both as a member and as chair. She was a member of the Agency for Healthcare Research and Quality Health

Information Technology Research study section from 2016 to 2019 and a member of the American Medical Informatics Association's Doctoral Dissertation Award Committee from 2017 to 2020.

Dr. Ogunyemi has an undergraduate degree in computer science from Barnard College and an MSE and a PhD in computer and information science from the University of Pennsylvania. She is an elected Fellow of the American College of Medical Informatics.

Ex Officio NIH Member: Lyric A. Jorgenson

Lyric A. Jorgenson, PhD, is Acting Associate Director for Science Policy and Acting Director of the Office of Science Policy at NIH. In this role she provides senior leadership in the development and oversight of cross-cutting biomedical research policies and programs considered to be of high priority to NIH and the U.S. government. Previously she served in many roles across the agency, including Deputy Director of the Office of Science Policy, and she has led the development of numerous high-impact science and policy initiatives, such as the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative and the National Center for Advancing Translational Sciences. Dr. Jorgenson also served as Deputy Executive Director of the White House Cancer Moonshot Task Force in the Office of the Vice President during the Obama administration, where she directed and coordinated cancer-related activities across the federal government and worked to leverage investments across sectors to dramatically accelerate progress in cancer prevention.

Dr. Jorgenson has a PhD from the Graduate Program for Neuroscience at the University of Minnesota Twin Cities, where she conducted research in neurodevelopment with a focus on learning and memory systems, and a bachelor's degree in psychology from Denison University.

Ex Officio NIH Member: Pamela Reed Kearney

Pamela Reed Kearney, MD, is Director of the Division of Human Subjects Research in the Office of Extramural Research (OER) at NIH. Prior to joining OER, she was the deputy chair of the Combined NeuroScience Institutional Review Board (IRB) in the NIH Intramural Program for approximately a decade. In this capacity she sat on three to four duly constituted IRBs, chairing one and serving as the vice chair of the others.

Dr. Kearney graduated with distinction from The George Washington University School of Medicine and completed an otolaryngology residency at The George Washington University. She was a Neurolaryngology Clinical Fellow for the National Institute of Neurological Disorders and Stroke in the Medical Neurology Branch's Laryngeal and Speech Section, and she later served as the staff clinician of the section. She has conducted clinical work at The George Washington University, Walter Reed Army Medical Hospital, and the NIH Clinical Center.

External Member: Carrie Dykes

Carrie Dykes, PhD, is Director of Research Services at the University of Rochester Clinical and Translational Science Institute (UR CTSI). Her primary role is to strategically plan, develop, implement, and evaluate the research resources and services of UR CTSI, and she provides leadership for the management and oversight of the Research Help Desk, Recruitment Unit, Clinical Research Center, Pilot and Incubator award programs, and Office of Regulatory Support. She also develops and assesses research education materials for a variety of constituencies across the University of Rochester Medical Center. Dr. Dykes serves as the University of Rochester's ClinicalTrials.gov Protocol Registration and Results System Administrator and is on the leadership board of the Clinical Trials Registration and Results Reporting Taskforce.

Dr. Dykes has a PhD from the University of Rochester and worked in the field of HIV drug resistance research for 20 years before joining UR CTSI.

External Member: Alissa T. Gentile

Alissa T. Gentile, MSN, RN, serves as the Dana–Farber Cancer Institute Research Nursing Manager for the Satellites and Collaborative. In this role she leads the design, implementation, and evaluation of clinical oncology research and services conducted at Dana–Farber satellite and Collaborative locations and is a key facilitator for the oncologists in the growth and development of the clinical research program across all Dana–Farber sites. Her responsibilities include providing nursing input for the review of prospective clinical trials and for retrospective review protocols; collaborating with study teams and network nurse leaders on hiring, training, and supervising satellite research nurses; and training and supporting Collaborative research nursing staff. She serves as the primary research nursing liaison between the satellite and Collaborative sites and Dana–Farber's main Longwood campus.

Prior to joining Dana–Farber, Ms. Gentile was the director of The Leukemia and Lymphoma Society's Clinical Trial Support Center, leading the efforts of a team of nurse navigators to educate people affected by blood cancers about the treatment option of clinical trials and to assist them in navigating the process of clinical trial enrollment. Previously she held the position of nurse educator at St. Elizabeth's Medical Center in Boston, Massachusetts, and early in her career she worked for many years as a Certified Emergency Department Nurse. Ms. Gentile has a bachelor's degree in nursing from the University of New Hampshire as well as an MSN focused on nursing management and education.

External Member: Sally A. Gore

Sally A. Gore, MS, MS LIS, is Manager of Research and Scholarly Communication Services for the Lamar Soutter Library at the University of Massachusetts Medical School. She oversees the library's collaborative efforts with basic science and clinical researchers on campus, including expanded support and instruction in data services. Her department leads all scholarly communication endeavors for the library, including providing bibliometric analysis;

tracking research impacts; ensuring funder-based public-access compliance; promoting open science initiatives; and managing eScholarship@UMMS, the university's open-access institutional repository. Ms. Gore also serves on the Board of Directors of the Medical Library Association and is Associate Editor of the *Journal of eScience Librarianship*.

Prior to assuming her current position, Ms. Gore was the research evaluation analyst for the University of Massachusetts Center for Clinical and Translational Science. She was also a National Library of Medicine grant–funded informationist at the Lamar Soutter Library, a reference and instruction librarian, and a consumer health librarian. Ms. Gore has an MS LIS from Syracuse University.

External Member: Barbara Kress

Barbara Kress, BSN, RN, is Executive Director of Clinical Data Disclosure and Transparency at Merck. She is responsible for registry and results disclosure, redaction operations, data sharing, and the return of plain language summaries to patients. Ms. Kress joined Merck in 1997 as a clinical scientist working on the successful development and submission of several compounds. In 2007 she was asked to assume an additional responsibility that she was told would take up only 5% of her time: ClinicalTrials.gov. Fifteen years and more than 30 staff members later, disclosure requires 100% of her time.

Ms. Kress currently participates in various Pharmaceutical Research and Manufacturers of America, European Federation of Pharmaceutical Industries and Associations, and TransCelerate disclosure work streams. She is also a member of the Executive Committee of the Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard, participating in the Data Sharing and Return of Results (aggregate and individual) working groups. Ms. Kress began her career as a critical care and emergency room nurse. She has a bachelor's degree in nursing science from Rutgers University.

External Member: Seth A. Morgan

Seth A. Morgan, MD, is a Fellow of the American Academy of Neurology who served as a clinical neurologist for more than 20 years before becoming an advocate for people living with multiple sclerosis (MS) following his own MS diagnosis in 2004. An activist for people with MS and other types of disabilities, Dr. Morgan is a member and the current chair of the National Multiple Sclerosis Society's (NMSS) Maryland Governmental Relations Committee and an NMSS District Activist Leader. He is a commissioner on and the current chair of the Montgomery County, Maryland, Commission on People with Disabilities, the vice chair of the Maryland Alliance of Disability Commissions and Committees, and a commissioner on the Maryland State Disability Commission. Dr. Morgan's other public service activities include serving as a member of the iConquerMS Research Committee, a reviewer for the Patient-Centered Outcomes Research Institute's Clinical Trials Advisory Panel, and a member of the NMSS Activism Advisory Committee. He was also a reviewer for the Congressionally Directed Medical Research Programs from 2014 to 2016.

Dr. Morgan earned his medical degree from The George Washington University School of Medicine and Health Sciences, and he completed a residency in neurology at The George Washington University Medical Center. He is a Fellow of the Stroke Council of the American Heart Association and a Diplomate of the American Academy of Pain Medicine. Dr. Morgan was inducted into the NMSS Advocacy Hall of Fame in 2015.

External Member: Stephen J. Rosenfeld

Stephen J. Rosenfeld, MD, MBA, trained as a hematologist. He spent 19 years at NIH, holding positions at the National Heart, Lung, and Blood Institute (NHLBI) and the NIH Clinical Center related to both basic and clinical research and, later, working in medical informatics and administration, and he ended his time at NIH as Chief Information Officer of the NIH Clinical Center. He subsequently served as Chief Information Officer of MaineHealth, a large, independent delivery network based in Portland, Maine, and as Chief Executive Officer of the Western Institutional Review Board (IRB) in Olympia, Washington. He was also the executive chair of Quorum Review IRB for seven years. Dr. Rosenfeld is a founder of North Star Review Board, the first nonprofit 501(c)(3) independent IRB, and is the president of Freeport Research Systems, a consulting firm focused on the people and systems of biomedical research.

Dr. Rosenfeld earned his medical degree from Cornell University, trained in internal medicine at Dartmouth College, and completed his hematology fellowship at NHLBI. He has an MBA from Georgetown University. Dr. Rosenfeld received the honor of Distinguished Professor of Medicine from Daegu Catholic University Medical Center in Korea in 2013. Also in 2013, he was appointed to the Secretary's Advisory Committee on Human Research Protections at the U.S. Department of Health and Human Services, and he served as chair of the committee from 2017 to 2021. In 2018 he was elected to the Board of Directors of Public Responsibility in Medicine and Research, and in 2019 he joined the Board of Directors of the Association for the Accreditation of Human Research Protection Programs, which he currently chairs.

External Member: Joseph S. Ross

Joseph S. Ross, MD, MHS, is Professor of Medicine (General Medicine) and of Public Health (Health Policy and Management) at the Yale School of Medicine, a member of the Center for Outcomes Research and Evaluation at Yale–New Haven Health System, and Co-Director of the National Clinician Scholars Program at Yale School of Medicine. With expertise in the development of performance measures and the translation of clinical research into practice, Dr. Ross examines the use and delivery of higher-quality care and addresses issues related to pharmaceutical and medical device regulation, evidence development, post-market surveillance, and clinical adoption. Dr. Ross co-directs the Yale University Mayo Clinic Center of Excellence in Regulatory Science and Innovation, the Yale University Open Data Access Project, and the Collaboration for Research Integrity and Transparency at Yale Law School. He has published more than 500 articles in peer-reviewed biomedical journals and is currently the U.S. Outreach and Research Editor at *The BMJ*.

Dr. Ross earned his medical degree from Albert Einstein College of Medicine and an MHS from Yale School of Medicine.

External Member: Steven Woloshin

Steven Woloshin, MD, is a general internist, Professor of Medicine and Community and Family Medicine, and Director of the Center for Medicine and the Media at The Dartmouth Institute for Health Policy and Clinical Practice, Geisel School of Medicine at Dartmouth. His research addresses the excessive fear and hope created by exaggerations and selective reporting in medical journals, advertising, and the health news. He has worked to improve the communication of medical evidence to physicians, journalists, policymakers, and the public, so they can make wiser decisions.

With Lisa Schwartz, Dr. Woloshin developed NIH's Medicine in the Media workshop and ran it for more than a decade. He is coauthor of the books *Know Your Chances* (selected for the National Center for Biotechnology Information's Bookshelf) and *Overdiagnosed* (winner of the Prescrire Prize). His essays have appeared in *The New York Times*, *The Washington Post*, and the *Los Angeles Times*. Dr. Woloshin is a founding organizer of the international Preventing Overdiagnosis meetings sponsored by *The BMJ*, The Dartmouth Institute, Consumers Union, and Oxford and Bond University (Australia). He collaborates frequently with the National Cancer Institute, serves on the editorial boards of *JAMA Internal Medicine* and the Cochrane Library, and is a strategic advisor to Cochrane Sustainable Healthcare. He and Dr. Schwartz were co-winners of the American Medical Writers Association John P. McGovern Award for preeminent contributions to research and enhancing the communication of medical evidence. Dr. Woloshin is also the founder and director of the Lisa Schwartz Foundation for Truth in Medicine.

Dr. Woloshin earned his medical degree from the Boston University School of Medicine, completed internal medicine training at NYU/Bellevue Hospital, and completed a research fellowship at the White River Junction VA Medical Center in Vermont. He has an MS from the Geisel School of Medicine at Dartmouth.

Appendix B: NLM Board of Regents Public Service Working Group on ClinicalTrials.gov Modernization Meeting Schedule: August 2021–September 2022

Date	Focus
Facilitated Meetings	
August 20, 2021, and August 30, 2021	NLM Board of Regents Working Group meetings: Discussed work completed to date, next steps and call for additional expertise, and plans for beta releases and related communications
September 14, 2021	NLM Board of Regents meeting
January 28, 2022	NLM Board of Regents Working Group meeting: Discussed recent ClinicalTrials.gov Beta and PRS Beta releases; updates on the Fast Healthcare Interoperability Resources and ClinicalTrials.gov Citation Format projects; status, metrics, and feedback for the first beta releases; and an update on the next releases
February 8, 2022	NLM Board of Regents meeting
April 29, 2022	NLM Board of Regents Working Group meeting: Discussed an overview of usage of and feedback on ClinicalTrials.gov Beta, the challenges involved in developing plain language content for the ClinicalTrials.gov website, and a review of recent initiatives related to plain language for clinical trials and their results
May 10, 2022	NLM Board of Regents meeting
September 2, 2022	NLM Board of Regents Working Group meeting: Continued the discussion about plain language in the Protocol Registration and Results System; discussed updates on the latest beta releases, including user feedback and plans for further development; discussed the modernization communications plan; and discussed plans for the Working Group in 2023
September 13, 2022	NLM Board of Regents meeting

Appendix C: ClinicalTrials.gov Modernization Team Members: September 2021–September 2022

Thank you to National Center for Biotechnology Information leadership and the many team members who have continued to support the ClinicalTrials.gov modernization effort, including:

- Laura Akinyode, Protocol Registration and Results System (PRS) Beta Business Analyst (contractor, former team member)
- Stacey Arnold, PRS Subject Matter Expert (SME)
- Ben Babics, PRS Beta Developer (contractor)
- Eric Babin, PRS Beta Developer (contractor)
- Richard Ballew, ClinicalTrials.gov Business/Data Analyst (contractor)
- Jayaram Basava, ClinicalTrials.gov Beta Website Developer (contractor)
- Gunnar Baskin, PRS Beta Business Analyst (contractor)
- Annice Bergeris, ClinicalTrials.gov Acting Assistant Director, Information Research Specialist, and Operations Team Product Owner
- Jackie Bhadange, PRS Beta Cloud Architect (contractor)
- Landon Bressler, PRS Beta Business Analyst (contractor)
- Elissa Bush, ClinicalTrials.gov Technical Information Specialist
- Walter Cerna, PRS Beta User Interface (UI) Designer (contractor, former team member)
- Qiao Chang, ClinicalTrials.gov Technical Information Specialist
- Aletheia Cooper, PRS Beta Lead Developer (contractor, former team member)
- Monica Corley, PRS Beta Business Analyst (contractor)
- Cassiah Cox, ClinicalTrials.gov Project Director (contractor)
- Vinod Danam, PRS Beta Developer (contractor)
- Mandy Davis, User Experience (UX) Researcher (contractor)
- Austin Devereux, PRS Cloud Database Architect (contractor)
- Nachiket Dharker, PRS Beta Product Owner (contractor)
- Sergey Dikunov, ClinicalTrials.gov Beta Lead Developer (contractor)
- Sarah DiPasquale, UX Researcher (contractor)
- Heather Dobbins, ClinicalTrials.gov Lead Results Analyst and PRS Beta Product Owner (former team member)
- Jolie Dobre, PRS UX SME (contractor, former team member)
- Josh Dorsey, PRS Beta Business Analyst (contractor)
- Kayode Enwerem, PRS DevOps Engineer (contractor)
- Zachary Feiger, ClinicalTrials.gov Results Analyst and PRS SME (contractor, former team member)
- Anna Fine, ClinicalTrials.gov Acting Director and Offering Owner (former Assistant Director)

- Beth Fordice, ClinicalTrials.gov Technical Information Specialist
- Jane Fun, ClinicalTrials.gov and PRS Beta Developer (contractor, former team member)
- Madhurima Gade, ClinicalTrials.gov Beta Website Developer (contractor)
- Rithika Ganni, ClinicalTrials.gov Beta Test Automation Engineer (contractor)
- John Gillen, ClinicalTrials.gov Developer (contractor, former team member)
- Jennifer Glas, PRS Beta UX Designer (contractor)
- Elisa Golfinopoulos, Automation Support Team Product Owner (former ClinicalTrials.gov Results Team Lead)
- Slava Gorelenkov, ClinicalTrials.gov Technical Program Manager
- Derek Griffing, ClinicalTrials.gov Policy Analyst (former team member)
- Stephanie Gutierrez, PRS Beta UI Designer (contractor)
- Karen Hanson, Technical Writer (contractor)
- Wendy Harman, ClinicalTrials.gov Beta Website UX/UI Lead (contractor)
- Jimithy Hawkins, ClinicalTrials.gov Beta Website Business Analyst (contractor)
- Alan Hutchison, PRS Beta Developer (contractor, former team member)
- Nick Ide, ClinicalTrials.gov Developer (contractor, former team member)
- Rafis Ismagilov, ClinicalTrials.gov Beta Website Developer (contractor)
- Catherine Kihara, UX Researcher (contractor)
- Bill Killam, PRS Beta UX SME/Lead (contractor, former team member)
- Mike Killeen, PRS Beta Developer (contractor, former team member)
- Ryan Koning, PRS Beta UX Architect (contractor, former team member)
- Carl Leubsdorf, Consultant (contractor)
- Russell Loane, ClinicalTrials.gov Developer, Senior Systems Architect (contractor)
- John Lopez, ClinicalTrials.gov Developer (contractor)
- Vitaliy Lyoshin, ClinicalTrials.gov Scrum Master (contractor, former team member)
- LaShawn McCann, PRS Beta Developer (contractor, former team member)
- Jesus Mendiola Gomez, PRS Beta Quality Assurance Engineer (contractor)
- Alma Morales, ClinicalTrials.gov Beta Website UI Developer (contractor, former team member)
- Star Morin, PRS Beta Developer (contractor)
- Hibah Nazir, ClinicalTrials.gov Product Manager (contractor)
- Ngoc Nguyen, ClinicalTrials.gov and PRS Beta Developer (contractor)
- Kenneth Ni, ClinicalTrials.gov Beta UI Designer (contractor)
- Erin Nomiyama, PRS Beta UX Designer (contractor, former team member)
- Hardik Parekh, PRS Beta Lead Developer (contractor) (former PRS Beta Deputy Lead Developer)
- Chris Pemberton, PRS Beta Developer (contractor)

- Alison Powell, Senior Communications Specialist (contractor)
- Rupinder Randhawa, ClinicalTrials.gov Modernization Project Manager (contractor)
- Alexandra Rayner, ClinicalTrials.gov Beta Website Senior Content Strategist (contractor, former team member)
- Christina Robinson, ClinicalTrials.gov Web Content and Outreach Coordinator and Beta Website Product Owner
- Mary Sanders, ClinicalTrials.gov Project Manager (contractor)
- Michael San Gabriel, PRS Beta Developer (contractor)
- Gurdeep Sayal, PRS Beta Developer (contractor)
- Max Shestopalov, ClinicalTrials.gov Scrum Master (contractor)
- Stephen Shoemaker, ClinicalTrials.gov Beta Website and PRS Beta Information Architect and Content Strategist (contractor)
- Colin Small, ClinicalTrials.gov Beta UX Architect (contractor)
- Scott Smith, PRS Beta Product Manager (contractor)
- Maureen Strange, SME (contractor)
- Lucy Street, ClinicalTrials.gov Beta Website Content Strategist (contractor, former team member)
- Jessica Toth, UX Researcher (contractor, former team member)
- Tony Tse, ClinicalTrials.gov Analyst
- Maria Vargas, ClinicalTrials.gov Beta Website UX Developer (contractor)
- Shanel Vicente, ClinicalTrials.gov Beta Website UX Developer (contractor, former team member)
- Rebecca Williams, ClinicalTrials.gov Acting Director and Offering Owner (former team member)
- Susan Wimmer, Senior Editor (contractor)
- Karl Wolf, ClinicalTrials.gov Developer (contractor, former team member)
- Tirsit Wondemu, PRS Beta Developer (contractor)
- BJ Wright, PRS Beta Developer (contractor, former team member)
- Becca Xu, UX Researcher (contractor, former team member)
- Allison Yu, ClinicalTrials.gov and ClinicalTrials.gov Beta Website Developer (contractor)
- Maya Zuhl, Automation Support Team Technical Lead (contractor)

Appendix D: Abbreviations

An alphabetical list of the abbreviations used in this report is provided below.

- AI: artificial intelligence
- API: application programming interface
- BMI: body mass index
- BOR: Board of Regents
- CRE: clinical research enterprise
- CSV: comma-separated values
- DIA: Drug Information Association
- FDAAA 801: Section 801 of the Food and Drug Administration Amendments Act
- FHIR: Fast Healthcare Interoperability Resources
- JSON: JavaScript Object Notation
- MeSH: Medical Subject Headings
- NCBI: National Center for Biotechnology Information
- NIH: National Institutes of Health
- NLM: National Library of Medicine
- PRS: Protocol Registration and Results System
- QC: quality control
- Working Group: NLM Board of Regents Public Service Working Group on ClinicalTrials.gov Modernization