Report on the ClinicalTrials.gov Modernization Effort

Summary of Progress: 2019–21

SEPTEMBER 2021

Prepared for the NLM Board of Regents Public Service Working Group on ClinicalTrials.gov Modernization by ClinicalTrials.gov Program Staff, National Library of Medicine

NIH National Library of Medicine

ClinicalTrials.gov

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Report Overview

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. The National Library of Medicine (NLM) initiated a modernization effort in August 2019 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 modernization approach involves three key activities: stakeholder engagement, product development, and technical infrastructure enhancements. This multiyear effort aims to deliver an improved user experience on an updated platform that will accommodate growth and enhance efficiency.

The NLM Board of Regents Public Service Working Group on ClinicalTrials.gov Modernization (the Working Group) was established during the September 2019 NLM Board of Regents meeting. The Working Group provides a transparent forum for communicating and receiving input on modernization, and its members represent a range of the perspectives needed to inform this effort. During the past two years, the Working Group has provided invaluable input to assist in formulating the vision and strategic goals for the modernization effort, including clarifying which challenges cannot be directly addressed and instead require attention from the wider clinical research community. NLM's modernization activities, together with the Working Group's input, have supported the development of beta versions of a stand-alone ClinicalTrials.gov website and components of the Protocol Registration and Results System, which are expected to be released for broad public use in late fall 2021.

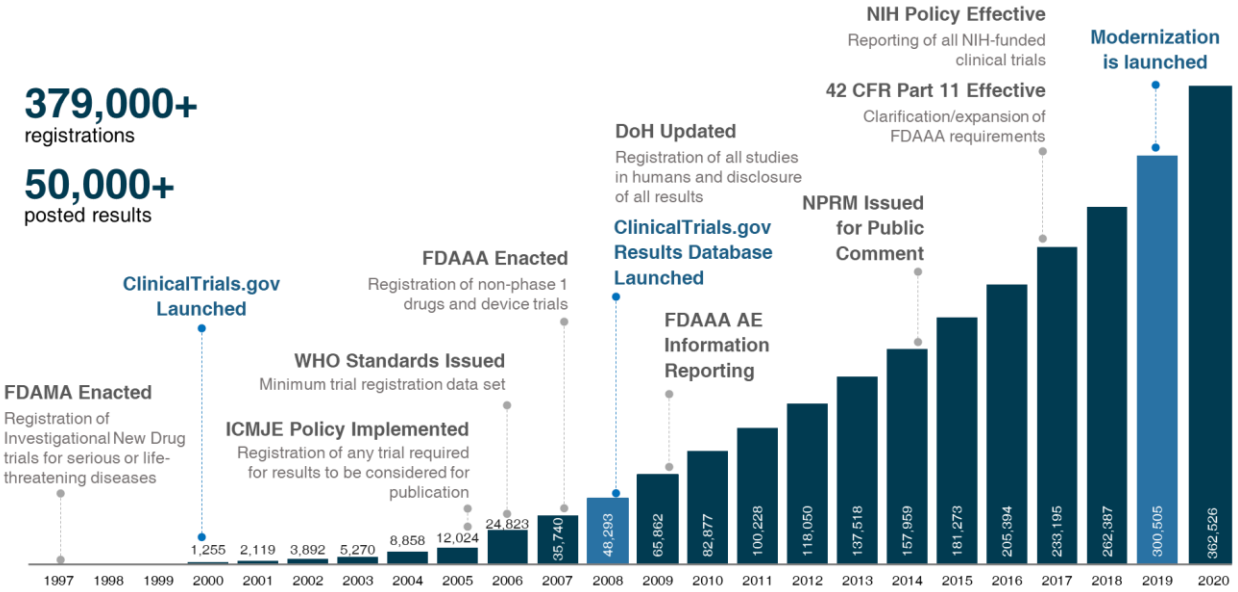
This report provides a summary of the ClinicalTrials.gov modernization effort from August 2019 to August 2021. It presents NLM's approach to modernization, presents the Working Group's input on various aspects of the modernization effort, describes user challenges and modernization priorities discussed by the Working Group for each strategic goal, shares NLM's product development plans and progress, and presents next steps for the Working Group and the modernization effort.

1. Introduction

ClinicalTrials.gov Overview

Launched in 2000, ClinicalTrials.gov is the world's largest public clinical research registry and results database, providing patients, families, health care providers, researchers, and others access to information on clinical studies for a wide range of diseases and conditions.[1] Operated by the National Library of Medicine (NLM), a component of the National Institutes of Health (NIH), this web-based resource lists records for nearly 400,000 clinical trials, observational studies, and expanded access programs. ClinicalTrials.gov makes available information provided directly by the sponsors and investigators conducting the research. More than 4.5 million unique visitors use the website monthly to find and learn about clinical studies, resulting in an average of 215 million page views each month. During more than 20 years of operation, ClinicalTrials.gov has grown considerably, both in terms of the number of records and the scope of information, following key policy and regulatory events (figure 1). This growth has better enabled ClinicalTrials.gov to advance and support the scientific and ethical goals of the clinical research enterprise while supporting a wide range of stakeholders who contribute to it and rely on it (figure 2).

Figure 1. Total number of posted study records per year on ClinicalTrials.gov and timeline of major events, from 1997 to 2020



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

The ClinicalTrials.gov reporting model (figure 3) relies on study sponsors and investigators to submit timely, high-quality clinical trial information about their research to the Protocol Registration and Results System (PRS), either voluntarily or to meet policy and regulatory requirements.[2,3,4,5,6,7,8] Following automated validation by the system, NLM conducts a limited manual quality-control (QC) review to check for apparent errors, deficiencies, and inconsistencies.[9] Following QC review, clinical trial information is posted on the ClinicalTrials.gov website and is also made available through its application programming interface (API).[10] The safety and scientific validity of studies listed on ClinicalTrials.gov is the responsibility of the study sponsors and investigators; listing a study on the site does not mean that it has been evaluated by the U.S. federal government.[11]

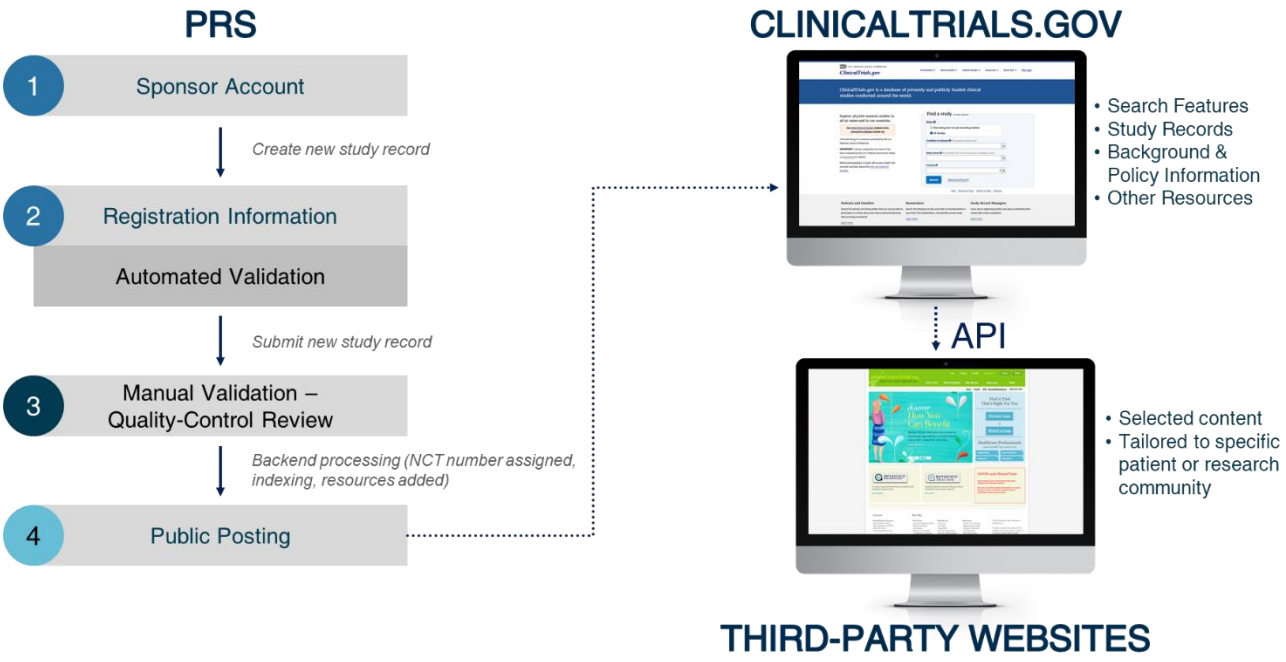
Figure 2. Benefits of comprehensive reporting

Benefits of Comprehensive Registration and Results Reporting

All contribute to increased public trust in clinical research

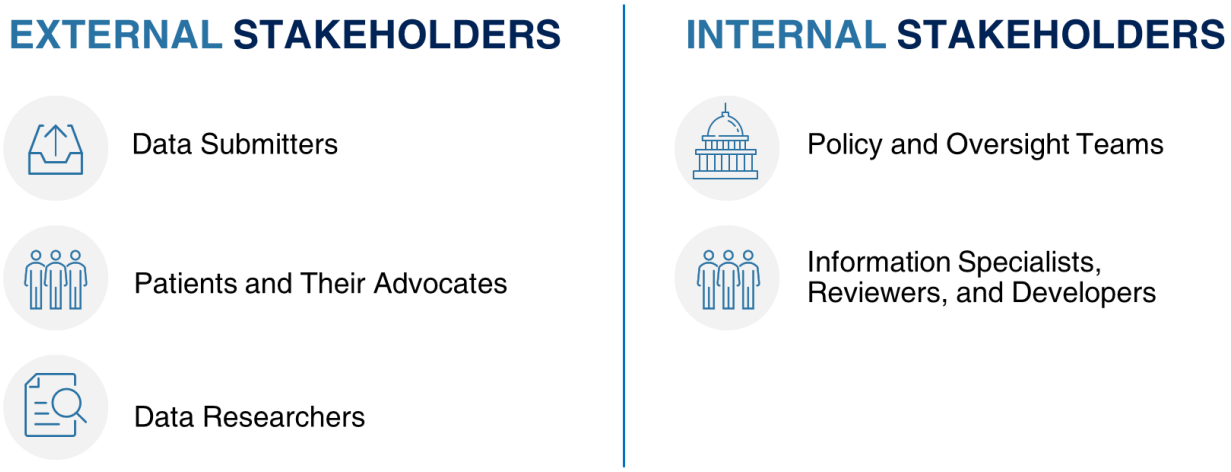
- Honor commitment to participants that their contributions will advance science; support enrollment
- Mitigate publication bias
- Advance stewardship and accountability
  - Identify unmet research needs
  - Facilitate complete reporting
  - Avoid unnecessary study duplication
  - Evaluate research integrity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

Figure 3. Schematic of the ClinicalTrials.gov reporting model information flow



The key stakeholder groups for ClinicalTrials.gov can be categorized as either external or internal stakeholders (figure 4).

Figure 4. Key ClinicalTrials.gov stakeholders



The three key external stakeholder groups, with substantial heterogeneity within and among them, are as follows:

- Data submitters, generally study sponsors and investigators, who are responsible for submitting, updating, and managing clinical trial registration and results information through the PRS. The information provided by this group is listed on ClinicalTrials.gov for use by others.
- Patients and their advocates, including health care providers, who find and use information about clinical trials for themselves or others, including to identify potential studies for participation
- Data researchers, including meta-researchers, medical librarians, and journal editors, who use clinical trial information to study the clinical research enterprise for detecting trends in research and gaps in medical knowledge, identifying trials for use in systematic reviews and meta-analyses, and validating reported outcome measures and study designs through ClinicalTrials.gov or its API

The two key internal stakeholder groups are (1) various clinical research management, policy, and oversight groups, such as federal regulatory and clinical research funding agencies, and (2) ClinicalTrials.gov staff information specialists, registration and results reviewers, and technical developers, who play a vital role in facilitating the information submission, QC review, and posting processes.

ClinicalTrials.gov Modernization Effort

NLM initiated this effort in August 2019 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.[12] The multiyear modernization effort aims to deliver an improved user experience on an updated platform that will accommodate growth and enhance efficiency.

NLM Board of Regents Public Service Working Group

To support this modernization effort, the NLM Board of Regents Public Service Working Group on ClinicalTrials.gov Modernization (the Working Group) was established in September 2019 by the NLM Board of Regents and was charged with providing a transparent forum for communicating and receiving input about the modernization effort.[13] It is specifically tasked with exploring ways that NIH can:

(1) Maintain the integrity of ClinicalTrials.gov as a trusted resource
(2) Maximize the utility of the growing corpus of information
(3) Connect with stakeholders through engagement to ensure that their evolving needs are understood

Working Group members represent a range of the perspectives needed to inform this effort, including those of patients and their advocates, health care professionals, journal editors, meta-researchers, and data submitters (appendix A). Several members, including the chair, were drawn from the NLM Board of Regents; external members were drawn from key stakeholder groups, including academic, industry, and nonprofit organizations; two ex officio members were from the NIH Offices of Science Policy and of Extramural Research; and the Acting Director of ClinicalTrials.gov served as Executive Secretary. The group met 10 times between December 2019 and August 2021 and reported regularly in open session to the full NLM Board of Regents (appendix B).

Modernization Progress

This report provides a summary of the progress of the ClinicalTrials.gov modernization effort during its first two years, from August 2019 to August 2021. It presents NLM's approach to modernization (section 2), presents the Working Group's input on various aspects of the modernization effort (section 3), describes user challenges and modernization priorities discussed by the Working Group for each of the three strategic goals (section 4), shares NLM's product development plans and progress (section 5), and presents next steps for the Working Group and the modernization effort (section 6). A list of the abbreviations used in the report is provided in appendix C.

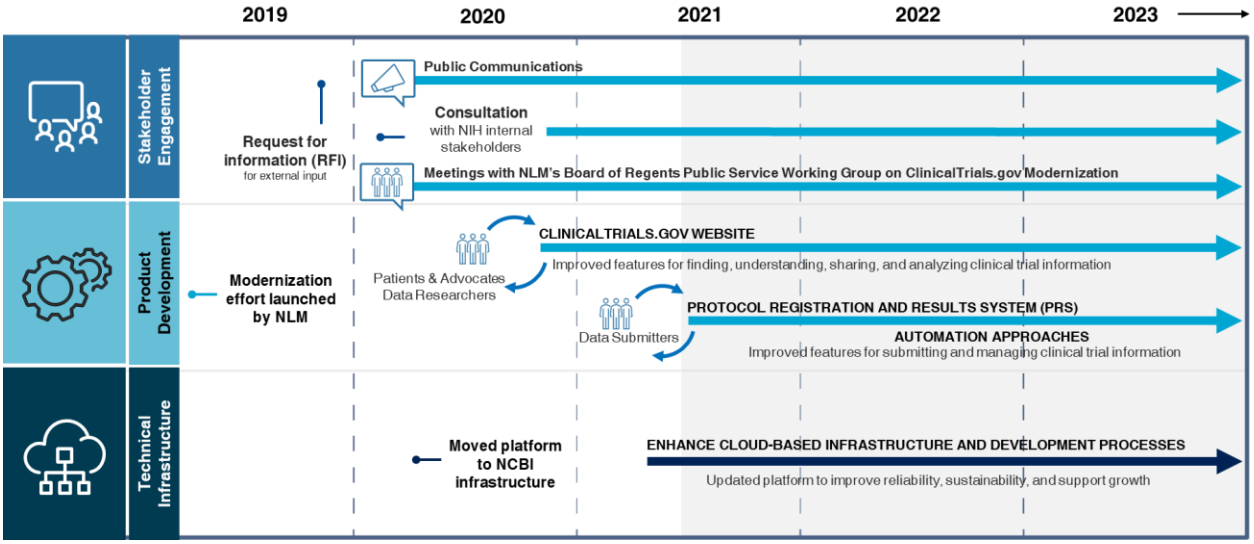
2. Approach to Modernization

NLM's approach involved first obtaining broad stakeholder feedback through a public request for information (RFI), followed by a narrowing of range to obtain focused, in-depth user feedback to inform the design and development of the beta ClinicalTrials.gov website and components of the beta PRS in order to ensure that these products addressed user needs. Next steps include releasing the beta versions to users and, again, obtaining broad stakeholder feedback; adding more features; and making further refinements. The modernization effort involves three key activities, also shown in the strategic roadmap (figure 5):

- **Stakeholder engagement** with internal and external stakeholders, including user research and a governance structure through the Working Group
- **Product development** involving Agile teams, user-centered design with continuous user feedback, and usability evaluation
- **Technical infrastructure enhancements** of the system platform and alignment with the NLM National Center for Biotechnology Information (NCBI) cloud-infrastructure strategy to improve system reliability and sustainability and to provide new features and capabilities to meet user needs

To support these activities, NLM organized the work effort across four primary teams focused on (1) the ClinicalTrials.gov website, (2) the PRS, (3) automation support for the PRS, and (4) coordination with and maintenance of the current website and PRS. This also required establishing new business processes to support efficiency, clear communication, and effective risk and resource management. A list of individuals involved in the modernization effort to date is provided in appendix D. The creation of these teams and processes was intended to not only support the modernization effort but also generate sustainable approaches for continuous innovation and professional growth that will endure long after the current effort ends.

Figure 5. Strategic roadmap for ClinicalTrials.gov modernization



Stakeholder Engagement

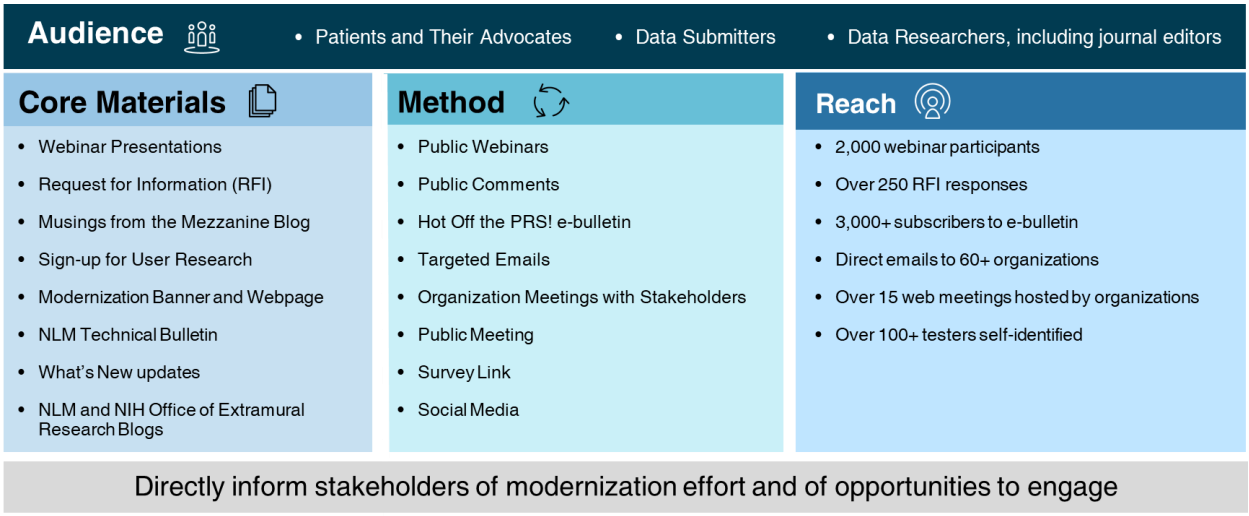
From the outset of the modernization effort, NLM sought to include input from individuals and organizations with diverse experiences and viewpoints to ensure that the process would be responsive to stakeholder needs. The approach to stakeholder engagement encompassed both broad stakeholder engagement activities and focused user research.

Broad Stakeholder Engagement Activities

The aim of stakeholder engagement activities was to understand how the system can better support stakeholders and to identify opportunities for improving its compatibility with existing clinical trial management tools and processes. NLM initially consulted leaders across the NIH Institutes and Centers to understand how ClinicalTrials.gov could better fulfill NIH's goals of clinical trial stewardship and transparency.[14] NLM subsequently expanded its engagement program outward, issuing an RFI to solicit public comments on the website's functionality, the information-submission processes, and the use of data standards.[15] More than 250 responses to the RFI were received from members of the public,[16] and the April 2020 virtual public meeting summarizing those responses and featuring presentations from members of the Working Group attracted nearly 400 attendees.[17] Subsequently, more than 600 individuals attended the February 2021 Modernization Update webinar, during which opportunities for user input were shared and the modernization roadmap was previewed.[18]

NLM continually updated stakeholders using a comprehensive communications strategy (figure 6) that included blog posts, the Hot Off the PRS! e-bulletin, information on the ClinicalTrials.gov Modernization webpage, targeted internal and external stakeholder meetings, and public webinars. All of the modernization materials are archived on a dedicated webpage and available for viewing anytime.[19]

Figure 6. Communications strategy



Focused User Research

After NLM analyzed the initial broad stakeholder feedback, staff subsequently identified topics for further exploration through focused user research. This research consisted of one-on-one interviews conducted by NLM with 70 individuals across the three external user groups (data submitters, patients and their advocates, and data researchers) to understand each user's journey, including how each individual interacts with the website and the PRS. Each person was asked about motivations, past experiences, and perspectives on the role that the website and the PRS play in the individual's life. NLM then coded, analyzed, and synthesized the information from the user interviews to produce reports that contain key findings and recommendations for modernization as well as user stories that suggest opportunities for feature development. The Working Group also considered the topics identified during user research, along with the reports and user stories, and made recommendations (section 3).

This user research validated previously obtained feedback and findings and provided additional input for product design and development during the modernization effort.

Product Development

The modernization teams have adopted Agile processes to support development of the modernized ClinicalTrials.gov website and the PRS. "Agile" design refers to software development methodologies that rely on iterative development, where requirements and solutions evolve through collaboration among cross-functional teams.[20]

Incorporating the input of real users into the design cycle helps ensure that their needs are understood and met.

The modernization teams work in two-week increments to deliver high-value designs and implement working software. Each user-centered design cycle is informed by formative research on user needs, development of new product features, feedback from prototype evaluation with a small group of actual users, and revisions to software coding. These activities are followed by usability research with actual users, and then the cycle repeats. Incorporating the input of real users into the design cycle helps ensure that their needs are understood and met.

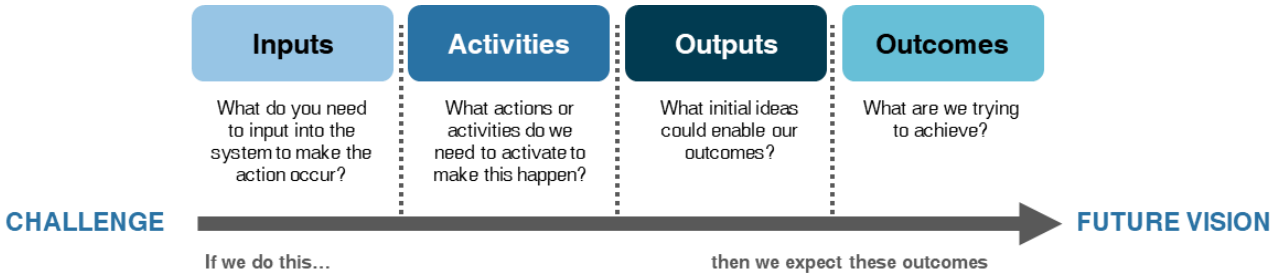
Technical Infrastructure Enhancements

Along with the development of specific products, NLM is building an updated technical infrastructure that leverages industry-standard technologies using a combination of off-the-shelf and customized solutions to improve system reliability and sustainability and to better support new features and capabilities to meet user needs. Changes to date include migrating the ClinicalTrials.gov development, testing, and production environments to NCBI's hardware, software, and development infrastructure; adopting NCBI's security posture (e.g., network, firewall, and patching methodologies); integrating new software development tools to support product development; and undertaking initial activities to migrate to a cloud infrastructure that will support the beta release of the website in late fall 2021.

3. Working Group Input on Modernization

As directed by its charge, the Working Group explored ways for NIH to maintain the integrity of ClinicalTrials.gov as a trusted resource for a diverse group of stakeholders, maximize the utility of the growing corpus of submitted information, and connect with stakeholders to ensure that their evolving needs are understood. The Working Group provided input on the vision and strategic goals for the modernization effort, its outcomes, the related challenges, and resources and key activities. A framework focused on developing a change strategy (figure 7) was used to integrate Working Group members' expertise with the feedback obtained from stakeholder engagement activities and the broader approach planned by NLM's modernization team.

Figure 7. Components of a strategy-for-change framework



Overall, this framework supplied a template for identifying changes that will benefit users as well as for planning the resources, or inputs, needed to conduct activities to achieve the desired outcomes directly through modernization. Input from the Working Group helped define the boundaries of the modernization effort and guided discussions about the user challenges and considerations central to achieving the goals of modernization.

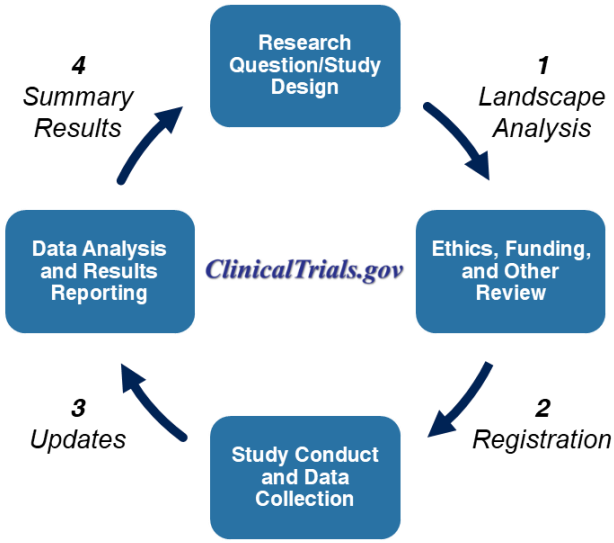
Vision and Strategic Goals for the Modernization Effort

Recognizing the critical role that ClinicalTrials.gov has played — and continues to play — in support of the clinical research enterprise and its many stakeholders, the Working Group endorsed a vision for a modernized ClinicalTrials.gov that enables it to serve as "an essential, transparent, and trusted part of the research ecosystem to advance medical knowledge."

This vision reinforces the role of ClinicalTrials.gov in supporting transparency throughout the study life cycle (figure 8). The Working Group also highlighted the importance of addressing the needs of all three primary external user groups as well as those of internal stakeholders. The Working Group noted that, among the external user groups, the needs of data submitters and data researchers appeared to be more tractable.

The Working Group emphasized that ClinicalTrials.gov's strength is its role as a central data aggregator, further bolstered by the laws and policies that require systematic registration and results reporting to ClinicalTrials.gov.[21] As such, the greatest value that ClinicalTrials.gov provides to stakeholders is enabling them to acquire clinical trial information of the highest quality and organizing that information for use on ClinicalTrials.gov and for reuse by third parties who can better customize information delivery to assist particular communities or specific research.

Figure 8. Role of ClinicalTrials.gov throughout the study life cycle



To realize the modernization vision, 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.
(3) Trial information, resources, and tools provide value to the research ecosystem.

Each of the strategic goals, with its corresponding user challenges and modernization priorities, is discussed in more detail in section 4.

In the pursuit of these goals, the Working Group noted the importance of adherence to the FAIR Guiding Principles for scientific data management and stewardship[22] to ensure that clinical trial information is *Findable*, *Accessible*, *Interoperable*, and *Reusable*. These principles reflect the importance of interoperable workflows across the clinical trial life cycle and the need for metadata to be easily accessible to support discovery.

Modernization Outcomes

The Working Group discussed and prioritized specific pragmatic as well as aspirational outcomes associated with trial registration and results reporting that the modernization effort should aim to better support. These outcomes included the following:

- Enhancing transparency across the clinical research enterprise to support public trust in clinical research
- Identifying research gaps and opportunities (e.g., facilitating landscape analyses)
- Providing greater insight into the clinical research enterprise to improve research quality
- Increasing public availability of information about ongoing and completed research
- Evaluating the integrity of reported research against the prespecified research plan

- Ensuring access to all trial results
- Finding trustworthy health-related information that meets various health-literacy needs
- Discovering all available trial results and related data sets (e.g., individual participant-level data)
- Supporting equitable and inclusive access to clinical research information and advancing efforts to evaluate diversity in clinical research

Challenges

The Working Group identified key high-level challenges, or obstacles, to accomplishing the modernization vision which must be considered and managed as part of the effort. Chief among them are the tensions inherent in serving a wide range of users and the necessity of balancing divergent user needs to ensure that the needs of all key stakeholder groups are met. Also, ClinicalTrials.gov has the obligation to convey the website's purpose and limitations clearly and prominently, in particular, the fact that a study's listing on ClinicalTrials.gov, by itself, does not mean that the federal government has endorsed or otherwise approved the research. The Working Group affirmed that the value of listing research not approved by the government for the purpose of supporting public accountability for clinical research activities outweighs the potential challenges involved. Finally, ClinicalTrials.gov needs to ensure that information provided by data submitters is timely and of high quality. The Working Group also noted that challenges related to the completeness and quality of the clinical trial information that appears on ClinicalTrials.gov depends, respectively, on the prevailing legal and policy framework and the quality of the information submitted by sponsors and investigators.

Key High-Level Challenges

- Balancing divergent user needs to ensure that the needs of all key stakeholder groups are met
- To convey the website's purpose and limitations clearly and prominently
- To ensure that information provided by data submitters is timely and of high quality

Resources and Key Activities

The Working Group identified resources needed for the modernization effort, including appropriate funding levels, timely access to staffing and expertise aligned with the needs of modernization, strong business processes to manage and coordinate the scale of the effort, appropriate technical infrastructure capabilities, and insights into current and evolving stakeholder needs.

The Working Group provided input on the three key activities (table 1) described as part of the modernization approach: stakeholder engagement, product development, and technical infrastructure enhancements.

Table 1. Key Modernization Activities and Related Working Group Support

Key Activity	Working Group Support
Stakeholder Engagement	• **Working Group Meetings:** Participated in meetings (appendix B) including three facilitated discussions using a strategy-for-change framework (figure 7) to discuss the scope and priorities of modernization activities • **Outreach Planning:** Supported broad and targeted outreach to key external stakeholder groups (figure 4) and suggested ways to optimize engagement and outreach activities • **RFI:** Provided feedback on draft RFI questions to solicit actionable information from stakeholders and identified gaps in proposed RFI topics (section 2) • **Public Meeting:** Assisted with planning the virtual public meeting (section 2). Several members participated in panel presentations, highlighting key challenges to consider. • **Roadmap Development:** Assisted with prioritizing themes identified by outreach and engagement activities for developing a project roadmap (figure 5) • **NLM Communication Strategy:** Shared feedback on NLM's approach to providing stakeholders with updates and a timeline of activities as soon as they become available (figure 6)
Product Development	• **User Evaluation Planning:** Provided feedback to help ensure transparency of the user prototype evaluations. The Working Group emphasized the importance of explaining to participants how their input will be used, even if specific suggestions cannot be implemented.
Technical Infrastructure Enhancements	• **Strategy Planning:** Provided feedback on NLM plans to enhance system components incrementally while minimizing disruptions for users and continuing to deliver improved services

4. Working Group Input on User Challenges and Modernization Priorities, by Strategic Goal

The Working Group provided input on the three strategic goals, focusing on external stakeholders. The Working Group's facilitated discussions helped identify stakeholder challenges that the modernization effort can address *directly,* as well as identified challenges that can be addressed only *indirectly* by NLM in order to encourage other leaders and stakeholders across the clinical research ecosystem to advance and address those user needs.

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

One strategic goal of the modernization effort is to provide clinical trial information that is current, complete, and reliable. This goal primarily affects data submitters (i.e., study sponsors and investigators), who need to register clinical trials and report summary results information in a timely and efficient manner to fulfill policy and regulatory requirements. The goal was prioritized because high-quality information is essential for meeting the needs of external end users of the data, such as patients, patient advocates, and data researchers, who rely on the availability of accurate and up-to-date clinical trial information. NLM staff responsible for QC review processes are also an important internal user group impacted by this goal, but they were not discussed directly by the Working Group.

Data submitters vary by level of scientific knowledge and experience with the PRS. Information is submitted by individual users through a PRS organization account affiliated with their organization. Currently, approximately 218,000 PRS users are associated with more than 28,000 organizational accounts. While most of these users are individually responsible for fewer than 10 study records, others have access to and manage more than 5,000 study records at different stages of reporting, many of which need to be monitored for updates to their registration and/or results information. Some organizations have developed their own systems or rely on third-party services for uploading clinical trial information but are still dependent on the API and related PRS services.

During a Working Group facilitated discussion, two members described data submission challenges from the perspectives of a large pharmaceutical company and an academic organization.[23] Drawing on the experience of Working Group members, the RFI responses, and findings from other stakeholder engagement activities and user research, we grouped data submitters into categories, based on their experience, training, and available resources, and defined specific challenges for each group (table 2).

Table 2. Goal 1 Challenges, by Data Submitter Category

Data Submitter Category	Challenges
All data submitters	• Understanding regulatory and policy requirements and their application to specific clinical trials • Accessing good reporting practices for a broad range of study designs and issues (e.g., master protocols) • Updating standard operating procedures (SOPs) and training materials as the PRS changes • Learning and optimizing the use of system features to meet individual needs • Countering a perceived lack of incentive for providing timely, high-quality data or, conversely, a lack of penalty for failing to do so
Frequent users with extensive institutional support (e.g., PRS Administrators for biomedical companies who may also use third-party services)	• Coordinating across a large organization • Reporting to multiple international registries with differing requirements • Assuming ownership of another company's portfolio after a corporate merger or acquisition
Frequent users with minimal institutional support (e.g., PRS Administrators for academic organizations)	• Managing frequent staff turnover (including principal investigators) and onboarding new PRS users (including support staff with little scientific training) • Lacking fully dedicated staff, resulting in dependence on PRS staff and resources to make up for a lack of expertise and support
Infrequent users with varying levels of institutional support (e.g., individual principal investigators, trial staff such as biostatisticians, study coordinators)	• Encountering a steep learning curve for using the PRS as well as for formatting clinical trial information to meet the QC review criteria

As noted, data submitters have differing needs based on their experience, training, and available resources. After considering those differences, the Working Group identified the goal 1 challenges that could be addressed directly through the modernization effort to support data submitters and, as a result, also support end users of the data. The priorities included the following:

- Enhancing features (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 to make them more flexible and customizable
- Expanding the reference library of PRS study record examples illustrating good reporting practices for specific study designs (e.g., master protocols) or approaches for specific reporting issues
- Improving automated just-in-time PRS support and resources to limit the need for one-on-one assistance, particularly with the QC review process

- Exploring how to improve access to one-on-one support (e.g., dedicated help line)
- Supporting best practices for reporting clinical trial information for underrepresented populations, including by sex, gender, race, and ethnicity
- Providing sufficient advance notice of planned PRS changes to give organizations ample time to update their SOPs, templates, and training and educational materials

During this discussion, it became clear that some challenges were out of scope for the current modernization effort because ClinicalTrials.gov, by itself, is unable to achieve them directly. Such challenges, which include the following, constitute a call to action for other stakeholders within the clinical research enterprise:

- Need for leadership at research institutions to instill an organizational culture that rewards transparency,[24,25,26], including the following:
  - Providing centralized, dedicated resources to oversee and support high-quality clinical trial information submissions by researchers[27,28,29]
  - Awarding academic "credit" for consistent submission of high-quality clinical trial information in a timely manner[30]
- Need for coordinated support systems throughout the clinical trial life cycle, including:
  - Protocol development, including structured protocol templates[31]
  - Institutional review board (IRB) processes to enhance oversight of the protection of human subjects before and during study conduct[32]
  - Adapting clinical trial management systems to better support summary results reporting

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

Another strategic goal is to ensure that all ClinicalTrials.gov users, including patients, patient advocates, and data researchers, can easily find and use information about clinical trials. This goal focuses on all users who rely on ClinicalTrials.gov for information.

A total of 4.5 million users visit ClinicalTrials.gov each month, and recent survey data (July 2019–June 2021; n = 12,515) indicate that about 55% of users are researchers, 35% are patients, and 10% are identified as "other" (e.g., students, journalists, financial analysts and investors, attorneys). Users are about evenly split between frequent visitors (45% use the site daily to monthly) and first-time visitors (45%), with the remaining 10% using the site occasionally (every six months or less).

During a Working Group facilitated discussion, two members described website user challenges from the specific perspectives of a clinical trial patient navigator and a data researcher with IRB expertise.[33] Drawing on the experience of Working Group members, the RFI responses, and findings from other stakeholder engagement activities and user research, we grouped website users into categories and defined specific use cases and challenges for each group (table 3).

Table 3. Goal 2 Challenges, by User Category and Example Use Case

User Category	Example Use Case	Challenges
All users	• Finding information about studies of interest, related studies, or a specific, individual study[34,35]	• Misunderstanding the role and scope of ClinicalTrials.gov • Using unstructured data elements (e.g., intervention name, condition, outcome measures, eligibility criteria) • Needing to keep search queries active to identify newly added trials that meet the search criteria • Saving complex search queries containing multiple fields and terms for future search-and-retrieval efforts[26]
Patients and their advocates (including health care professionals)	• Learning about clinical research • Identifying potential studies for themselves or close contacts to participate in	• Lacking familiarity with clinical research terms, concepts, and processes • Narrowing search results after retrieving many studies • Finding information related to personal logistics (e.g., insurance, travel) • Understanding the information in a study record • Knowing what to do next after identifying trials of interest • Needing general health information • Distinguishing higher-quality trials from lower-quality trials
Data researchers (e.g., journal editors, meta-researchers, clinical trialists, medical librarians, funders)	• Better understanding the research landscape for a particular topic[36] • Conducting meta-research on the clinical research enterprise to characterize research challenges and needs[37] • Evaluating the reporting of a specific clinical trial against the prespecified research plan (e.g., for biomedical journal editorial and peer reviews)[38]	• Knowing which search terms will retrieve which study records • Encountering inconsistent quality and completeness of study record information[39] • Encountering export formats that do not fully support analytic needs • Identifying when results are available (on ClinicalTrials.gov or in publications) • Understanding which data are available on ClinicalTrials.gov • Encountering incomplete XML-formatted data or download tools • Distinguishing major changes from minor changes when comparing study record versions

Although patients, patient advocates, and data researchers use the website for different purposes, the groups share certain needs and challenges. After considering those commonalities, the Working Group identified the goal 2 challenges that could be addressed directly through the modernization effort. The priorities included the following:

- Improving the search experience: Add features to better manage search results, such as 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).[40,41,42]
- Enhancing user resources: Help users learn about website functions specific to their group, for example, a glossary of common site terms, background information on study participation, and training on tools for advanced functions such as the API.

Although patients, patient advocates, and data researchers use the website for different purposes, the groups share certain needs and challenges.

- Adding plain language content and improving accessibility: Provide an accessible and inclusive website experience by using plain language to support all users and ensure that the site can be easily used on all devices and by anyone with a physical disability. The Working Group noted that informed consent documents could be leveraged as a source of vetted information in plain language.
- Providing contextual support: Connect 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: Evaluate opportunities to improve standardization for key data fields, including conditions, interventions, eligibility criteria, and outcome measures. This is especially important in relation to the search experience.
- Increasing the visibility of the ClinicalTrials.gov website: Consider whether the website's resources should be shared more broadly through an educational campaign or search engine optimization.

As with goal 1, the Working Group considered other goal 2 challenges to be out of scope for the current modernization effort because ClinicalTrials.gov, by itself, cannot address them directly. The group identified the following challenges as ones that might be addressed by others who contribute to the clinical research enterprise:

- Need for consistent, high-quality clinical research with social and clinical utility, which includes, for example, addressing the issue of "uninformative" clinical trials[43] and considering how to develop quality indicators and involves the following:
  - Addressing patients' expectations that listed studies meet a certain quality standard

  - Addressing data researchers' desires for appropriate tools to support independent evaluation
- Need for support for external stakeholders to continue the development of targeted solutions to best serve individual communities, for example:
  - Encouraging trial navigation services provided by third-party organizations to benefit patients
  - Allowing the combining of data from multiple sources (e.g., disease prevalence, U.S. Census) to support research analyses
- Need for support related to clinical trial information listed on ClinicalTrials.gov, including:
  - Ensuring that the contact persons listed for a study are reachable, knowledgeable, and able to assist with queries from potential participants
  - Addressing challenges related to adequately preparing health care professionals to support patients who have questions about the research and participation in clinical trials

The Working Group noted that NLM should continue to:

- Focus on a limited QC review of submitted information for apparent errors, deficiencies, and internal inconsistencies.
- Play a role in providing tools that support data reuse by third parties to serve community needs.

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

The final strategic goal addresses how the modernization effort can ensure that the trial information, resources, and tools on ClinicalTrials.gov provide value to the clinical research ecosystem (e.g., in response to the COVID-19 pandemic). This goal focuses on NLM's role as a central data aggregator and the importance of making relevant contextual information (e.g., publications, systematic reviews, related data sets) discoverable and ensuring that clinical trial information is reusable by others. Although this goal was not the focus of a Working Group meeting, future Working Group activities could address the topic specifically and more fully.

This goal focuses on NLM's role as a central data aggregator and the importance of making relevant contextual information (e.g., publications, systematic reviews, related data sets) discoverable and ensuring that clinical trial information is reusable by others.

The Working Group noted that the clinical research ecosystem beyond ClinicalTrials.gov contains challenges that users would like addressed, including the need to improve

research quality and to advance greater inclusion of underrepresented populations in clinical research. While NLM cannot directly address such challenges, it will, where possible, ensure efficient access to information on ClinicalTrials.gov, with appropriate tools and resources to support others who undertake these endeavors.

Key aspects of achieving this goal include the following:

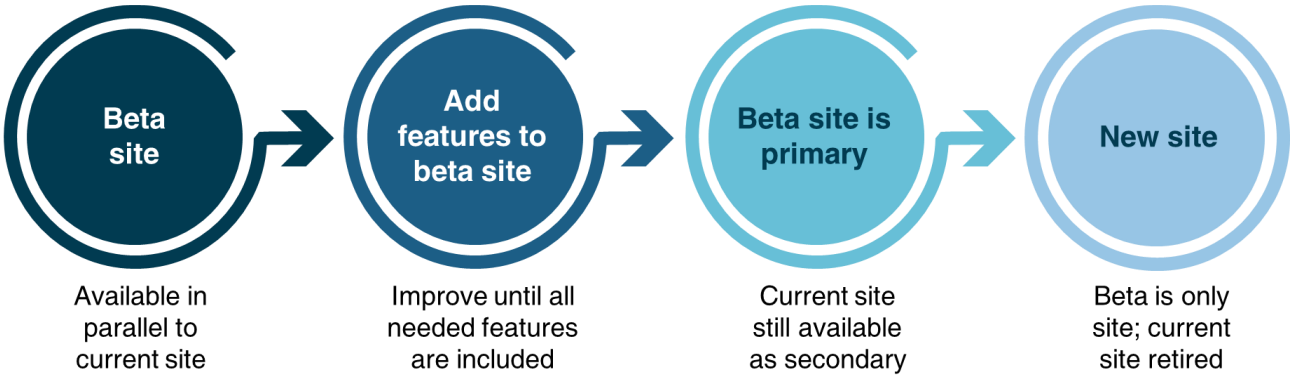
- Advancing common data formats that support interoperability of clinical trial information submission with data sources such as protocol templates and clinical trial management systems
- Supporting best practices for data reporting, including important patient demographics such as sex, gender, race, and ethnicity, to better support data reuse
- Evaluating opportunities to standardize unstructured text in key fields (e.g., condition, intervention, eligibility criteria) that currently limits ease of reuse
- 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 clinical research enterprise or the clinical research landscape or who create customized dashboards
- Providing resources that allow users to find important contextual information such as related health information, results publications, systematic reviews, and data sets

5. NLM Product Development Plans and Progress

NLM has made significant progress in the development of the modernized ClinicalTrials.gov website and PRS. A core principle of the implementation is to minimize disruption to users while continuing to deliver improved services to maximize the value of these systems to the people who rely on them. NLM has developed continuity of service approaches for the website and the PRS to ensure a smooth and efficient transition to updated features (figure 9). Making the new user experiences available in parallel to the current systems will allow for adequate testing and refinement and for the addition of more features and functions without disrupting the current user experience. NLM will gradually transition users to the new sites, or site components, when they are complete and retire the legacy sites. Stakeholders will continue to receive timely updates, which will provide transparency regarding the modernization process and set appropriate expectations.

Making the new user experiences available in parallel to the current systems will allow for adequate testing and refinement and for the addition of more features and functions without disrupting the current user experience.

Figure 9. Transition from the current site through the beta site to new products during modernization



New PRS Experience

The new PRS experience is being developed with a new technical infrastructure that is being integrated into the current PRS. The modernization approach segments the work effort into discrete components, allowing for the phased delivery of enhancements to improve the overall user experience.

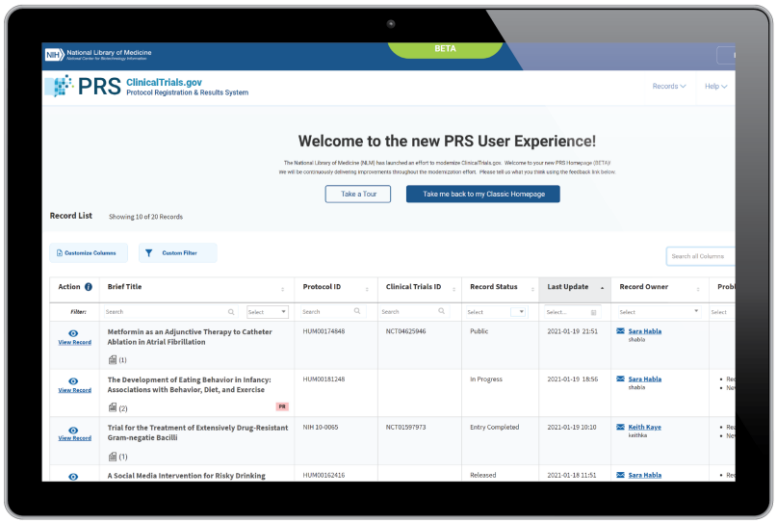
The first beta PRS release, planned for late fall 2021, incorporates the priorities identified by the Working Group to provide a more intuitive experience, add more flexible and customizable workflows, and help data submitters more easily identify trials that may be subject to reporting requirements. This first release will introduce users to a modern and intuitive design (figure 10) and will include new workflow and portfolio management features, such as the following:

- A customized portfolio display with multicolumn filtering so that users can easily find specific records
- The ability to email clinical study staff directly from the record list so that users can reduce the number of steps in their daily workflow
- Additional information about the records in a portfolio so that users can view more data at a glance
- Multiple file-format download options to accommodate a variety of user needs

The goals for this first set of PRS improvements are to:

(1) Introduce users to the new interface technology and evaluate its real-world performance
(2) Provide users with improved functionality to manage their record portfolios and workflows
(3) Collect user input to inform future development activities

Figure 10. Preview of the beta PRS home page (in development and subject to change)



Following validation of the technology's performance and iterative incorporation of revisions based on user feedback, the next release is expected to include additional advanced features to help users manage their record portfolios. These may include information and tips to assist with planning for upcoming dates and events, features to easily identify and carry out action items, and the ability to execute more functions directly from the record list.

Future releases of the beta PRS product will focus on other priorities identified by the Working Group and will include components of the processes for submitting registration and results information, addressing QC review comments, and managing accounts. Specific details of each component and release will be communicated to stakeholders as that information becomes available.

New ClinicalTrials.gov Experience

The modernized ClinicalTrials.gov website is being developed on a new technical infrastructure in parallel to the current site. The beta website will be launched with basic features to ensure that its underlying technical platform is functioning as expected before incorporating more advanced, complex features. Once the beta site is complete, it will become the primary website, and the current website will gradually be phased out.

The product design goals derived from user research (figure 11), as well as from the Working Group's input, are being applied during development of the new website experience. These design goals correspond to the overall goals for improving the ClinicalTrials.gov user experience and will be achieved incrementally as new releases are added to the beta site.

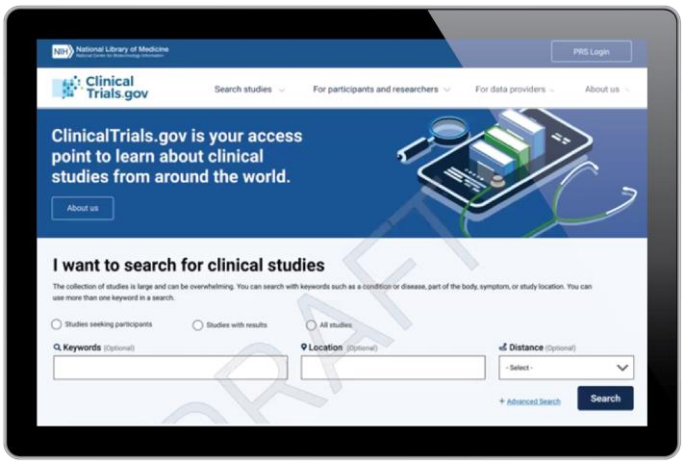
Figure 11. Modernization product design goals from user research

Onboarding	Make site's purpose clear to users, regardless of entry point.
Search Experience	Easily find studies of interest and narrow search results. Be able to implement complete parameters from the outset.
Study Record Experience	Easily navigate study records and comprehend content areas. Organize study records to be fit-for-purpose.
Information Architecture	Intuitive navigation and enable users to efficiently provide feedback.
Easy-to-Understand Content	Visually present background information with clear next steps.
Appropriate Context	Connect users with trustworthy content related to the research.

The first beta release incorporates the priorities identified by the Working Group by introducing a modern look and feel, with responsive design to better support users on mobile devices, and providing content in plain language and contextual educational information. Limited in scope, this release will include the following features:

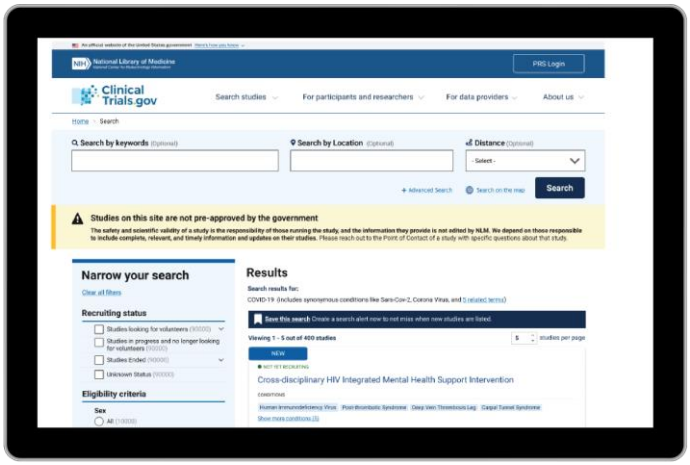
- A new home page with a welcome message and a simple search with different underlying search technology (figure 12)
- A search results page with filters to refine search results (figure 13). New features will include an updated algorithm for capturing potentially relevant results and study cards that highlight key information such as study and recruitment status, study locations relevant to the user's search, and related terms within the study record.

Figure 12. Preview of the beta ClinicalTrials.gov home page (in development and subject to change)



- A redesigned study record page with an in-record navigation menu, collapsible sections, interactive study results tables for data researchers, and an integrated Google Maps API for viewing study locations
- Updated background information about ClinicalTrials.gov and clinical research studies, presented in plain language

Figure 13. Preview of the beta ClinicalTrials.gov search results page (in development and subject to change)



Following validation of the technology's performance and implementation of any revisions in response to user feedback, subsequent releases will incorporate other priorities identified by the Working Group that are expected to address additional patient, patient advocate, and data researcher needs, such as:

- Updates on saved searches
- Customizable downloads with multiple file-format options
- Easy-to-find and easy-to-view record histories
- Advanced search functions
- An upgraded API
- Technical support information
- Help content specific to using the website
- Easy connections to trusted health information
- Standardization of key items, where feasible

6. Next Steps

NLM is grateful to the Working Group for the input provided during this initial phase of the modernization effort: It has helped validate priorities and more clearly identify which outcomes can be directly or indirectly addressed. The Working Group also helped to guide NLM's stakeholder engagement activities and provided suggestions for reaching critical stakeholder communities. The influence of the Working Group on the product development process and the impacts of its input have been helpful in guiding the new beta site experiences planned for late fall 2021.

We will continue to ask the Working Group for feedback to guide priorities and suggestions for functionalities to be added in future releases.

We aim to keep the Working Group apprised of the impact of the beta releases on the user experience, using both qualitative and quantitative metrics that can be compared to the current sites. We will continue to ask the Working Group for feedback to guide priorities and suggestions for functionalities to be added in future releases, while also seeking input on outcomes that have not been fully explored.

Working Group Membership

NLM seeks the Working Group's input on membership through September 2022, recognizing the contributions made to date and providing an opportunity to consider how the expertise of group members may need to evolve as the modernization effort continues. Specifically, we ask the group to consider whether additional expertise may be needed through Working Group membership or through invitations to subject matter experts to participate in a specific meeting. Additionally, Working Group members will have the ability to transition off the group easily, as needed.

Public Communications Related to the Beta Releases

Three phases of public communications about the upcoming beta releases are planned: (1) a public webinar prior to availability of the beta releases to preview what can be expected, (2) a broad announcement of beta release availability through a public webinar complimented by e-communications and social media outreach, and (3) targeted communications to specific user groups about beta release features and functionality that address additional information needs. These communications are intended to generate excitement about what is to come while managing expectations for what the first releases

will include, reassuring users that the aim is to minimize disruptions to workflows while providing useful new features, and provide general information about what to expect regarding continued improvements over time. Working Group input will be considered on the timing and specific approaches for these communications.

Following outreach about the beta releases, the ClinicalTrials.gov modernization team will continue to keep key audiences (both public and internal NIH) informed of ongoing efforts and future updates.

The ClinicalTrials.gov modernization team will continue to keep key audiences (both public and internal NIH) informed of ongoing efforts and future updates.

More Information

Additional information about the ClinicalTrials.gov modernization effort is available online at https://clinicaltrials.gov/ct2/about-site/modernization.

Minutes from past Working Group meetings are available online at https://www.nlm.nih.gov/od/bor/bor.html.

Appendices

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

1. Maintain the integrity of ClinicalTrials.gov as a trusted resource, particularly among an ever-expanding research enterprise
2. Maximize the utility of the growing corpus of information, including through submission practices and user-focused technical functionalities
3. 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: Rebecca (Becky) J. Williams, PharmD, MPH, NLM, NIH

Board of Regents Members:

- Kent J. DeZee, MD, MPH, FACP, COL, MC, U.S. Army Office of the Surgeon General
- Jennifer (Jennie) S. Lucca, MSW, The Children's Inn at NIH

Ex Officio NIH Members:

- Lyric A. Jorgenson, PhD, Office of Science Policy
- Pamela Reed Kearney, MD, Office of Extramural Research

External Members:

- Carrie Dykes, PhD, University of Rochester Clinical and Translational Science Institute
- Alissa Gentile, MSN, RN, Dana-Farber Cancer Institute
- Sally A. Gore, MS, MS LIS, University of Massachusetts Medical School
- Carlos R. Jaén, MD, PhD, University of Texas Health Science Center at San Antonio (former BOR member and Working Group chair)

- Barbara Kress, BSN, RN, Merck
- Seth A. Morgan, MD, National Multiple Sclerosis Society
- Stephen J. Rosenfeld, MD, MBA, Freeport Research Systems, LLC and North Star Review Board
- Joseph S. Ross, MD, MHS, Yale School of Medicine
- Steven Woloshin, MD, The Dartmouth Institute

Former Member:

- Gary A. Puckrein, PhD, National Minority Quality Forum

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 a tenured Professor of Preventive Medicine and the 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 National Institutes of Health-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: REBECCA J. WILLIAMS

Rebecca (Becky) J. Williams, PharmD, MPH, 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, National Institutes of Health. She assumed this role after serving as Assistant Director of ClinicalTrials.gov for more than a decade. Dr. Williams is responsible for technical, scientific, policy, regulatory, and outreach activities related to the operation of ClinicalTrials.gov. Her research interests relate to improving the quality of the reporting of clinical research. Her prior experience includes regulatory affairs consultant and reviewer and supervisory roles at the U.S. Food and Drug Administration in the area of prescription drug advertising and promotion.

Dr. Williams has a PharmD from the University of Wisconsin–Madison and an MPH from the Bloomberg School of Public Health at Johns Hopkins University.

BOARD OF REGENTS MEMBER: JENNIFER S. LUCCA

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

Ms. Lucca's career began in Anchorage, Alaska working for The Arc of Anchorage, an organization dedicated to serving individuals with disabilities. Since that time her focus has primarily been on developing and managing family support programs in community and health care settings. She is passionate about supporting families during times of significant stress and 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 a master's in social work with a focus on policy, planning, and administration from The Catholic University of America.

EX OFFICIO NIH MEMBER: LYRIC A. JORGENSON

Lyric A. Jorgenson, PhD, is Deputy Director for the Office of Science Policy (OSP) at the National Institutes of Health. She provides senior leadership in the development and oversight of policies and programs associated with emerging, high-impact issues of importance to the biomedical research enterprise and the federal government. She 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, directing and coordinating cancer-related activities across the federal government and working to leverage investments across sectors to dramatically accelerate progress in cancer prevention, diagnosis, and treatment.

Prior to joining OSP, Dr. Jorgenson was a Health Science Policy Advisor and Analyst under the Deputy Director for Science, Outreach, and Policy at NIH, playing a central role in creating new signature initiatives such as the Brain Research through Advancing Innovative Neurotechnologies Initiative and the National Center for Advancing Translational Sciences. She was also a Science and Technology Fellow for the American Association for the Advancement of Science and has received numerous awards in recognition of her accomplishments and service.

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.

EX OFFICIO NIH MEMBER: PAMELA REED KEARNEY

Pamela Reed Kearney, MD, is Director of the Division of Human Subjects Research within the Office of Extramural Research (OER) at the National Institutes of Health. Prior to joining OER, she was the deputy chair of the Combined NeuroScience Institutional Review Board 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 done clinical work at The George Washington University, Walter Reed Army Medical Hospital, and the NIH Clinical Center.

EXTERNAL MEMBER: CARRIE DYKES

Carrie Dykes, PhD, serves as 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. Dr. Dykes develops and assesses research education materials for a variety of constituencies across the University of Rochester Medical Center. She 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 GENTILE

Alissa 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. She 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 patients affected by blood cancers about the treatment option of clinical trials and 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, MA, 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 a Master of Science in Nursing 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.

EXTERNAL MEMBER: CARLOS R. JAÉN

Carlos R. Jaén, MD, PhD, is the Holly Distinguished Chair, Patient-Centered Medical Home, Professor and Chair of Family and Community Medicine, and Professor of Population Health at the University of Texas Health Science Center at San Antonio. Dr. Jaén's research interests focus on improving preventive care for individuals of all ages and preventing complications from chronic diseases such as diabetes, high blood pressure, and heart disease. He is passionate about building and studying high-performance primary care offices. He served on the panels that published smoking cessation guidelines in 1996 and 2000 and was co-chair of the panel that published an update in 2008. In 2005 he was appointed to the National Advisory Council of the Agency for Healthcare Research and Quality, and he was also an appointed member of the New York State Public Health Council. He was Co-Director of the Center for Research in Family Medicine and Primary Care, which studied more than 500 mostly independent primary-care practices over the last 20 years. He received a Generalist Physician Faculty Scholar Award from the Robert Wood Johnson Foundation and a Cancer Control Career Development Award for Primary Care Physicians from the American Cancer Society. His interests include building a healthier San Antonio through efforts in community wellness.

Dr. Jaén has a PhD in epidemiology and community health and an MD, both from the State University of New York at Buffalo, and an MS in oncology from Niagara University. He completed a residency in Family Medicine and a Primary Care Research Fellowship at Case Western Reserve University. He is a practicing family physician and has been among the Best Doctors in America annually since 2002. He was chair of the Board of Directors of the

American Board of Family Medicine in 2014 and was elected to the National Academy of Medicine (formerly the Institute of Medicine) of the National Academies in 2013.

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. She joined Merck 23 years ago as a clinical scientist working on the successful development and submission of several compounds. In 2007 Ms. Kress was asked to assume an additional responsibility that she was told would take up only 5 percent of her time: ClinicalTrials.gov. Twelve years and 28 staff members later, disclosure requires 100 percent of her time.

Ms. Kress began her career as a critical care and emergency room nurse. She currently participates in various Pharmaceutical Research and Manufacturers of America, European Federation of Pharmaceutical Industries and Associations, and TransCelerate disclosure work streams. Ms. Kress is 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.

EXTERNAL MEMBER: SETH A. MORGAN

Seth A. Morgan, MD, was 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. As an activist, Dr. Morgan has been involved in a number of efforts to support people with MS and other types of disabilities. He has been an advocate/activist for the National Multiple Sclerosis Society Greater DC-Maryland Chapter, serving on the Governmental Relations Committee and as a District Activist Leader since 2014. He has been a commissioner on the Montgomery County, Maryland, Commission on People with Disabilities since 2009 and has chaired the commission since 2015; he has also been a member of the Maryland Alliance of Disability Commissions and Committees since 2012 and has served as vice-chair since 2015. Dr. Morgan's other public service activities have included being a member of the iConquerMS Research Committee since 2016, the Patient-Centered Outcomes Research Institute's Clinical Trials Advisory Panel from 2016 to 2019, and the National Multiple Sclerosis Society Activism Advisory Committee since 2018. He was also a reviewer for the Congressionally Directed Medical Research Programs from 2014 to 2016.

Dr. Morgan received 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 American Academy of Neurology, 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 National Multiple Sclerosis Society Advocacy Hall of Fame in 2015.

EXTERNAL MEMBER: STEPHEN J. ROSENFELD

Stephen J. Rosenfeld, MD, MBA, is a hematologist. He spent 19 years at the National Institutes of Health, 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. He ended his career 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, ME, and as Chief Executive Officer of the Western Institutional Review Board in Olympia, WA. Most recently, Dr. Rosenfeld served for 7 years as the executive chair of Quorum Review IRB.

Dr. Rosenfeld earned his medical degree from Cornell University. He trained in internal medicine at Dartmouth College and completed his hematology fellowship at NHLBI. Dr. Rosenfeld also has an MBA from Georgetown University. He 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 Department of Health and Human Services and served as Chair of that 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 where he is currently Vice-Chair.

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 issues related to pharmaceutical and medical device regulation, evidence development, postmarket surveillance, and clinical adoption. Dr. Ross codirects 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 400 articles in peer-reviewed biomedical journals and is currently an Associate Editor at *JAMA Internal Medicine*.

Dr. Ross earned his medical degree from the Albert Einstein College of Medicine and an MHS from the 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 health news. He has worked to improve the communication of medical evidence to physicians, journalists, policy makers, and the public, so they can make wiser decisions.

With Lisa Schwartz, Dr. Woloshin developed the National Institutes of Health'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 Library of Medicine bookshelf) and *Overdiagnosed* (winner of the Prescrire Prize). His essays have appeared in *The New York Times*, *The Washington Post*, and *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 board of *JAMA Internal Medicine*, is a series consultant for *The BMJ*, 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 in research and enhancing the communication of medical evidence. He is also the founder and director of the Lisa Schwartz Foundation for Truth in Medicine.

Dr. Woloshin received 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.

FORMER MEMBER: GARY A. PUCKREIN

Gary A. Puckrein, PhD, is President and Chief Executive Officer of the National Minority Quality Forum (NMQF). NMQF strengthens efforts to use evidence-based, data-driven initiatives to eliminate premature death and preventable illness for racial and ethnic minorities and other special populations.

Under Dr. Puckrein's leadership, and with support from the Department of Health and Human Services, the Health Resources and Services Administration, and the Robert Wood Johnson Foundation, NMQF launched the ZIP Code Analysis Project (ZCAP) in 1998. ZCAP is the predecessor database of the National Health Index (NHI).

NHI is a comprehensive database that links vital statistics, demographic, environmental, claims, prescription drug, clinical laboratory values, health care access points (e.g., hospitals, physicians' offices), and other data elements in one centralized data warehouse, organized around ZIP Code. NHI measures and forecasts health status in small geographic areas, evaluates the impact of scientific interventions, monitors changes in health

outcomes, and undertakes risk assessments (i.e., health care utilization and its financial implications). NMQF uses NHI to provide a common set of indicators—geographic and health status referents—to stratify communities by health status.

In addition to his work for NMQF, Dr. Puckrein possesses a unique business and academic background. He has a PhD and a master's degree from Brown University, where he graduated Phi Beta Kappa.

Appendix B: Board of Regents Public Service Working Group on ClinicalTrials.gov Modernization Meeting Schedule

Meeting Date	Meeting Focus
	Initial Meetings and Preparations
September 10–11, 2019	NLM Board of Regents meeting: Formation of a Public Service Working Group for the modernization of ClinicalTrials.gov
December 13, 2019	NLM Board of Regents Working Group meeting: RFI review and input
December 20, 2019	NLM Board of Regents Working Group meeting: Communications strategy
February 3, 2020	NLM Board of Regents Working Group meeting: Preparation for public meeting
February 4–5, 2020	NLM Board of Regents meeting
April 30, 2020	Virtual public meeting
May 1, 2020	NLM Board of Regents Working Group meeting: Debriefing after the public meeting
May 12, 2020	NLM Board of Regents meeting
August 28, 2020	NLM Board of Regents Working Group meeting: Preparation for September 11, 2020, Working Group meeting
	Facilitated Meetings
September 11, 2020	NLM Board of Regents Working Group meeting: Strategy-for-change framework introduced, and modernization vision and outcomes discussed
September 15, 2020	NLM Board of Regents meeting
December 11, 2020	NLM Board of Regents Working Group meeting: ClinicalTrials.gov challenges for website users
February 9, 2021	NLM Board of Regents meeting
February 26, 2021	NLM Board of Regents Working Group meeting: ClinicalTrials.gov challenges for PRS users
May 11, 2021	NLM Board of Regents meeting
	Recently Held and Upcoming Meetings
August 20, 2021, and August 30, 2021	NLM Board of Regents Working Group meetings: Summary of work completed to date, next steps and call for additional expertise, and plans for beta releases and related communications
September 14–15, 2021	NLM Board of Regents meeting

Appendix C: Abbreviations

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

- API — application programming interface
- IRB – institutional review board
- 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
- RFI — request for information
- SOPs — standard operating procedures
- Working Group — National Library of Medicine Board of Regents Public Service Working Group on ClinicalTrials.gov Modernization

Appendix D. Modernization Team Members

Thank you to NCBI leadership and the many team members who have supported the ClinicalTrials.gov modernization effort, including:

- Laura Akinyode, PRS Business Analyst (contractor)
- Stacey Arnold, PRS Subject Matter Expert (SME)
- Richard Ballew, ClinicalTrials.gov Business/Data Analyst (contractor)
- Annice Bergeris, ClinicalTrials.gov Information Research Specialist and Operations Team Product Owner
- Caitlin Bowler, User Experience (UX) Researcher (contractor, former team member)
- Elissa Bush, ClinicalTrials.gov Technical Information Specialist
- Qiao Chang, ClinicalTrials.gov Technical Information Specialist
- Cassiah Cox, ClinicalTrials.gov Project Director (contractor)
- Vinod Danam, PRS Developer (contractor)
- Dina Demner-Fuschman, SME
- Nachiket Dharker, ClinicalTrials.gov Registration Team Lead and PRS SME (contractor)
- Sergey Dikunov, ClinicalTrials.gov Website Lead Developer (contractor)
- Heather Dobbins, ClinicalTrials.gov Lead Results Analyst and PRS Product Owner
- Jolie Dobre, PRS UX SME (contractor)
- Zachary Feiger, ClinicalTrials.gov Results Analyst and PRS SME (contractor)
- Anna Fine, ClinicalTrials.gov Assistant Director
- Beth Fordice, ClinicalTrials.gov Technical Information Specialist
- Jane Fun, PRS Developer (contractor)
- Madhurima Gade, ClinicalTrials.gov Website Developer (contractor)
- Rajiv Ghatak, ClinicalTrials.gov Scrum Master (contractor, former team member)
- John Gillen, ClinicalTrials.gov Developer (contractor)
- Jaime Goff, ClinicalTrials.gov Website UX Architect/Analyst (contractor, former team member)
- Elisa Golfinopoulos, ClinicalTrials.gov Results Team Lead and Automation Support Team Product Owner (contractor)
- Slava Gorelenkov, ClinicalTrials.gov Technical Program Manager
- Derek Griffing, ClinicalTrials.gov Policy Analyst
- Wendy Harman, ClinicalTrials.gov Website UX/User Interface (UI) Lead (contractor)
- Nick Ide, ClinicalTrials.gov Developer (contractor)
- Rafis Ismagilov, ClinicalTrials.gov Website Developer (contractor)
- Casey Jennings, PRS UX Analyst/Strategist (contractor, former team member)
- Dmitrii Kishchukov, PRS Lead Developer (contractor)
- Ryan Koning, PRS UX Architect (contractor)
- Alex Kostyukovsky, ClinicalTrials.gov Developer (contractor)
- Carl Leubsdorf, Consultant (contractor)
- Russell Loane, ClinicalTrials.gov Developer (contractor)
- Vitaliy Lyoshin, ClinicalTrials.gov Scrum Master (contractor)

- Jacob McAdams, PRS Developer (contractor, former team member)
- Jesus Mendiola Gomez, PRS Quality Assurance Engineer (contractor)
- Alma Morales, ClinicalTrials.gov Website UI Designer (contractor)
- Hibah Nazir, ClinicalTrials.gov Product Manager (contractor)
- Toobie Nguyen, PRS UX Architect (contractor, former team member)
- Alison (Ward) Powell, Senior Communications Specialist (contractor)
- Alexandra Rayner, ClinicalTrials.gov Website Senior Content Strategist (contractor)
- Christina Robinson, ClinicalTrials.gov Web Content and Outreach Coordinator and Website Product Owner (contractor)
- Mary Sanders, ClinicalTrials.gov Project Manager (contractor)
- Maureen Strange, SME (contractor)
- Lucy Street, ClinicalTrials.gov Website Content Strategist (contractor)
- Tony Tse, ClinicalTrials.gov Analyst
- Shanel Vicente, ClinicalTrials.gov Website UX Designer (contractor)
- Rebecca Williams, ClinicalTrials.gov Acting Director and Offering Owner
- Susan Wimmer, Senior Editor (contractor)
- Karl Wolf, ClinicalTrials.gov Developer (contractor)
- Becca Xu, UX Researcher (contractor)
- Allison Yu, ClinicalTrials.gov Website Developer (contractor)

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