

**Summary of Responses to Request for Information (RFI):  
ClinicalTrials.gov Modernization**

**April 28, 2020**

## Contents

Background.....	1
Methods.....	1
Results.....	2
1. ClinicalTrials.gov Website Functionality .....	3
1a. Examples of New Uses of the ClinicalTrials.gov Website.....	3
1b. Resources to Link to from ClinicalTrials.gov.....	3
1c. Examples of Current Uses of the ClinicalTrials.gov Website .....	4
1d. Scope of the Primary Uses of ClinicalTrials.gov.....	4
2. Information Submission through the PRS .....	5
2a. ClinicalTrials.gov Registration and Results Submission Process and Improvements.....	5
2b. Alignment of the PRS Submission Process with Organizational Processes.....	5
2c. Novel Methods to Enhance PRS Information Quality.....	5
2d. Useful Submission-Related Materials.....	6
2e. Incentives and Recognition for Information Submission .....	6
3. Data Standards to Support ClinicalTrials.gov .....	6
3a. Balance Between Standards and Flexibility .....	6
3b. Examples of Useful Standards.....	6
Conclusions.....	7
Appendix: Questions from the Request for Information (RFI):	
ClinicalTrials.gov Modernization .....	8

## Background

[ClinicalTrials.gov](https://clinicaltrials.gov) is the world's largest public clinical research registry and results database. This resource provides information on more than 336,000 clinical studies and 42,000 results for a wide range of diseases and conditions. More than 3.5 million visitors use this public website each month to find and learn more about clinical trials. The National Library of Medicine (NLM) maintains ClinicalTrials.gov on behalf of the National Institutes of Health (NIH).

NLM has launched an effort to [modernize ClinicalTrials.gov](#) to improve the user experience by updating the platform to accommodate growth and enhance efficiency. To obtain detailed and actionable input, NLM issued a request for information (RFI), [NOT-LM-20-003](#), on December 30, 2019. The RFI's purpose was to solicit comments on the ClinicalTrials.gov website's functionality, information-submission processes, and use of data standards. NLM accepted comments and attachments via a web-based form until March 14, 2020.

The RFI questions were grouped into three broad topic areas:

1. Functionality of the ClinicalTrials.gov website, including how the site is currently used and potential improvements, resources that could be linked to from the site, and new ways the site could be used
2. Information submission, including initiatives, systems, or tools for supporting the assessment of internal consistency and improving the accuracy and timeliness of information submitted through the ClinicalTrials.gov Protocol Registration and Results System (PRS)
3. Data standards that could support the submission, management, and use of ClinicalTrials.gov information content

See the appendix for the RFI questions and sub-questions. This report provides a high-level summary of the responses received for each sub-question. However, in preparing this report, NLM did not correct any of the comments and did not address or comment on their contents.

## Methods

To analyze the responses to the RFI, NLM first assigned each comment or portion of a comment within a submission to the corresponding RFI question (i.e., 1, 2, or 3) and sub-question (e.g., 1a, 1b, 1c, 1d). NLM then assigned keywords or a domain code that described, in a few words, the topic of the comment. For example, NLM assigned the domain code "Search" to responses to sub-question 1a that discussed the ClinicalTrials.gov website's search function and the domain code "Linking" to responses that suggested online resources to which ClinicalTrials.gov could link.

When a single comment addressed multiple topics in response to a single prompt, NLM assigned a separate code to each component of the comment. For example, if a respondent offered three examples of unsupported, new uses of the ClinicalTrials.gov website for sub-question 1a, NLM gave each example its own code. Depending on the content of the examples, NLM sometimes

assigned the same code to two or more of them or a different code to each. Some respondents submitted a comment more than once, using the same or only slightly different wording. Whenever possible (e.g., when respondents provided identification or contact information), NLM removed verbatim duplicate comments from the counts provided in the Results section of this report.

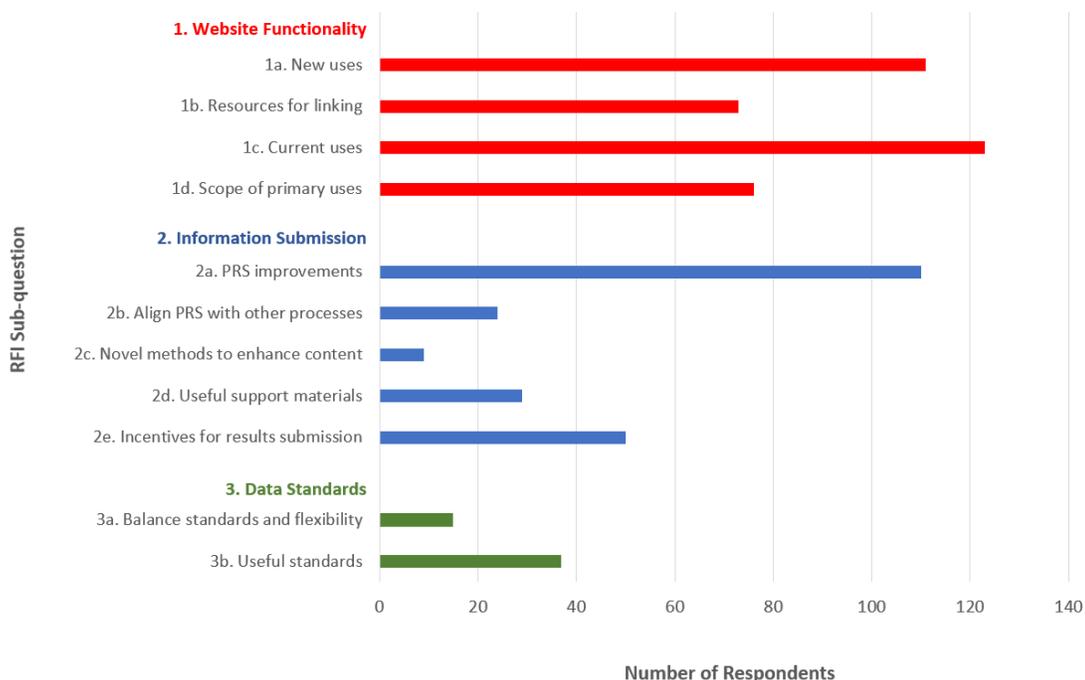
## Results

NLM received 268 submissions from 259 unique respondents.<sup>1</sup> Of those responses, 84 were submitted anonymously. The tentative breakdown of the 268 submissions is as follows:

- Data providers: 76 (28%)
- Researchers and others: 56 (21%)
- Patients and caregivers: 52 (19%)

Not enough information was provided in the remaining 84 submissions (31%) to identify the apparent user role. Respondents also submitted attachments, including seven supplementary documents (e.g., graphs to accompany their comments, a list of open clinical trials at one institution, PRS screenshots).

The total number of respondents who provided a comment in response to each question and sub-question in the RFI is shown in figure 1.



**Figure 1. Number of respondents who answered each question**

<sup>1</sup> Six submissions were blank, and one respondent requested that the comments provided be excluded from the public posting (but included in the summary statistics in this report).

The feedback clearly shows that stakeholders value ClinicalTrials.gov highly and want it to be as useful a resource as possible. For example, one respondent commented:

The ClinicalTrials.gov site provides an important public service, and it's invaluable to have the registry information freely available to the public. As the ClinicalTrials.gov platform continues to evolve, in both form and function, it will become even more widely used and beneficial to the patient, research, and funding communities. Thank you for your efforts on this project!

Common responses are summarized below, by sub-question. Responses addressing issues that pertained to multiple sub-questions or to none of them are not included in this summary.

## **1. ClinicalTrials.gov Website Functionality**

### ***1a. Examples of New Uses of the ClinicalTrials.gov Website***

Sub-question 1a asked for examples of unsupported, new uses of the ClinicalTrials.gov website. Some respondents offered suggestions for the ClinicalTrials.gov search function, such as making searches more user friendly by walking users through the steps for building a search query. Others requested changes that would allow displays of lists of studies similar to the one being viewed and customization of the level of technical detail provided in the search results by type of user (e.g., patient, researcher). Respondents also requested the ability to search by genetic mutation or biomarker, disease subtype, type of intervention, inclusion or exclusion criteria, physical distance of study sites from participant locations, and study purpose (diagnostic, preventive, or therapeutic). The ability to sort search results by fields—such as date of last update, geographic region, disease or condition, and intervention—was also suggested. In addition, respondents asked that the search results page indicate the relevance of each record retrieved.

Other common suggestions were to allow lists of clinical trial records identified through searches to be downloaded and to standardize the nomenclature used to describe studies. Respondents suggested more prominent displays for each study of inclusion and exclusion criteria, funding sources, study status, contact information, and changes to the study record. Information and formats that respondents thought would be valuable to potential study participants included videos that explain each study, detailed maps of study sites, details on out-of-pocket costs and reimbursement rates for participants, and descriptions of the risks to participants. Some respondents requested that ClinicalTrials.gov study records include plain language information or link to plain language summaries of study findings.

### ***1b. Resources to Link to from ClinicalTrials.gov***

For sub-question 1b, respondents were asked to describe resources that could be linked to from ClinicalTrials.gov and explain why those resources would be useful. By far, the most common suggestion was for ClinicalTrials.gov study records to include links to PubMed citations and PubMed Central records of published journal articles containing the study's findings. Another frequent suggestion was to link ClinicalTrials.gov study records to PubMed citations of

publications about study interventions. Several respondents also suggested linking ClinicalTrials.gov entries to MedlinePlus and other NIH databases, as well as to U.S. Food and Drug Administration and European Medicines Agency databases. Others proposed linkages to repositories of studies' individual participant data and to advocacy group websites that provide online educational and support materials for patients and families.

### ***1c. Examples of Current Uses of the ClinicalTrials.gov Website***

Sub-question 1c requested examples of how the ClinicalTrials.gov website is currently used. Respondents described a number of common uses, such as the following:

- Patients or health care providers searching for studies that are recruiting participants
- Researchers conducting systematic reviews
- Advocacy groups and various stakeholders accessing study information to display on websites tailored to particular audiences

Respondents also offered a range of suggestions for enhancing ClinicalTrials.gov study records, including new options for printing or sharing these records, using addresses and other contact information for study sites, displaying details of eligibility criteria, and providing plain language summaries of study descriptions. Other suggestions were related to improving the study records themselves by, for example, displaying the eligibility criteria and study sites more prominently, adding a method for searching study record contents, and providing structured information for the inclusion and exclusion criteria.

As with sub-question 1a, many respondents commented on the search function. Some said that the ClinicalTrials.gov search engine is excellent, while others identified limitations. Some listed potential improvements, such as enhancing the ability to find exact matches for search terms and expanding the search fields available for the Advanced Search feature. Some respondents suggested simplifying the basic search options, and others requested support for more complex searches. Respondents' comments also addressed tools for saving searches or specific study records and notifications when saved records are updated.

### ***1d. Scope of the Primary Uses of ClinicalTrials.gov***

Sub-question 1d asked respondents whether they use ClinicalTrials.gov primarily to find a wide range of studies or a more limited range. Responses were split fairly evenly between the two, and several respondents said that they seek both a wide and a narrow range of studies. In most cases, respondents who use ClinicalTrials.gov to find a limited range of studies are seeking studies on a specific disease or condition. Other reasons to look for a narrow range of studies included the need to find ongoing (not completed) studies or to find studies with a particular design or that use a specific intervention. Many of the respondents seeking a wide range of studies did not specify why. Of those that did, reasons included wanting to choose from a broad range of studies for a given patient or wanting to see all the studies in a country on a given indication, different types of studies, or studies on different types of interventions.

## **2. Information Submission through the PRS**

### ***2a. ClinicalTrials.gov Registration and Results Submission Process and Improvements***

Sub-question 2a asked respondents to identify steps in the ClinicalTrials.gov registration and results submission processes that could be improved. Many respondents requested additional standardization of data elements, such as eligibility criteria, contact and location information, and study arms and interventions. Others suggested greater standardization of data elements to increase compatibility with other platforms. Many respondents also suggested making it easier to submit information on nontraditional studies that does not easily fit the current required data elements. Examples of these nontraditional studies included cluster-randomized, adaptive, and pragmatic trials; longitudinal studies; basic experimental studies in humans; and master protocols.

Respondents offered suggestions for streamlining the data entry process, including automatically perpetuating updates to fields within or across study records and allowing Microsoft Excel files to be uploaded or information to be imported directly from electronic data-capture systems. Others proposed providing greater support during the quality-control review process, including more opportunities for one-on-one assistance and just-in-time support for responding to review comments.

Respondents requested customizable tools and features to help manage the information workflow within the PRS, dashboards with PRS account-wide metrics, notifications of events and deadline reminders, and more flexible reports. Many suggested ways to enhance the consistency and searchability of the information entered in the PRS, including adding a dictionary of standardized common outcome measures to choose from, drop-down menus to populate fields, and a library of standard inclusion and exclusion criteria.

### ***2b. Alignment of the PRS Submission Process with Organizational Processes***

In answer to sub-question 2b, respondents described opportunities to better align the PRS submission process with their organization's processes. Suggestions included greater integration of local institutional review board (IRB), NIH, and ClinicalTrials.gov reporting requirements; automated transfers of information and updates between IRB documents and ClinicalTrials.gov; and interoperability of ClinicalTrials.gov, IRB, and other systems that manage clinical trials information. Some respondents suggested expanding the PRS feature that allows uploads of adverse events information to include other types of information (e.g., demographic characteristics, site details) from institutional clinical trial management systems to facilitate tracking and reduce data entry errors.

### ***2c. Novel Methods to Enhance PRS Information Quality***

Sub-question 2c asked about novel methods for enhancing the quality of the information submitted to the PRS and displayed on the ClinicalTrials.gov website. Of the small number of responses to this sub-question, the main suggestion was to use natural language processing (possibly in combination with optical character recognition) to code study variables using

standard vocabularies and ontologies. Implementation of this suggestion would facilitate secondary data analyses.

### ***2d. Useful Submission-Related Materials***

Sub-question 2d asked about submission-related informational materials that respondents would find useful and other materials that would make the submission and quality-control processes easier. A few respondents suggested that ClinicalTrials.gov include definitions, ideally in Microsoft Excel format, of the data elements (e.g., recruitment status, race); these definitions would be particularly useful for studies other than randomized controlled trials. Other suggestions were to provide descriptions of common data-entry problems and how to solve them as well as guidance on submitting data for nontraditional clinical trials and on writing plain language titles and brief summaries.

### ***2e. Incentives and Recognition for Information Submission***

For sub-question 2e, respondents identified ways to provide credit, incentives, or recognition for individuals and organizations that submit complete, accurate, and timely registration and results information to ClinicalTrials.gov. A few respondents suggested incentives such as letters of recognition; plaques; labels or icons indicating on-time submission; publicly available compliance rates, by data provider; ratings by the public or NLM; and mentions in ClinicalTrials.gov Hot Off the PRS!, the email bulletin for PRS users.

## **3. Data Standards to Support ClinicalTrials.gov**

### ***3a. Balance Between Standards and Flexibility***

For sub-question 3a, respondents described ways to balance the use of standards while retaining flexibility to ensure that the information submitted to ClinicalTrials.gov is accurate. A few respondents suggested standardizing the vocabulary for clinical trials reporting by encouraging greater use of common terminologies (e.g., RxNorm, SNOMED CT, LOINC). Suggestions for maintaining or increasing flexibility included using machine learning and natural language processing for mapping free text to controlled terms and concepts as well as increasing character limits for free-text fields.

### ***3b. Examples of Useful Standards***

Sub-question 3b asked about standards that might be useful for improving data quality, enabling the reuse of data, or improving the consistency and management of ClinicalTrials.gov data. Some respondents suggested ways to standardize the names used for diseases and conditions, including adding new, more specific terms to the Medical Subject Headings (MeSH) thesaurus to precisely identify the condition studied and using coding systems other than MeSH (e.g., NCI Thesaurus, International Classification of Diseases) to identify diseases and interventions with greater granularity.

## Conclusions

Based on a preliminary review of all of the responses to the RFI, the main themes of the suggestions for modernizing ClinicalTrials.gov are to:

- Enhance search options and improve the tools for managing and monitoring search results
- Improve the formatting and content of study records using, for example, data standards and normalization
- Provide more plain language content in study records, on the public site, and to support information submission
- Enhance information discovery through linkages to other study-related resources
- Evaluate approaches to the data structure and format, including greater standardization and flexibility
- Streamline the information-submission and quality-control review processes
- Develop additional tools to give users insights into their PRS accounts and to support workflow management
- Enhance support for PRS users, including resources related to submitting nontraditional clinical trials

NLM is grateful to the individuals and organizations that provided detailed responses to the 11 sub-questions in the RFI. The preliminary analyses summarized in this report will be complemented by additional, in-depth, quantitative and qualitative analyses of the feedback received. NLM will use the input from the RFI, as well as from additional stakeholder engagement, user interviews, and a public meeting on April 30, 2020, to inform its roadmap for modernizing ClinicalTrials.gov.

## Appendix: Questions from the Request for Information (RFI): ClinicalTrials.gov Modernization

The RFI ([NOT-LM-20-003](#)) asked respondents to answer the following questions:

1. **Website Functionality.** NLM seeks broad input on the ClinicalTrials.gov website, including its application programming interface (API).
  - a. List specific examples of unsupported, new uses of the ClinicalTrials.gov website; include names and references for any systems that serve as good models for those uses.
  - b. Describe resources for possible linking from ClinicalTrials.gov (e.g., publications, systematic reviews, de-identified individual participant data, general health information) and explain why these resources are useful.
  - c. Provide specific examples of how you currently use the ClinicalTrials.gov website, including existing features that work well and potential improvements.
  - d. Describe if your primary use of ClinicalTrials.gov relies on (1) a wide range of studies, such as different study types, intervention types, or geographical locations or (2) a more limited range of studies that may help identify studies of interest more efficiently. Explain why and, if it applies, any limiting criteria that are useful to you.
  
2. **Information Submission.** NLM seeks broad input on initiatives, systems, or tools for supporting assessment of internal consistency and improving the accuracy and timeliness of information submitted through the ClinicalTrials.gov Protocol Registration and Results System (PRS).
  - a. Identify steps in the ClinicalTrials.gov registration and results information submission processes that would most benefit from improvements.
  - b. Describe opportunities to better align the PRS submission process with your organization's processes, such as interoperability with institutional review board or clinical trial management software applications or tools.
  - c. Describe any novel or emerging methods that may be useful for enhancing information quality and content submitted to the PRS and displayed on the ClinicalTrials.gov website.
  - d. Suggest what submission-related informational materials you currently find useful and what other materials would make the submission and quality control process easier for you.
  - e. Suggest ways to provide credit, incentivize, or recognize the efforts of individuals and organizations in submitting complete, accurate, and timely registration and results information.
  
3. **Data Standards.** NLM seeks broad input on existing standards that may support submission, management, and use of information content (e.g., controlled terminologies for inclusion and exclusion criteria).
  - a. Provide input on ways to balance the use of standards while also retaining needed flexibility to ensure submitted information accurately reflects the format specified in the study protocol and analysis plan.

- b. List names of and references to specific standards and explain how they may be useful in improving data quality, enabling reuse of data to reduce reporting burden, or improving consistency and management of data on ClinicalTrials.gov.