ClinicalTrials.gov Modernization Public Meeting
April 30, 2020
9:30 a.m.–12:30 p.m. ET

Transcript

Moderator: This is Wendy, your moderator. I'm welcoming you to make sure everyone can hear me and so you know that the sound is working before we get started here in just a couple of minutes.

Recording 1 – Introduction and Overview Session (0:00:06)

Becky Williams: Good morning, everyone. I am Becky Williams, the Acting Director of ClinicalTrials.gov at the National Library of Medicine. And welcome to this public meeting on ClinicalTrials.gov modernization.

I really appreciate you spending your time with us this morning, especially when there may be many things competing for your attention with new and difficult challenges amid COVID-19.

In this day, I think the importance of ClinicalTrials.gov and the expectations of our users have only been reinforced as we all respond to COVID-19. We really have been honored to provide this service at a time having up-to-date information on clinical research is essential.

The modernization effort is intended to ensure that ClinicalTrials.gov is well positioned to continue to deliver this value well into the future. And we can really only do this with your involvement, and input, and are really so grateful for your contributions in responding to the Request for Information and for being here today.

I want to recognize quickly the contributions of our dedicated staff who make this effort possible and have shown incredible flexibility, creativity, and commitment during these times and in bringing this meeting into its virtual existence.

We also have the pleasure of working with many dedicated partners across NIH, and we are really pleased to benefit from their input and support of this modernization effort.

One of these supporters is the team at NIH's Office of Science Policy, and today I'm happy to have the honor to introduce the director of that office, Dr. Carrie Wolinetz. She serves as the Associate Director of Science Policy as well as the Acting Chief of Staff, and she advises the NIH Director on, really, basically any science policy matter of significance to the NIH, to the research community, and the public.

We're really pleased that our own work overlaps with that of Carrie's work and her office, and she's joining us today to launch our meeting. And I will turn it over to you, Carrie.

(0:02:26)

Carrie Wolinetz: Great, thank you, Becky. And please, allow me to join the mutual admiration society here for the team at the National Library of Medicine and your leadership of ClinicalTrials.gov. It's really an incredible partnership, and I know I speak for the entire Office of Science Policy team and the NIH Director, Francis Collins, when I say that we could not be more excited about this modernization effort.

In many ways, ClinicalTrials.gov is a victim of its own success in the most positive way possible. When I think about the things we've been able to accomplish as an agency, whether it is our broad stewardship efforts to ensure that the clinical trials that NIH funds are of the highest quality and meet our greatest standards of rigor, that we are meeting our commitment to participants in clinical trials by ensuring that there is rigor and transparency around the results of those trials, or whether it's really leading the way in informing the public about what's going on in any given area of science, ClinicalTrials.gov has proven to be an incredibly important tool to a variety of users, and so this effort to improve the user experience and update the technology platform is really critically important for so many things that we do at NIH, our partnerships across the government, and our commitments to the American public, the taxpayers, and research participants.

So I want to echo Dr. Williams's thanks for all of the input that we received through the RFI and from all of you and through this meeting today; it's really, really important, and I think to have a real-world example of the importance of ClinicalTrials.gov as we face the midst of the COVID-19 crisis. Certainly, we are seeing a high usage of people search for the information related to COVID-19 on ClinicalTrials.gov. I think as of last week there were more than 700 COVID-19-related studies listed.

And of course, just yesterday we saw the announcement of some really positive results from the remdesivir trial that NIH is supporting. And so, again, it has proven itself to be a critically important tool when both the scientific community and public are seeking important information about public health issues and scientific opportunities.

Just to briefly touch, when talking about COVID-19, to keep people aware that NIH is really serving at the forefront of leading the research efforts on COVID-19. We are launching a number of rapid-fire efforts, including, as you may have seen, the Accelerating COVID-19 Therapeutic Intervention

and Vaccine Partnership, the ACTIV partnership, which is really an extraordinarily fast-moving public–private partnership with more than a dozen industry partners, a number of cross-government activities to really coordinate our clinical trials related to the development of vaccines and therapeutics on a really massive and global level, and that's everything from developing massive protocols to sharing candidates and data, and I'm sure Dr. Brennan will be saying more about NLM's efforts related to data sharing and building infrastructure for COVID-19, and we also have a number of research efforts really stretching across all of our Institutes and Centers, trying to accelerate everything from diagnostics to treatments to recovery efforts related to the ongoing pandemic.

So, NIH is "all in," and as you might imagine, it's taking up a fair amount of our bandwidth right now.

So, let me just close by saying thank you again for participating in this meeting, for weighing in and engaging as stakeholders in ClinicalTrials.gov. I remain incredibly excited about this effort and really look forward to engaging with all of you and watching the National Library of Medicine's continuing efforts on modernization.

Thank you again for the opportunity to speak with you, and I will turn it back to the moderator.

(0:07:25)

Moderator: Thank you so much, Carrie. Hi, everyone. My name is Wendy Harman and I will be your moderator today, which means you'll hear my voice at various points through the event this morning. And right now, I just want to offer a few housekeeping tidbits.

First, let's take a little tour around Adobe Connect. The presentation slides, so everything that all of our excellent speakers and panelists will be talking about today, the visuals, will be in that main view that you see there.

Just to the right of that is speaker information. So, if you want to know who is speaking at any given time, the image there with the title will reflect exactly who is talking to you.

Right below that speaker information you'll find the links to the meeting agenda, the RFI comment summary, the consolidated RFI responses, a link to the closed-captioning service for the duration of this meeting, as well as the meeting website overall, the public meeting website.

In the bottom right-hand corner of your screen, you should see a Q&A pod. And we're going to talk a little bit more about that, but this is where we want you to submit your questions.

So first let's go over the agenda a little bit. We have three big events this morning. The first will be an overview of the ClinicalTrials.gov modernization effort, as well as a summary of the RFI responses that you all have submitted. We're going to meet the Board of Regents, then we're going to have a more in-depth panel discussion on the information submission process, followed by a panel that will discuss website functionality, and then we're going to wrap up for the day.

So, a couple of housekeeping tips here. First of all, you're going to be muted for the entirety of this meeting, but that doesn't mean that we don't want you to participate. So, we're going to be conducting polls throughout the meeting.

And, again, if I can direct your attention to that Q&A pod in the bottom right-hand corner of your screen, please go ahead and submit any questions and comments that you have through there. We're not going to respond directly to every single one of those, but we are going to collect all of the input for future communications.

We'll also have that open chat pod available at various points; some of you may have experienced that before the meeting got started this morning.

So, let's go ahead and practice a poll before we get started.

As you'll see loading now is a polling tool on the bottom half of your main screen. There's a blank box. In the open text box to the left of the send button, all we want you to do right now is type in where you're joining us from. And if you see that someone else is in the same location as you, you can click the +1 to the right of their response to upvote them.

So, let's all give that a try — I see lots of you are doing it already.

You're good at this!

We'll give you a few more seconds. I think everybody is getting the hang of it. It's great to see so many people participating today.

And it looks like Maryland is the winner, followed closely by North Carolina and Illinois. I can't believe we didn't see anyone say they were in their kitchen! Or maybe we did and it's a little bit lower.

So, great job — that was an excellent warmup! And now I would love to welcome Becky Williams, Acting Director of ClinicalTrials.gov, back

again to share an overview of the modernization effort and a summary of the RFI public comments.

(0:11:37)

Becky Williams: Thank you, Wendy. It's really great to see where everyone was joining us from today, both geographically and I can only envision the different parts of people's homes in which you're occupying at the moment.

This is me broadcasting from my living room, which is certainly a first. But I'm very glad that we were able to make this happen today.

What you see on the right-hand side of the image on this slide is where we were supposed to be physically gathering today on the NIH campus, but again I'm really happy to be sharing this virtual space with you instead.

Our goals for the day are to provide some basic background on ClinicalTrials.gov, as well as an overview of the modernization effort that we are undertaking.

We are aiming to share a high-level summary of the Request for Information comments that we received, as well as the themes that seem to be emerging from your input.

We're really happy to bring together today so many different types of users and stakeholders and are really hoping that we can have an opportunity to share some of our mutual interests and needs. And I expect we'll also see some examples of where those needs may diverge.

We're hoping, as Wendy introduced, to be able to engage you throughout this morning, through additional polling, chat, and questions, to really continue to get your input on these topics and themes.

I can tell you, just to set expectations, that we're not going to be sharing any grand vision today. But instead, this is really an opportunity for us to thank you for your contributions to the RFI and to be able to share quickly with you what those contributions look like.

One of our main goals throughout this modernization effort is to ensure that we are engaging with you continuously and communicating transparently, which is clearly embedded within our own mission. And so, part of the goal for today's meeting is really to be sharing back information with you as quickly as we can.

To help ensure that there's appropriate context for folks that may be joining us today, around the RFI comments, I'm going to start with a little bit of background, and also just talking a little bit about some of our efforts here at ClinicalTrials.gov in the context of COVID-19.

As many of you are aware, we have a tremendous amount of content that's hosted on ClinicalTrials.gov, and all of this has really been possible because of the strong foundation of laws and policies that have been put in place, primarily to reinforce yours and our expectations around clinical trial information being made available, including the results of clinical trials, in a timely and transparent manner.

People expect this transparency because of the widely recognized benefits of registration and results reporting.

It's clearly a method in which we can honor the promise that has been made to participants when they choose to be part of research, that their contributions will advance science. And it also supports the enrollment of participants into research.

The site is also a centerpiece for ensuring accountability in the reporting of clinical research.

It's really meant to ensure that we know about all of the trials that are being conducted so that we can help ensure that those studies are ultimately reported and, ideally, in the same way in which the prespecified research plan was laid out.

And all of these efforts really do support better stewardship of the clinical research enterprise, ensuring that funders like NIH can be making wise investments in future clinical research, knowing what has already been conducted in the past and what will be conducted going forward.

And all of these things really do contribute to, hopefully, enhancing increased trust in the clinical research enterprise.

And the way that we at ClinicalTrials.gov really seek to fulfill the benefits and to make sure they are realized is by focusing on two primary aims.

That first aim is around how we collect information about clinical studies, and the second aim is focused on how we facilitate the use of that information.

And these two aims align well with the input that we were seeking from you through the RFI process and are really the two main themes that we'll be focusing on today.

In terms of that first aim, for those of you who use the public site you may be less familiar with some of the processes involved throughout the process of the information actually getting listed on the public site.

We maintain a submission portal at ClinicalTrials.gov called the PRS, in which organizations have accounts that they manage to submit information.

And that clinical trial information is really a combination of free-text fields and structured data items, much of the information being required but with other, optional items as well.

Before the information is submitted to ClinicalTrials.gov, it must first meet automated validation rules that are really looking at the completeness of the information and some aspects of internal consistency.

And after meeting those automated validation rules, there's a manual process in place that we call the quality control review process, and you'll be hearing more about this in one of the panels today.

That manual review process that I mentioned is really focused on assessing the information in the study record itself. It is not intended to assess the quality of the study.

There are other processes in place that are aimed at addressing that. Our process is really focused on the information that's been submitted, to help ensure that there aren't any obvious errors or inconsistencies in that content.

You can see from this slide we process a relatively high volume of clinical trial information each week.

Registration information is typically reviewed within 2 days, and results information is processed and reviewed in less than 25 days.

Throughout this year, we have continued to see a pretty significant number of study registrations, sort of continuing along the same trajectory, and we've seen our registration volume remaining steady but with COVID-19 studies really accounting for larger portions of the new studies we've been receiving.

We have been prioritizing these studies in our review processes to help ensure that they are disseminated to the public as quickly as possible.

Also, as part of our submission process, we develop many different support materials that are aimed at submitters to support the processes that they have in place.

These materials are intended both for training purposes as well as for reference purposes, and, again, this will be a theme that you'll hear about in the information submission panel later today.

In the context of COVID-19, though, there's been a lot of developments with research activities, with many research activities being paused as staff are redeployed to high-priority areas, while at the same time we're seeing an increase in COVID-19-related research.

In the context of all of this happening, there's been a lot of questions and needs coming from the research community, and we've been providing information to our submitters that continues to be updated, to continue to support them with their emerging needs and questions.

And now switching gears to that second aim of facilitating use of information on ClinicalTrials.gov, what you see here are kind of two different views.

One, you see our own interface, the primary way in which many people interact with the information that we make available.

But then you also see reference to the ClinicalTrials.gov API, which is an application programming interface that basically allows computers to talk to each other and pull information from our site.

And what you're seeing is another third-party organization that is targeting their own community with clinical trial information specific to those needs.

I'm highlighting this because we know that with the thousands of diseases and conditions represented on ClinicalTrials.gov, it is a challenge to be able to equally serve all of the communities represented by those diseases and conditions. And believe, really, that this model is complementary because it can provide more targeted support to these communities.

And this afternoon you'll be hearing from a group that does provide such targeted support to their users.

In terms of use of ClinicalTrials.gov, we really have seen a tremendous amount of interest and growth as compared to last year.

We do suspect that some of this may be, in part, due to interest in COVID-19, but, again, it just sort of reinforces the importance and the value that people are seeing in using ClinicalTrials.gov.

To support people in finding information in COVID-19 content on our site, we've had to ensure that the latest terms and synonyms for the disease are part of our search — that's been a constantly evolving space.

And we've provided direct links to more easily find information about COVID-19-related research, as well as making information available from the WHO portal that aggregates content from other trial registries.

We are one of many international registries that exist to provide the public with clinical trial information.

And, along that theme of third-party websites and users, we've seen significant use of our content by other users, including government, private, and nonprofit sites.

Some of these are patient focused, while others are focused on the accountability and better understanding of the overall landscape of research that's happening in the context of the COVID-19.

And there's been some publications that have also reflected on and leveraged the information within ClinicalTrials.gov to show these types of landscape analyses related to that content. And this is another topic we'll be touching on later today.

And so the public benefits of a trial registry have really never been so obvious among this time of COVID-19, both in connecting people to research but also in ensuring the integrity of reporting.

It's really an opportunity to continue to see how essential registries can be in ensuring that results are disseminated in a timely manner. And that reporting matches what was prespecified in the research plan.

And all of these activities further reinforce the role of ClinicalTrials.gov in connecting to research-related communications that may exist.

If you've been following some of the research announcements here at NIH and by NIAID and others, anytime that they have a press release they're referring to ClinicalTrials.gov in the study that is listed there. And this is a common practice in other places, and one that is useful to further reinforce.

You can see that ClinicalTrials.gov is potentially a way to further connect to journal publications that exist, as well as other information related to individual participant-level data that may be available, not posted on ClinicalTrials.gov, but helping people to discover that information when it does exist.

On the site itself, we support full protocol documents, statistical analysis plans, and informed consent form posting as well as the summary results information in the results database itself.

And this is another topic that we planted in the RFI, to understand what type of resources people found valuable for linking.

So with that, I'm going to shift to providing a little background on the modernization effort itself. And keeping this backdrop of COVID-19 in

mind, all of the things that we're talking about today really do continue to be reinforced.

This year at ClinicalTrials.gov, we are celebrating our 20th anniversary, and we've had this incredible opportunity of incremental growth over the years.

But now we really have an opportunity to think to the future and what is necessary to ensure that ClinicalTrials.gov continues to be a trusted and valued public health resource and really to make sure that we're providing maximum value to the public.

Modernization is serving, really, two key audiences. Internally it's partially for us at NLM and NIH to really enhance our own infrastructure and internal processes and operations, but all of this is with the ultimate goal of ensuring that we can deliver timely improvements to you as our external users.

The modernization effort is a multiyear effort that we're planning over the next 4 to 5 years.

This first year is completely focused on the engagement process as an emphasis.

We really want to ensure that we are understanding the needs of our users as we move forward with developing a roadmap for what modernization will look like, and the RFI and your input is a key aspect of that.

I also just want to mention that we really do intend to consider this modernization effort in the context of the entire clinical research ecosystem in which we serve and operate.

We know that all of this is interconnected, and really thinking about opportunities for interoperability that can enhance efficiency and also improve information quality throughout this entire life cycle of dissemination of information.

I want to mention that even though the year has been focused primarily on engagement, we have also been sort of doing things that might appear to be invisible to you.

We've initiated some infrastructure work that helps to account, I guess, for a lot of what our team has been doing over the last year, but the main task has really been to shift our development framework from the Lister Hill Center over to the National Center for Biotechnology Information, or NCBI, which many of you may recognize as the home of PubMed.

There, we're able to leverage some of their existing framework, while also allowing us to plan for new components. So, this year has really been focused on sort of establishing a new baseline for us to be able to develop off of, from that infrastructure standpoint.

And as we move forward today with our discussion, we ask you to think about this broader ecosystem that ClinicalTrials.gov serves, but also is an integral part of, and to reflect on the opportunities that may exist to better meet the needs throughout this entire life cycle.

And so, one part of our engagement process this year is not only the RFI, but we've also been engaging with the NLM Board of Regents and the Public Service Working Group.

And I'm really pleased to be able to pause here and to introduce the Director of the National Library of Medicine at NIH, Dr. Patti Brennan.

She's been a very strong supporter of ClinicalTrials.gov and really a champion for advancing data science at the National Library of Medicine, to leverage the Library's vast digital information and to ensure that it's serving as a platform for biomedical discovery and data-powered health.

Patti will be here to provide a welcome and to introduce the working group that has been providing us with input on modernization.

We're working on connecting, I believe, Patti's microphone, and so I'm just going to pause for a second as we move into that aspect of connection.

(0:30:45)

Patti Brennan: Becky, let me check, I believe I've connected.

(0:30:46)

Becky Williams: You have connected. I can hear you. Wonderful!

(0:30:54)

Patti Brennan: I wasn't due for another minute, ladies and gentlemen.

Good morning. I'm going to change to controlling my slides also, is that correct? Or are you advancing my slides?

(0:31:06)

Moderator: That's correct, Patti. You advance them.

(0:31:11)

Patti Brennan: Okay. Good morning, everyone. I'm Patti Brennan, I'm the Director of the National Library of Medicine.

I want to thank all of you who are in attendance on this call today.

And thank you for joining us, but, most importantly, thank you for what you are doing to provide to the American public and the world the very, very best platform for accessing information about clinical trials and the access to the trials for opportunities to participate as well as for opportunities to learn the results of trials.

I want to spend a few minutes telling you about how the National Library of Medicine is responding to the COVID-19 event that is surrounding all of us.

I'm incredibly proud of our workforce. We've been on mandatory maximum telework for several weeks now, but we have done things such as expanding access to over 40,000 machine-readable articles related to COVID-19 and have taken that corpus, which has already received over 2 million accesses from NIH, and shared it to be able to exploit machine-readable strategies to access the literature, a challenge through Kaggle to answer the questions posed by the National Academies, a TREC-COVID Challenge, which is going to generate new kinds of search engines, and a specialized subset research, LitCOVID, that allows for access to the literature to explore COVID-specific information but indexed in a way that gets to unusual features such as the geographic location.

As you've heard already, ClinicalTrials.gov indexes over 900 studies for COVID-19, and we also are providing partnerships with WHO to be able to access and expose their repositories.

Our GenBank exposed the first full sequence of the virus on January the 13th, and we now have fully automated, 24-hour submission and release of data.

We're providing clinical standards terminology related to COVID-19 to support the hospitals and clinics, and we're also providing assistance to libraries around the country through our 8,000-member National Network of Libraries of Medicine.

You know, during this crisis many libraries have closed, and over the last 5 years many hospital libraries have restricted their services, so never before has the NLM been as important.

The National Library of Medicine is also a research engine, so we are working to provide and strengthen the infrastructure to ensure access to

this literature, to also provide more deeply — the clinical and chemical structures related to COVID-19, to enhance that our collections be electronically available anywhere in the world, and ensuring that it's easy for investigators to submit their new sequences through GenBank and through VirusHub.

Our Sequence Read Archive, which is the largest publicly available biological repository in the world, that's now available freely for access in AWS and Google, allows for explorations such as identifying new metagenomic sequences that may provide indicators of the evolutionary aspects of the virus.

In addition, we continue to support the implementation guidelines, training for standardization, and use of LOINC codes; these are laboratory codes that are essential for the testing, both for the antibodies as well as for the presence of the virus.

We're assisting institutions by expanding our Value Set Authority Center with professional society-defined value sets, FHIR implementing these to ensure that clinical facilities can monitor the cost and the quality outcomes related to the clinical profile of a patient with COVID-19.

Our research activities are taking our skill in advanced analytics and doing data mining of clinical data for deep phenotyping, trying to determine how we detect the sense of COVID phenotype in the clinical record.

We're applying AI and machine learning analytics to both visualization of clinical and molecular images. We're also using these analytics to support clinical decisions in real time.

And we're assisting in public health surveillance using viral genomics, health data, and social media data to identify spread.

So our research and service operations are supporting the COVID-19 strategies that the country is taking on to handle this complex and terrible disease.

But you're here today for a very special reason. Under the auspices of the Board of Regents, we've empaneled this group to help us understand and guide public engagement around the modernization of ClinicalTrials.gov.

The National Library of Medicine, which predates NIH — we trace our founding to 1836 — we became part of the Public Health Service in 1956, when our Board of Regents was established by statute.

This Board of Regents serves as advisory to the Secretary of HHS and also is an advisor to the Assistant Secretary of Health.

We meet three times a year; it draws from the clinical, library science, and data science communities.

We run the Board of Regents to address problems and challenges that face the National Library of Medicine; they serve as advisory to me. I also provide their reports to Dr. Collins.

But we use the National Library of Medicine's Board of Regents as a way to engage with the public, such as through this particular working group.

The working group that's been empaneled here has a charge to serve as our public engagement, to explore topics related to the modernization of ClinicalTrials.gov. They maintain the integrity of ClinicalTrials.gov as a trusted resource; maximize the utility of the growing corpus of information; and also connect with stakeholders through engagement, such as the one we're having today, to ensure that evolving needs are understood and carefully considered.

I want to personally thank all of the members of the working group who have joined in this activity at this very busy time. And I'm going to take a few minutes to introduce you to them.

Dr. Carlos Jaén has been a colleague and friend of mine for almost 20 years. He joined the National Library of Medicine Board of Regents about 2 years ago, and today stands as the chair of this committee.

This committee meets as needed, reports to the Board of Regents three times a year through Dr. Jaén's leadership.

The executive secretary of the Board of Regents Working Group — Public Service Working Group on the ClinicalTrials.gov Modernization is Becky Williams. Dr. Williams has been with the NIH and the National Library of Medicine for a long period of time; she serves as the Operations Director and the vision behind the ClinicalTrials.gov and its modernization pathway.

Lourdes Baezconde-Garbanati is a member of our Board of Regents and serves as one of the four members of the Board of Regents who are supporting this working group.

In addition to Carlos as chair and Lourdes as a member, we also have Dr. Kent DeZee and Gary Puckrein as members of our Board of Regents who have taken on the additional task of serving on the Board of Regents Working Group.

Through Dr. Williams's efforts and guidance from Dr. Jaén, we created a fantastic panel for this working group, and let me introduce you to them.

Their biographies are in your package. You'll notice that we have a mixture of researchers, of clinicians from many disciplines, of representatives of patient advocacy groups, and of librarians.

Carrie Dykes from the University of Rochester, Alyssa Gentile from The Leukemia and Lymphoma Society, Sally Gore from the University of Massachusetts Medical School, and Barbara Kress from Merck Pharmaceuticals.

In addition, on the working group, we have Seth Morgan from the National Multiple Sclerosis Society; Stephen Rosenfeld, who's with the Secretary's Advisory Committee on Human Research Protections; Joseph Ross from the Yale School of Medicine; and Steven Woloshin from The Dartmouth Institute.

Finally, we have members from within our NIH operations, Lyric Jorgenson from the Office of Science Policy and Pamela Reed Kearney from the Office of Extramural Research.

Those of you who are listening today or to the broadcast may learn more about the National Library of Medicine's Board of Regents and the Public Service Working Group on ClinicalTrials Modernization through the URL that's posted on your screen, or if you Google "NLM Board of Regents," you'll be able to find the page that describes our working groups.

I believe that I have left enough time for one or two questions, Becky, if there are any; otherwise, I'll turn you over to your important work.

Thank you for your time.

(0:39:59)

Becky Williams: Thank you so much, Patti. It's been wonderful to have you with us here this morning, and it's been very clear how well positioned we are being within the National Library of Medicine, in terms of the modernization effort going forward.

I see that we don't have any direct questions to be addressed at this time, so we'll be moving on to the next part of the program.

And so with that, I plan to provide now a high-level summary of the RFI public comments that we received. Many of you are here today because you also contributed to that RFI, and I'm very pleased that you are able to join us.

This is a little background — the Request for Information was available for about two and a half months this year; we closed around the time that everything related to COVID-19 was starting to increase and demand more people's attention.

The comments were collected in a web-based form through the guide notice that we have listed here.

The RFI itself covered three primary topics. One was around website functionality, which we've already talked about to a certain extent this morning. The second was information submission. And the third is data standards.

The third topic is not one that we're necessarily — that we didn't — we haven't set aside a specific panel on today, but as you'll quickly see, that topic ends up quickly overlapping with the other two topics of website functionality and information submission.

I also want to clarify that one of the things that we made available with the RFI was that this Request for Information wasn't intended to modify any of the existing legal and policy requirements for registration and results submission.

The purpose was really to think about how we can maximize the baseline that has been established by those requirements to, again, ensure that we're providing maximum value for you.

I wanted to talk a little bit about the process that we went through before listing the RFI, to give you a sense of how much time and effort that we've been putting into this aspect of it.

Before we started, we really wanted to make sure that we were spending enough time learning about the needs of our own partners here at NIH.

NIH is a very large place, with many Institutes and Centers, with lots of overlapping needs, but, again, some diverging needs as well.

Many of the themes that you see listed on this slide are themes that were also reflected in your RFI comments.

But I just wanted to mention a couple of the topics here.

The first one was engagement.

I'm mentioning this because NIH and our partners in the other Institutes and Centers really encouraged us throughout this process to ensure that our engagement had broad representation, and we really took this to heart, aiming for our outreach around the RFI to be broad and inclusive. And this

is a value that we intend to carry forward beyond just this phase of the RFI itself.

The other topic that was really important among the Institutes and Centers was reinforcing the importance of clinical research itself being inclusive of the people it's intended to benefit.

And they were really interested in considering and evaluating where there may be opportunities to reinforce this principle within ClinicalTrials.gov and, really, that entire clinical research life cycle that we have been discussing.

And so, this slide pulls together many of our different engagement activities, leading up to the RFI itself. Obtaining input from our Board of Regents Public Service Working Group on the approach that we're taking, obtaining input, again, from our partners here at NIH to ensure that we were understanding their needs, and then shifting to outreach outside of NIH.

And even though this slide ends in September of 2020, in terms of what we're identifying in terms of continued external engagement, which will occur through additional stakeholder meetings and participation in conferences and other types of interaction, I just want to reassure you that, really, this is just the beginning, and we are completely committed to engaging with you throughout this entire process.

We think it will be important as we lay out next steps and priorities to continue to hear from you to make sure that we're sort of on the right track and know quickly whether and where we might have gotten something quite wrong.

So in terms of strategy for the RFI, it was really designed to reach many different audiences, with a wide range of communication methods.

And we really do have to thank all the individuals and organizations that helped us throughout this outreach process to get the word out to allow for the robust response that we received.

We received 268 submissions to the RFI, and this really represented a range of different individuals and organizations.

We attempted to categorize the respondents based on role, and that's what you see here. About half of the respondents were researchers and data submitters, which does correspond with use of our public site — about half of our users on the public site are researchers and data submitters. And about 20% from patient communities.

And others are unknown, either because they were anonymous or it was not quite possible to categorize them.

So, one thing that this does tell us is that there may be a need to further reinforce our engagement with health care providers and patient communities as we continue to move forward.

Again, we're really happy, sort of, with this overall representation.

I thought, sort of, given the context of the respondents that we received from the RFI, it might be a useful time to take a pause and to do a poll to allow us all to get a sense of who is joining us today and to identify what role you identify with in your use of ClinicalTrials.gov.

I know many of us wear more than one hat. In this case, we're just asking you to choose one primary role.

We have patient, friend, family, or advocate; health care provider; a data provider, someone who submits information to ClinicalTrials.gov; scientist/researcher; institutional review board member; clinical research support, someone who might be part of a clinical research team that's supporting submission or otherwise supporting clinical research; medical librarian or information specialist; and then there's the great catchall category of "other."

And the votes are still coming in, so I'm just going to let that run for a second.

One observation is our "other" category sort of aligns in terms of representation today to what we say in the RFI, approaching sort of a quarter people who aren't quite categorized, so we appreciate that.

And really, clinical research support seems to be the most highly represented, with data providers following.

Great.

Thank you, everyone.

And so, moving on to the analysis itself, we have made the summary comments available. You can see that under my name, over on the right-hand side. And it's also available on our modernization website.

The analysis that we conducted was performed by NLM subject matter experts.

We basically assigned codes to each comment. And sometimes comments could have more than one code because it covered more than one area.

We ended up with about 200 unique codes related to the comments that we received.

I have to say we were very impressed, sort of, with the care and attention that people took in the comment submissions, really paying attention to our request to be specific and to provide detail within the comments. It really has given us a lot to work with. And a lot to think about.

And I also just need to pause and give quick kudos to the analysis and writing team for completing this analysis in just over a month and allowing us to share it with you today. These have been really unique working conditions, and performing this analysis in a month at any point in time would be challenging, but doing it in these conditions was even more unique, so I really thank the team for that.

The next slide that I have here is just providing an overall view of where we received comments. It's obviously quite striking that the majority of comments were around enhancing website functionality and improving the submission process.

And so, we'll be talking a lot about those things in our panels that follow this session.

And we'll be reviewing each of these in a little bit more detail. And, like I mentioned earlier, the data standards topic really does end up getting incorporated into the other section.

Overall, I think what struck us most in reading the comments, and in understanding sort of the range of people that responded, was that from all the comments, whether they were constructive or critical, they really did convey the value that people see in ClinicalTrials.gov. And your desire to

increase that value by having it better serve your needs, whatever they may be.

And so, we're really appreciative of those sentiments, and being able to see how much people really do value the site.

Another sort of interesting observation from the comments was that in many cases, the needs of our different users, no matter what role you identify with, many of those needs overlap, which makes our job a lot easier.

But then there's also examples where there are competing needs and interests. I'm just showing a couple quotes from the comments that we received that focus on contact information.

If you're a participant, someone who is potentially looking to participate in research, being able to have clear contact information and understanding who you can reach out to is a really important item and data element within a study record.

But then what you see is sort of the competing interest of an investigator or research team who is listing their contact information, in which that might end up creating extra burden or workload for them, and have less of a desire for that to be as prominent on the study record itself.

And so, as we're moving through the RFI comments, coming along, then we will continue to examine these different competing interests and really where they do overlap.

So I thought now might be a good time to pause and take another poll.

One thing that I'll note is, on some of our polls, if there is a long list of options, you may need to use the scroll bar to scroll down to actually find all of the possible options. That's on the right-hand side of that polling pod.

So today, one of the questions, again, sort of getting to know our audience: What is your primary purpose for using ClinicalTrials.gov?

To register a trial or submit results information? Again, we heard a lot from our data provider community, so I bet you are well represented today.

Searching for trials for yourself or someone else?

Conducting research on clinical trials, such as landscape analysis or systematic review?

Or none of the above?

All right, it looks like we have, again, sort of a lot of folks that are representing our data submitter community today. Thanks for responding. Hello and welcome.

As well as many people who are relying on content for the public site, searching for trials for themselves or for someone else, or using the site to do research. So, welcome to all of you as well.

And so with that, I'm going to turn it back over to our moderator, Wendy.

(0:55:10)

Moderator: Thank you so much, Becky, and Carrie, and Patti, and all of the Board of Regents Public Service Working Group. That was a terrific overview.

As a reminder, you can submit a question or comment via the Q&A pod. We're not going to be responding individually, but we have seen a number of questions about whether the meeting is being recorded and slides will be available.

And the answer to that is yes, within the next 30 days you will be able to find the recording and the slides on the ClinicalTrials.gov Modernization webpage. And we'll also announce they are live via the Hot Off the PRS! newsletter.

We're going to move right along.

Up next will be the information submission panel with Heather Dobbins, Carrie Dykes, Sally Gore, and Barbara Kress.

Recording 2 – Information Submission Panel (0:00:00)

Up first, I'm delighted to introduce Heather Dobbins, the ClinicalTrials.gov Lead Results Analyst, to lead the discussion about information submission.

(0:00:19)

Heather Dobbins: Hello, everyone. I am happy to be here today to talk to all of you, and following my presentation [indiscernible] organizational perspective [indiscernible].

I'm working on advancing the slides.

Okay.

So, our goal [indiscernible] the RFI topics [indiscernible] to get some input from you, especially since a lot of us [indiscernible].

First a brief background to provide context.

(0:01:18)

Technical Support: Excuse me, Heather, I'm going to interrupt momentarily. I apologize. We seem to be having some issues with your audio cutting in and out.

If you could check the placement of your microphone and be sure to project very loudly; also, as we practiced, you might want to check the drop-down arrow next to the microphone up there to make sure the proper mic is selected.

But let's go and try that again.

(0:01:50)

Heather Dobbins: Okay. Is this any better?

(0:01:57)

Moderator: Yes, that sounds great, Heather.

(0:02:00)

Heather Dobbins: Okay. Unfortunately, I'm not doing anything differently and I am practically on top of my microphone, so I apologize that I don't know what's causing the interruption.

So, I believe I just summarized our session goals. And I moved to this: So I'm going to provide some brief background to provide context for the topic today.

As Becky described earlier, we issued an RFI to seek public comment on different topics [indiscernible].

Using the protocol system [indiscernible].

(0:03:02)

Moderator: Heather, I'm sorry to interrupt you again, but we are having trouble hearing you again.

So, let's troubleshoot a little bit.

(0:03:11)

Heather Dobbins: Okay.

I am really sorry.

Is this any better?

(0:03:25)

Technical Support: Heather, I don't think this is on your end. Again, this is Jeff. Apologies for interrupting, I believe that it may just be internet congestion.

But if you could, what we're going to do is provide you with a dial-in number, and you can try calling.

Actually, if you can disconnect for me and reconnect, asking the room to call your phone instead of using your microphone, we might be able to get a better connection this way.

So, if you go up there next to where your microphone is and click on disconnect my audio, and then reconnect, but this time make the selection of having the room call your cell phone, and we'll try to get you reconnected that way.

(0:04:15)

Becky Williams: Hi, this is Becky, and while you're working on that with Jeff, Heather, I'll go ahead and just jump in and sort of say a few words to fill the time, if that works well for everyone.

I'm going to go back to your title slide here, on the information submission panel, and just provide a little bit more background about how we set up the agenda for today.

We decided to focus first on the information submission panel, primarily because how information is submitted and the needs of those who are providing information greatly influences the information that is then available on the public site.

There's a process sort of in between, as well. Once information is submitted, we do some back-end processing on that content in order to make it available on the public site.

And some of the things that we do around that relate to adding synonyms for search that makes things easier to find.

We add resources such as publications; we add information and links to resources like MedlinePlus, to allow consumers to sort of find more general health information about their disease and topic.

So we thought it would be useful today to be able to start with the information submission side before talking about the website functionality side.

I also want to mention, in terms of creating the different panels that we have today, one of the goals was to allow the audience to hear different perspectives. And so represented on this panel are Carrie Dykes, who's at an academic institution; Barbara Kress, who is at a company that is responsible for disclosure; and then Sally Gore, who works at a medical library, who supports researchers and others in different aspects related to using the site as well as submitting and managing information.

And the panel around website functionality, same thing. It will allow you to hear from different voices who have different perspectives on some of these different topics.

I'm sort of tracking along in our little pod here, and it looks like Heather might be back on board. Did you want to test her audio?

(0:06:56)

Heather Dobbins: Hello? Can you hear me?

(0:06:59)

Becky Williams: I can hear you.

(0:07:04)

Heather Dobbins: Okay. Great. I am looking in our little presenter chat, and it does appear that I may be better connected by my phone.

Okay. So, I have received a suggestion to start from the top, since I have been broken up a lot and so that the message is not broken up.

Thank you, Becky, for filling that time in, for providing that additional background information. That's very helpful for us today.

I will apologize one more time, and let's try this again.

I will just start by saying I'm happy to be here and to talk with all of you.

So the goals for our session today are: to share a summary of responses to the RFI topic of information submission; to provide some examples of ClinicalTrials.gov within the context of different organizational workflows; and to get some additional input from you, our participants, especially since our data providers are well represented today, on some of the topics that were raised in the information submission RFI item.

So first a brief background to provide context. I won't go through this bit because I feel like we've been through the information submission topic thoroughly.

The other bit of background information, as Becky mentioned, in Becky's slides you saw the flow, the diagram that's over on the left-hand side, which is related to process of registration. And then on the right-hand side, you'll see that the process looks very similar for submitting results.

So there are a lot of details in this process, and the big idea that you need to know for the purposes of this talk are that both registering a study and reporting results, to do that a user will enter information into the PRS, that information goes through an automated validation process, and then reviewers perform a manual QC process, and Becky went through some of the goals of that manual QC process.

When the information passes both the automated and manual QC, it is then posted to ClinicalTrials.gov on the public site.

And so here is a summary of what you all had to say in the RFI comments.

Right here, this is part of one of the slides that Becky showed you, so this is the number of submissions or unique responses to the RFI, and as you see, most commenters chose to provide input about the data submission process itself and how to improve the PRS.

Further breaking that down, each submitted comment was coded by more than one subject matter expert here at ClinicalTrials.gov to examine the frequency with which commenters mentioned specific issues or areas of interest, and this is a summary of the distribution of those codes in the "how to improve the PRS" topic responses.

You can see that “Data Entry” was mentioned the most, at 140 times, at around 33% of the overall coded comments.

“Data Element Definitions” were mentioned 55 times, and so on.

That last catchall “Others” category consists of all the code that occurred at a frequency less than the category above it — the “Updates” with nine responses at 2.1%, and we’ll dive a little bit deeper into these data in a couple of slides and note that you can find more information about our coding methods in our summary report.

Here’s a brief qualitative summary of the responses to subtopics 2b through 2e.

For 2b, the most frequent request for interoperability was with Clinical Trial Management System. Other examples included processes such as IRB reporting.

For 2c, the most frequently mentioned emergent technology to enhance the PRS was natural language processing, with other examples of API and machine learning, or artificial intelligence.

For 2d, the most frequent request was for clearer data element definitions, and often the request for “clearer” was intended to mean plain language or layperson language. Other examples were additional study design templates and more expanded review criteria.

For 2e, most frequently respondents suggested that public recognition was the best incentive for timely reporting of quality results. Other incentives — sorry, it looks like somebody else — so, other incentives mentioned were providing statistics for PRS users, so how users are rated with respect to each other, and enforcement.

As I mentioned before, we’re going to take a closer look at the responses to 2a, which was how to improve the PRS, and in our coding we noticed all of the responses fell into one of three key themes: comments discussing the data structure and format in the PRS; comments about the process of data entry, submission, and QC review; and comments suggesting features to improve the overall workflow management for organizations and administrators in those organizations.

Within the comments about data structure and format, some commenters were requesting more standardization in some of the data elements, such as eligibility, contacts and locations, arms and intervention; some of the requests for more standardization expressed a desire to do so in order to enhance compatibility across multiple platforms.

On the other hand, some commenters suggested that more flexibility in some of the data elements and record structure would be improvements to the PRS.

We saw requests for more flexibility through simple changes, such as increased character limits, to more complex changes, such as the ability to describe different stages of study design at the time of registration. For example, if the number of arms or blinding will change throughout the course of the study, commenters wanted the ability to specify that at the time of registration, using a flexible PRS structure for that purpose.

Some commenters requested structural support within the PRS for a variety of study designs. For example, PRS study designs that you could select as an option and then have the PRS structure some of the tables and data elements specifically for the study design that you selected.

The next theme revolves around data entry, submission, and the QC review process.

Some commenters requested tools to simplify the data entry and submission process. These requests included: just-in-time help during data entry to clarify the information that is needed in each data element; libraries of pre-written outcome measures that you could select that were relevant to what you assessed in your own study; the ability to upload data from different file formats such as Excel spreadsheets or publications; minor updates to the PRS user interface, such as shortcuts for getting to different places of the records or to copy changes from one place to multiple places.

And then other comments in this theme talked about additional streamlining of the QC review process. Those comments requested easy access to one-on-one help with reviewers, a process to dispute and remove QC review comments, and requests to address a perceived inconsistency between record reviews.

Here in this last theme, the comments were focused on more customizable features to manage organizations' workflows. Requested features included such things as a PRS dashboard that displays metrics and a to-do list of actionable items; record tags that could be customized to label records falling under different policies or regulations, and these record tags would be used to flag data elements and timelines specific to each policy; customizable email lists; additional, movable columns within the different record lists; streamlined record edits, such as ability to edit the same information in more than one record; and, finally, different organizations may have different staff that need to review and process the record at different stages, so commenters requested an information submission

process that could be customized to uniquely meet each organization's workflow.

And so I think I went slightly over because of my technical difficulty.

But that was the summary of that bit of information submission responses to the RFI.

And so now it's time for a poll question.

We would like to pose this question to you. So, you just heard me describe three key themes in the RFI comments with sub-themes and examples from our RFI comment analysis. We are interested in learning which of these sub-themes would be of the most interest to you in a modernization effort.

Again, you saw the polling frame pop up below the presentation slides.

In this instance, we're asking you to pick two of the sub-themes that are here in the slide.

This is looking great.

It looks like we actually are having some of the competition of the different requests from different people, additional standardization versus more flexibility both shine through, and those are some of the competing interests that we have been reviewing through input.

Okay. So, I believe I'll leave that open for — okay, we'll go ahead and stop. That's perfect.

And so I wanted to thank you for your input, and with that I will turn it over to the moderator to introduce our next speaker.

(0:18:22)

Moderator: Sure. Thank you, Heather, and thanks, everybody, for participating in the poll there.

Up next, we will hear from Dr. Carrie Dykes from the University of Rochester Medical Center.

(0:18:36)

Carrie Dykes: Thank you. Good morning, everyone.

I’m the PRS administrator for the University of Rochester, and I was asked to provide some background about academic institutions, including unique characteristics that influence how academic institutions manage ClinicalTrials.gov, the roles that administrators play at our various institutions, some information about the Clinical Trials Registration and Reporting Task Force, and types of metrics that we use to ensure compliance with ClinicalTrials.gov.

Academic institutions have several unique issues that impact compliance with regulations and how ClinicalTrials.gov is managed.

Most principal investigators have competing responsibilities. They have their research projects, but they also have clinical responsibilities, teaching responsibilities, and academic service responsibilities.

In their research role, the level of responsibility may vary, depending on the project or their role on the project, and they often have several different types of projects they’re working on, such as behavioral studies, interventional studies, or observational projects, all which have different rules and requirements.

In academic institutions, faculty act as individual entities. The management of research at most institutions is decentralized. Their research projects are managed like their own small businesses. And collaborations often require crossing departments, colleges within a university, or across institutions.

Different faculty, and even whole institutions for that matter, also have different levels of risk aversion.

There’s a fair amount of turnover for both PIs and their team members, such as study coordinators, and many institutions lack a formal exit communication strategy, which can create problems for administrators when records in the PRS require action, but the research team is no longer at the institution.

Finally, academic institutions are academic. They teach the research process to the next generation of principal investigators.

Often, PRS administrators are working with employees who are learning the ropes and therefore require a more hands-on approach with many more educational opportunities.

This is a list of some of the roles that academic administrators have: They create accounts for university study teams, help investigators determine if their study needs to be registered, walk investigators through the registration process, and either register studies with them or do it for them.

Same goes for results.

We often help them enter their results or do it for them, we track problem records for the institution and help investigators resolve those problems, and we track institutional metrics and provide education to study team members.

Academic medical centers vary widely in size and how each manages ClinicalTrials.gov. I've put examples of Johns Hopkins and Rochester here so you can see the difference between a larger and a smaller institution.

Johns Hopkins has five separate PRS accounts, whereas Rochester only has one.

Again, Johns Hopkins has over 1,800 total records in their PRS, and Rochester has only about a quarter or a third of that.

Finally, the number of FTEs varies widely. Whereas Johns Hopkins has two and a half total full-time efforted employees to manage PRS, Rochester has 10% of an FTE.

The Clinical Trials Registration and Results Task Force was created to help academic institutions understand and apply requirements for registration and reporting; identify best practices; develop tools for management of records; and provide communication among institutions, between institutions and the PRS team. There are over 220 institutions in the group and almost 500 members.

You can see our website listed here on the slide.

The group is managed the by Sarah White at MRCT and Tony Keyes at Johns Hopkins, and they lead calls each month featuring people from PRS, the FDA, and OHRP.

You can join the task force if you're an academic institution with a PRS account, and membership details can be found on the website.

Finally, I wanted to provide some examples of metrics that academic institutions often use to track compliance. These are items that would be helpful to have on a dashboard, for instance.

The number of total records, the number of active records, the number of problem records, new registrations, or records with results due.

And it would be good to be able to see these within a particular time frame, such as the past month or the past year.

In addition, having a way to count down when records have results due, say at 3, 6, 9, and 12 months, would help us remind investigators to complete analysis of study results.

Being able to identify the various types of records such as ACTs or NIH-funded or BESH studies.

Other things we track are percent compliance for both registration and reporting, registration cycle time, and the number of cycles it takes to get a record registered, and the same metrics for results reporting as well.

Hopefully, this gives you an idea of how academic PRS administrators manage records and the unique environment of medical centers that impacts compliance and management practices.

Thank you for your attention today.

(0:25:20)

Heather Dobbins: Thank you very much, Carrie, for that perspective from academic medical centers.

And so what we wanted to say is that we know investigators and clinical trials staff at academic medical institutions are well versed in taking advantage of a service that we provide to anyone reporting results, where we assign a results reviewer to help complete a results record and submit the results information. Through this service, reviewers are happy to provide general answers to questions or walk you step by step through data entry.

In the RFI comments, we heard a request to have easy access to one-on-one assistance, so we are curious to know how many of you are aware that you can currently request this one-on-one assistance from a results reviewer to help you with results submission.

And it looks like people are split, about half and half. Half were aware and half were not aware.

So, if you'll look at the slide right above the survey, that tip is that you can request this service via email to our general email address: register@clinicaltrials.gov.

Thank you.

(0:26:43)

Moderator: Thanks, Heather. Great job on the polling once again.

Next we're going to transition and hear from Sally Gore from the University of Massachusetts Medical School.

(0:26:59)

Sally Gore: Thank you, everyone. I hope you can hear me okay. I've had some interesting or difficult connectivity issues this morning. It's a little stormy here; I think that's not helping.

I just want to thank you for the opportunity to spend a few moments with you this morning.

I was asked to offer some perspectives from those of us who work as librarians in academic medical libraries or hospital libraries and other special libraries that support clinical research.

I think Carrie just gave a wonderful overview of how clinical research happens at academic institutions, and in many ways, she described the same environment where I work at UMass Medical School.

So let me see if I can just add another layer to that, to how different departments and people support clinical research and use ClinicalTrials.gov and, in particular, that of libraries and more librarians like myself.

I'm doing two screens at once. Let me see if I can get in.

So, I start here as a reminder for some and perhaps a new insight for others; this is a slide that my department, Research and Scholarly Communication Services, walks through with our incoming PhD students each fall.

In a world where so much information is right at our fingertips, I think it's easy for people to not know, or maybe have forgotten, the valuable expertise and resource that librarians bring to researchers throughout the entire research workflow.

From the very beginning, when one is formulating a research question, to creating effective search strategies for bibliographic databases or, in particular as we heard earlier, searching ClinicalTrials.gov when you're doing systematic reviews, to managing data and using electronic notebooks effectively, to taking advantage of information management and citation management tools, to seeking out the proper place to publish, to understanding copyright and users rights, tracking the impact of

research outcomes. In each and every one of these areas, we bring skills and knowledge to support the efforts of the researchers.

And, in particular, when it comes to supporting clinical research and the work that we do in helping folks with ClinicalTrials.gov, I think these are the points in the process where we're most often called upon to help.

These are the aspects of the modernization project where, I believe, academic medical librarians and others special librarians who support clinical research focus our attention.

We think about the aspects of using this system, of course, registering trials, reporting, understanding compliance issues, and the like. But also, really what's important for us is all the ways that information in ClinicalTrials.gov is seamlessly tied to other outputs. Things like publications and patents and policy data and the like.

As Carrie stated very well in her presentation, there is no one-size-fits-all when it comes to describing the users of ClinicalTrials.gov.

The support we provide as librarians in general focuses on clinical and basic science researchers both. These are two groups that are certainly different, and more within the groups themselves, there are a lot of differences.

There are differences in the numbers and types of staff, there are differences in experience, differences in funding, and all of these affect the types of help that we're called upon to provide.

For example, a well-funded, highly experienced clinical or basic science researcher is afforded a lot more staff and a lot more time to work with to understand a tool like ClinicalTrials.gov, as compared to a physician–scientist who might be early in his or her career, with very limited time to do research on top of balancing clinical duties that they're called upon to do.

Think about right now the folks who are on the front lines trying to treat the issues like COVID-19 as they're also doing research, which is happening, and it's amazing how much it is, but we can kind of think of the toll that can take.

So you can imagine how, when, and where librarians support these individuals varies quite a bit.

And so, with that in mind, the things that we need most in our work are clear, easy-to-access, and up-to-date instructions. We need training opportunities, we need consistency, and we need contact.

While NLM provides a great deal of help via ClinicalTrials.gov, those of us who are on the front lines in a different way, meaning right where the researchers are, are those who are asked to serve as go-betweens.

Whatever NLM can provide in terms of instructions and training, plus whatever we can add locally to enhance these things, benefits all.

We can answer questions and troubleshoot a lot faster than an email sent to a help form, we can offer in-house training that's customized to our folks, we can build repositories of materials like examples of study designs that are not meant to replace those provided by NLM but to enhance them and are personalized for our own particular setting.

Because, again, we all work with a variety of different audiences who have a variety of different needs and who desire help in a way that works best for them.

It's much more feasible to do this in some ways from a local perspective than from a national or even international purview. However we can do this, again, for enhancement, not for duplication of efforts, is a win.

So, lastly, I just want to speak a few minutes again, as Carrie did as well, on the efforts we do particularly as scholarly communications librarians to track and report the impact of research done at our institutions. This is really a growing field, with lots of new opportunities emerging.

We have a number of tools and means to track compliance and grant funding and to build faculty portfolios, lots of things around bibliometrics and alternative metrics, publications being a standard, but patents, of course, and policy statements and social network activities.

These things are all available by us now, and as I noted earlier, any and all of the information and data in ClinicalTrials that can be linked with other NLM resources where some of these things are stored, it's just a huge bonus.

Becky outlined some of these things when she was filling that time in the — when we were having a little tech issues before the panel began, and I think any enhancements here are always most welcome.

Bottom line: Research is competitive. Funding is tight. Everyone's work is deemed important. So the need to demonstrate the real impact of one's research from the individual lab level all the way to an institution as a whole is really vital.

And we try to support that as librarians in all these different ways.

(0:34:34)

Heather Dobbins: Thank you very much for that, Sally.

As you heard, there are many resources that a library can offer to help different audiences at different levels of information requests.

And we like to offer resources.

One of the resources that ClinicalTrials.gov offers are example study designs intended to demonstrate how to enter results information for different study designs.

As you see here in the slide, up at the top, those are currently example study designs that we offer. Under that, we have some that are currently in development. Of course, we hope they will be released sooner rather than later, but they are coming.

And this is an upvote question — so, we're interested in what other example study designs would be useful to you.

So, for this one, you type your answer into the — oh, people are saying they lost the picture?

So, I'm not sure how to troubleshoot that.

But for this one, what you can do is type in your answer, hit "send," and then you can use that +1 to vote for somebody else's answer or you can continue adding your own answer.

I am seeing a lot of people requesting observational example study designs. And that is great information to have.

I'm seeing pragmatic clinical trials.

I did see some people enter the master protocol research program, so hopefully those basket umbrella trials resources that we have coming will be of great use.

Step wedge design.

A lot of really good answers here.

They come in so fast, it's hard to read them all.

The smart adaptive, so that will be really good that we have that one coming out.

Okay. Thank you all very much for that input.

We have all of that recorded. And I will pass this to Wendy to introduce our next speaker.

(0:37:21)

Moderator: Thanks, Heather. Up next, we have Barbara Kress giving us her perspective from Merck.

(0:37:31)

Barbara Kress: Thank you, Wendy, and good morning, everyone.

I'm the Director — Executive Director of Clinical Data Disclosure and Transparency at Merck. And I've been working in this space since 2007.

Today I'll share what posting on ClinicalTrials.gov looks like for industry.

So, I think it's noteworthy to show how posting to ClinicalTrials.gov has evolved in head count as well as departmental structure over the years.

We started with a decentralized model. My group was only responsible for registrations, and the researchers conducting the clinical trials posted their results. Around 2009, we changed to a centralized model, absorbing results posting as well.

Although researchers know their trial results, they didn't know the requirements under FDAAA, and they may not use the system, frankly, for years between trials.

And so we now have a department of 30 people dedicated solely to the disclosure and transparency initiative.

My company has well over 2,000 trials on ClinicalTrials.gov at various stages. And it's imperative to have a very sound tracking process, so we can submit records within company and ICMJE timelines.

Daily, we receive notifications from our document repository system when protocols and amendments and CSRs are finalized.

And from our Clinical Trial Management System, or CTMS, we run weekly and monthly reports. CTMS houses protocol milestone dates, and so we run site, study change, and scoping reports.

The site report is as it sounds, it adds site or changes site status. The study change report highlights date changes along the trial. And the scoping report helps us to identify trials for posting on critical milestone dates.

So putting these reports together, our posting process kicks off, based on the scoping and notification of finalized documents. A therapeutically aligned medical writer authors the posting in the transparency management system, which we'll talk about. Once completed, the record goes for a quality control review and then for approval. The record is then released through this transparency management system to the NIH, and then we simply monitor for acceptance or for comments.

So over the lifetime of a trial, which can last, as you know, for many years, there are many updates that have to be made to a record along the way. To capture those changes, we run weekly change and insight reports.

As I said, my team and I have been doing this for a long time, and we've learned a lot over the years, and I think the most important tip is to have a dedicated transparency team.

I think subject matter experts really make all the difference. They know the law, the format, system limitations, timing and data requirements, and I think there's a higher probability of acceptance using this centralized model, and it's a game changer for us.

Trained medical writers make a huge impact. Medical writers certainly have an advantage in this role, but writing for ClinicalTrials.gov is a skill unto itself, and it requires training and mentorship.

SOPs and guidance documents are roadmaps, right, that define process and standards and expectations, particularly for our medical writers; of course SOPs are extremely important in audits.

Quality control review has been an important step for us. The record that is authored is checked against the source document and our QC checklist. This checklist is based on our experience, comments received from the NIH, and from the NIH's own checklist that they have.

Medical writer meetings occur weekly, and review comments are discussed, knowledge is shared; process and guidance document suggestions are also discussed.

The big issue here is major NIH comments are discussed, which is really important. This allows every writer to hear the issues, to problem solve as

a group, and to learn, and all these comments are logged for future reference, and this helps to identify trends for us and to make adjustments in how we're writing.

We also contact the NIH, and they've been very, very responsive to us, and all feedback that they give us is shared with our team, and often added to our guidance documents.

For all the talk about process steps and guidance documents and meetings, there is only one way to know if all your efforts are working. And you have to collect and analyze metrics.

And to be honest, we collect metrics for everything. But I think there are a few that are critical. I think authoring time is critical — it's critical to know if you have enough head count, right, to get the job done, based on your book of business.

Review and approval time is important. If you're rushing your authoring time to meet deadlines, now the record is sitting waiting for whoever approves in your organization, all your efforts really could be for naught, right? This also tracks repeat offenders who are delaying approvals.

Quality control review time should not take as much time as authoring the document, right? You want it to be thorough and efficient. And adherence to your process is an important indicator of a processing control.

Internal process audits, I think, are foundational and should be done frequently. If your process is not in control.

And, of course, compliance with the law is of the utmost importance here. What is your rate of compliance? Do you track this internally? Do you report it quarterly or yearly to someone in your organization?

And the NIH acceptance/rejection rate is really important.

This is where I think having a dedicated group is key because we can incorporate feedback into the process again to make it stronger.

And last but not least, there are tools and services that can help you with all of this.

TransCelerate is a nonprofit organization that collaborates with biopharma to create solutions and to simply processes. They recently created a common protocol template that provides common structure and language.

Most protocols are not written for a cut and paste into ClinicalTrials.gov, and this template really enables end points that map to objectives and it

supports CDISC standards as well. You can find the template on the TransCelerate website.

We talked a bit about the Clinical Trial Management System before; it's a great trial-tracking system. You have the ability to run reports, and you can directly connect it to a transparency management system to automatically upload dates.

And, lastly, of course there are vendor services to help as well, full- or partial-service companies you can contract for experienced medical writers or, quite frankly, for the whole process.

There are several companies out there that provide transparency management platforms that I discussed. Right, these platforms provide audit trails, authoring capabilities, review and approval capabilities, and metric readouts. They also can provide staff with disclosure expertise; they can streamline your current processes or create one for you.

I'll stop there. Thank you. Wendy or Heather, back over to you.

(0:46:13)

Heather Dobbins: Hello. It is me, Heather, again. And so it's time for the last poll question of this session.

Thank you, Barbara, for your presentation and talking about the different things from Merck's perspective.

From our panelists, each of our panelists, you've heard different things that they may track within their own workflow to keep tabs and report on their institution's to-do list, their progress, their successes, and maybe areas of improvements.

And as part of modernization, if we were to design a PRS dashboard, what metrics would you like to see for your organization?

To make this a little easier for you, we've listed some of the example metrics that the panelists have mentioned, but this is a free-text answer, so feel free to provide any metrics that you can think of and enter in the time that we have.

This one is just a free-text answer. So, this is not one where you can vote on somebody else's answers. You just have to answer all of your own.

And I am seeing a lot of people say − I'm seeing ACTs come up a lot. I'm assuming that means the number of ACTs that they have in their workload.

Upcoming results, people are interested in learning about upcoming results.

Oh, thank you. That was made bigger.

People are interested in − yes, due dates, cycle times, different percentages of records that meet registration and reporting results timely.

Okay.

Consent uploading. Oh, I'm guessing that's the number of records that have informed consent uploaded.

Okay. That's a lot of answers. Thank you very much for that input.

And with that, this session is over.

We can take a couple of easy questions that we've received during the time that people were talking. And then we will take a break.

So, let me look through the questions really quickly.

What somebody did ask was the ability to − for that help, that one-on-one assistance, people want to know if that's available for registration records.

We do offer email assistance for registration records. You can email the same address, and you will get an answer that should be tailored to your question. So, in that sense, it is a one-on-one assistance.

We don't typically schedule teleconferences for registration records because of the volume and nature of the questions. But you can get the same help through that same address.

And then the other questions that I'm seeing, people are asking specifically about what we foresee in response to these modernization input, and we'll be communicating — during this meeting today, we're not going to be addressing any of those specifics, but we will be communicating publicly going forward with our modernization, about our modernization efforts.

And with that, our time is up.

So I would just like to thank all of our panelists again for their time and listening today, and then I will turn it over to Wendy to adjourn us for a quick break.

(0:05:23)

Moderator: Thank you, Heather. Terrific job. I know I learned a lot and was excited to see those results in that discussion.

So we are going to take a short break right now.

I believe we're going to put up the chat pod again, and if you all would like to continue talking with each other about this ClinicalTrials.gov modernization effort, that would be terrific.

And if you need to take a break for a few minutes to check your email or take care of a couple of other things, we are going to resume right at 11:30 with the website functionality panel.

[Brief Recess]

Moderator: This is Wendy again. We're going to get started with the website functionality panel.

Hopefully, everyone had a chance to stand up and stretch, and you're ready to engage again with this wonderful upcoming panel that we have.

Recording 3 – Website Functionality Panel (0:00:00)

So, it is once again my pleasure to introduce and hand over the mic to Becky Williams, who is the Acting Director of ClinicalTrials.gov.

Becky?

(0:00:14)

Becky Williams: Thank you, Wendy.

I just want to also take a moment and thank the previous panelists. I think that each of their contributions really demonstrates this context of the entire research ecosystem that we are operating in and how different organizations have different types of needs and approaches.

And how, really, when we think about modernization, there's this issue about how studies themselves are evolving, and different study designs and approaches to research that are also things that we need to be evolving with at ClinicalTrials.gov to meet those informational needs around that.

And I just love the role of the library and medical librarians and the role that they play in supporting researchers and really serving as a hub for this field of data science that everyone focuses on these days, as the new buzzword.

It's really great to hear from each of our panelists. So, thank you.

And moving forward, we're going to be focusing on the website functionality aspect of the program, and as you can see here, I'm really glad to be joined by a whole new set of panelists that sort of will be bringing really unique insights into their own experiences overall and in interacting with information on ClinicalTrials.gov.

Similar to Heather's session, the goals here are to share the responses and themes that we've heard from the RFI around website functionality; we want you to be able to hear different perspectives from panelists that really do also align with some of the different perspectives that we heard in the RFI comments themselves.

And then, again, we have the joy of more polling and interaction to be able to obtain your input, and then just a reminder you can continue to submit questions through that pod that we'll be collecting and using as well as we move forward.

The topic of website functionality had focused on four key areas.

One was really around new uses of the site, as well as current uses, and how some of those could be enhanced. And those items, a and c, are the ones that we're going to be focusing on during this panel.

But item b was another topic, just in terms of resources for possible linking from ClinicalTrials.gov. And I had shown previously the slide that had sort of — I guess I'm skipping my order of my slides here.

I'm jumping ahead on topics. I'm so excited to get to that.

Just to ground us here in the topic of website functionality again, the comments that we had thought had really focused on both the website itself, as well as opportunities for leveraging the application programming interface and how that could also be improved, as well to support various uses of the site.

And for all of those out there who aren't familiar with it, I'm just including a reference here, but, again, it's really designed to support that third-party use, and we've made a lot of new formats available as well as many more fields available to be able to interact with the information on the site.

You can see here from our responses that most of the responses really focused on both new uses and current uses of the website, so, again, as I mentioned earlier, that's really what I'm going to be focusing on today.

And as I started to talk about earlier as well, resources for linking was certainly a topic that people provided input on and that we covered in the summary report, and I just thought I'd mention briefly that sort of the top responses and requests in that space are really on that upper left-hand corner, focusing on journal publication and linking to the NIH resource PubMed and PubMed Central to provide content there.

We do already do this, but a lot of the comments focused on sort of strengthening and improving the way that this functionality works.

Some folks commented on linking to other NIH resources, such as MedlinePlus, which is operated here at the National Library of Medicine, as well as connecting to other government databases here or websites here in the U.S., the FDA, and abroad, the European Medicines Agency, which runs a clinical trial registry and results database.

People also mentioned the desire to be able to connect and find individual patient data when it's available to support further research; again, this would be de-identified data that would be stored in other repositories with other safeguards.

As well as advocacy organization websites that can provide support and educational materials for patients.

When we go to look at, in a little bit more detail, the new uses that people were requesting, you can see at the top there that a lot of comments really focused on the study record itself and how that information was organized, or what information was available within it.

And then you see a bunch of categories that are related to different aspects of search and using search results.

And the second category that you see there, related to alerts, really sort of helped to − is reinforcing all that effort that might have gone into finding a particular study or conducting a particular search. People wanted ways to be able to save and manage those search results and get alerts about changes or additions to those going forward.

Also, downloading content for analysis as well as wanting additional information that might be in plain language format around results information.

I'll also just point out here, and for a lot of our comment categories, there's sort of a long tail, if you will. And that we received, you know, lots

of other types of comments that aren't necessarily represented on this slide.

Switching to current uses and how people use and interact with the site, again, the comments were very similar in nature, focusing on the study record and the way in which they interact with search. A topic that didn't appear on the other one, which is focused on data quality and the information that's available and ensuring that it's as useful as possible going forward, as well as just general usability principles related to website functionality.

So, when you take kind of a step back and look at the coding that we did, we've abstracted that information into top response themes really focusing on, again, this category of search options and managing search results. The study record format and content. And then a theme that was really cross-cutting across all of the categories was the desire for additional plain language information.

I'm going to drill down into each of those in just a little bit more detail to give you a sense of what some of the comments and what people were speaking to there.

In terms of search options and managing search results, people really desired for search to be more user-friendly. What user-friendly meant, though, meant different things to different types of people.

And so some wanted a step-by-step approach to building a search, others wanted to customize the approach based on the user type, and a general comment to sort of simplify it. Yet at the same time you'll see later that people really want more options to be able to search, so they want it to be user-friendly and simple, yet at the same time having lots of options to be able to search for content. And so there's adding more search options focused on the existing structured data elements that we have, which are relatively easy to accommodate, as well as some of the nonstructured data elements like eligibility criteria, and then other information that we don't necessarily collect in a structured format, things like genetic mutations or biomarkers, that might be really relevant to finding information on the site.

And then again, all this effort you put into developing a search that meets your needs, then how can you manage those search results, with different tools for sorting and filtering, downloading, and again that theme of notifications I already mentioned.

I've just included some quotes here that represented some of the different comments, just in terms of, again, varying views on the nature of how well

or how not well, I guess, the site works based on different people's viewpoints and perspectives.

The second theme was around study record format and content.

As we saw with the information submission topic, there was, again, sort of a desire for more standardization around certain content, particularly interventions and eligibility criteria.

And then comments around what information should be displayed and where; depending on sort of what your own role or need is, some of that content may change in terms of prominence.

There were also comments related to making more content available, things that aren't necessarily currently available on the site, including information related to out-of-pocket costs that people might incur or payment to participants, as well as potential risks associated with study participation.

And then, again, in study record comments, content, people had desire to add features to make using content easier, so how you might be able to more easily share a study record with someone else, as well as more printer-friendly formats that can be reused.

And again, just some comments about standardizing content from our users and what people found is a challenge, but then also what might be helpful within this space.

Finally, the last theme is plain language information. And there was lots of comments in different spaces around that. Some around just general health information and learning about study information or study participation. So some of the general content, background informational materials we make available on the site.

People thought that resources for using the site features, both targeted at patients and researcher audiences, would be useful. So thinking about how to better coach and help people understand the vast array of tools that are available, and that will continue to improve over time.

And then, finally, around the study record content itself, focusing on study descriptions, and some people also mentioned study results.

And as you heard from Heather's talk, plain language content for data submitters was also another important theme, just in that being able to understand both the legal requirements as well as the submission requirements; the simpler you can make it, the higher probability of success you may have in that process.

So, pausing to think about the themes that we've covered and talked about in website functionality, a key theme was the study record content and format.

And so, among this audience, I'm curious: Within this theme, which of the following categories are most important to you?

There should be a poll hopefully popping up.

And the options are to standardize more record content.

More prominently display certain record content — that would mean different things to different people.

Make more content available within study records.

Or add features for making using that record content easier, like we talked about sharing or printing, emailing, those types of things.

Wow, we have two very popular options: standardizing more content and also adding features to make using that record content easier. I think it is clear who gets the gold medal and the silver medal on this particular poll.

We'll let it run just another second.

Thank you. This is great.

And with that, I will turn it back over to Wendy.

(0:13:48)

Moderator: Thanks, Becky. I will transition us to our next panelist, and I would love to introduce Alissa Gentile from The Leukemia and Lymphoma Society.

(0:14:04)

Alissa Gentile: Thank you, Wendy, for that introduction. And it's my pleasure to be part of the NLM Board of Regents and this program. It's been wonderful.

I’m hoping to provide a perspective how advocacy groups use ClinicalTrials.gov and services to support patients who want to consider clinical trials as a treatment option.

As we know, clinical trial landscapes can be complicated and overwhelming for patients who are already dealing with cancer and deciding what treatment is right for them. Finding and enrolling patients into clinical trials is often difficult, and there’s no easy way for patients and caregivers to go about that.

The Leukemia and Lymphoma Society, we also refer to the CTSC, Clinical Trials Support Center, serves the blood cancer community help overcome obstacles to clinical trials, help patients find clinical trials, and speed the development of new treatments.

The clinical trial nurse navigators increase patients’ opportunities for clinical trial participation, and we do that by facilitating informed decision-making and minimizing logistical barriers for the patients and their families.

Our patients come to us one of three ways. First and most often, our patients come to us through the Information Resource Center, which is the call center at LLS staffed by social workers, health educators, and nurses.

Patients or caregivers can also self-refer using our online referral form, and we also have physicians who are members of the American Society of Hematology can come to us using the ASH portal to refer their patients directly to our team.

When physicians refer the patients to our team, our nurses work directly with those patients, in addition to their providers, to help find and support clinical trial enrollment.

The Clinical Trial Support Center is composed − is a comprehensive patient navigation service, and we’re staffed by nine clinical trial nurse navigators.

Our nurses are advanced practice nurses, we have adult and PD nurse practitioners and research nurses, all who have experience in hematological malignancy, treatment methods, stem cell transplantation, genomics, and clinical trials.

Each nurse has their own caseload of patients whom they work with, from the time a patient or caregiver is first in contact with the CTSC going forward. Our nurse navigators get to know our patients. We want to understand their unique situations and really recognize what their needs and wants are.

We educate patients about clinical trials and help them understand the clinical trial process, including their rights and obligations as a participant.

We gather details about the patient's diagnosis, their tumor profile, their past medical treatment, medical history, as well as review the patient's financial and social situations when it comes to clinical trials. We then research clinical trials and give the patient an individualized, patient-friendly list of appropriate clinical trials to ultimately discuss with their health care team.

We help with enrollment by reaching out to clinical trials sites; connecting with the sites' research nurses or PIs; and assisting with logistics, often with the help from the Information Resource Center. Even after a patient is enrolled, the same nurse remains available for support throughout the trial or treatment choice that patient chose.

Last year alone, we helped over 600 patients and we had more than 8,000 interactions to help facilitate enrollment. So, as you can see, that number really explains the in-depth navigation that the nurses do provide to these patients.

In our process in developing a patient-friendly list of trials to give to the patients and caregivers or their treatment teams, we utilize ClinicalTrials.gov in many different ways.

We do have a proprietary navigation hub that uses the ClinicalTrials.gov API, and it allows us to search detailed information within the eligibility criteria for over the 1,500 blood cancer clinical trials that are available.

We make use of almost all the ClinicalTrials.gov search fields, including but not limited to the brief summaries, eligibility criteria, sites, and site contact information.

In combination with the ClinicalTrials.gov information, we have our own proprietary information that we also use.

Like many others, we will link our NCT numbers to the trial page on ClinicalTrials.gov to find more information.

If or when a study result or links to articles are available within that study page, nurses find that information very useful for them, in terms of looking at that particular trial.

Our list of trials is then sent to patients and caregivers, and each one is unique in its own way. If a nurse has taken steps to reach out to the site about a particular trial, it is noted on that report.

The more accurate the information is on ClinicalTrials.gov, it has less barriers for us nurses to have to go through that support and patient process to taking steps to be considered for a clinical trial. And ultimately that patient would have more information.

It's important to note that the goal of the Clinical Trial Support Center is not to enroll every patient into a trial, but increase the opportunity for participation; facilitate informed decision-making about clinical trials; and really minimize those logistical barriers if the patient, in collaboration with their health care team, decides that a clinical trial is right for them. Ultimately, we want to educate, support, and empower those patients to be active participants and have some control over their treatment decisions.

The ClinicalTrials.gov is a large part of increasing that patient's opportunity for informed decision-making.

And I'll stop there and turn it back over to you, Becky or Wendy.

(0:20:04)

Becky Williams: Yeah, that was great. Thank you so much, Alissa.

And your organization really does offer an important service and resource, and I think you really helped to illustrate the level of detail and depth that providing patient support in this space can require.

Your group has never been shy about telling us what we could do to help improve the site, to better improve your use of it, and we hope that that continues and are grateful for your involvement and input in this process.

I thought I'd pause and take a moment and ask a poll question.

There are many patient-focused organizations like The Leukemia and Lymphoma Society that support patients with their health information needs, and we're just wondering if you could share with us your experience with those organizations, whether you're aware that they exist; whether you've actually used health information available from a patient organization; and, one step further, if you've used any clinical trial-related information services from a patient organization; or if you're sort of new to learning about the role of these organizations.

So it looks like we have a pretty good general level of awareness, raising more awareness today it looks like with some folks saying that they're new to the role of patient organizations.

And a fair number actually using organizations for either health information or clinical trial information.

It's really great. Thank you so much for your responses.

And with that, I will turn it over to Wendy.

(0:21:55)

Moderator: Thanks, Becky. And next we're going to hear from Seth Morgan, who is coming from the National Multiple Sclerosis Society. And looking forward to hearing his perspective.

Go ahead, Seth.

(0:22:07)

Seth Morgan: Great. Thanks, Becky, and good morning, everybody.

Both as a physician with experience caring for individuals with incurable chronic and progressive diseases and as a person with such a disease, I've been tasked with presenting the patient perspective, the experience that patients have in learning about medical diagnosis and their informational needs.

In order to really understand the topic, however, you need to know what the patient is going through and understand as best possible the psychological effect that the diagnosis of such a chronic and possibly progressive disease has.

And a few statements gleaned from the internet.

Okay, we got them there.

Okay, so the first one is from Debi Wilson: "Fear of the future will likely rear its ugly head more often than you'd like…It can be difficult to keep your mind from wandering to a very dark place."

The second one is "People are afraid of the dark because they don't know what's in it. People are afraid of the unknown," from Matt Alan G.

And "More time on the internet caused my fear to spiral out of control." That was Judy Lynn.

Thank you.

And "How I can save myself from despair? How I can take back control of my body, my mind, and my spirit?" from Cathy Chester.

And advance it again.

And in the current time, those quotes could very well have been about COVID-19, if you think about it. But they're not.

They were all made online before the COVID-19 experience and, specifically, by people with multiple sclerosis.

However, given the general public's taste of the pandemic, I think they've gotten a flavor for what it's like to go through having a chronic disease that you don't know what is going to hold in store for you.

So just imagine that going forward as a chronic, never-ending process because these are incurable conditions.

The highlighted quotes represent probably millions, certainly thousands if not millions, of comments that you can find online, and I'm sure there are some better ones out there, but those are the ones I decided to share.

Just as an educational point, multiple sclerosis is a chronic, often progressive, disease that is different for each person with it, and there are no real rules to how it's going to manifest. The reason for that is there are approximately 100 billion, 100 billion, with a "b," nerve cells in the average adult brain and spinal cord, pretty much all of which can be injured by MS, so hence the symptoms are different from person to person. It's very rare to find two people who have absolutely the same constellation, and it adds to the uncertainty of what is going to happen because you can't really extrapolate from your current situation to what other people have experienced.

So, questions like, will this interfere with my plans for my life?

Will I be able to have the career I had been planning for? Or even whatever job I have right now, will I be able to keep it?

What will this mean for having a significant relationship with a life partner?

Should I start a family?

Will I even survive this condition?

These and so many other terrifying questions cascade over each other, and these unknowns create what I call the Frantic Fear of chronic disease.

So most people on this call I'm sure are very familiar with these different topics; at different points and in variable order, the emotions that people go through with chronic disease span a wide spectrum.

A brief comment about denial. Even though I am a specialist in neurology, studied neurologic diseases, and am a neurologist with published peer-review journal articles and board-certified fellow of the American Academy of Neurology with over 26 years of experience managing patients, when I was diagnosed with multiple sclerosis, and other diseases of the nervous system obviously, even with all that experience I was not immune to the whole denial process.

When I knew I had multiple sclerosis clinically, I got my own scan, I found the lesions that were typical, I contacted a colleague who is a specialist in the condition, and informed my family that I had the disease and was going to see someone.

In that 2-week period from the diagnosis that I made to seeing the individual in their office, I convinced myself that I did not have this disease and that I had to explain to my family why I had made that terrible error in my assessment.

So, eventually, after you go through the depression, the withdrawal, the grieving, the education about the disease is what you start wanting to get. And then you can start considering research participation, or considering alternative medication options, including vitamins, healthy living, and all the other good things that can happen.

However, you can also start grasping for anything, regardless of the scientific validity or the risk potential, and that's where the danger is.

Access to research options and information is a very strong positive; it gives hope. It offers the possibility of a future and helping at least, if not finding the cure, or maybe finding it and starting on a medication, which will help you survive the situation that you're in.

I want to share a short vignette about what happened when I was early in practice; this was before I had the multiple sclerosis diagnosis myself. I saw a very young individual who I had diagnosed with multiple sclerosis about a month before, and she came in for a follow-up and informed me she had had all of her teeth extracted, and I asked her why she had done that, and she said, "Well, I did research on the web," and it led her to believe that MS was caused by the amalgams that she had had for dental care over the years.

So, the Frantic Fear of chronic disease often puts a damper on your own logic and logical thinking, and it can be a very powerful and very dangerous phenomenon, and the quality of the research that we get is as important I think as the information, probably more important than the information that we get.

So that, to me, is the perspective of the patient.

And I just am concerned by the fact that people go through…

(0:30:41)

Becky Williams: Thank you, Seth. I really appreciate you sharing your insights with us today. That phrase, "Frantic Fear," it just really sort of strikes you to the core.

And it really just reinforces how traumatic this experience can be for patients, and those stages that you presented were just oh so helpful in understanding the process that we all go through when trying to grapple with new information that's so critical to yourself.

And I think you've also reinforced sort of the need for trusted health information with the story of your patient.

And so we thought we'd just take a moment and poll the audience. This poll is kind of fun because you can choose as many as you would like, and we're interested in what sources do you use to find health information. And they've expanded the poll so hopefully we can see all of the options that are listed there; you can scroll down. There's a few more that might be there if you can't see them all.

But click away. I'll let that run just for a little while.

Google and your doctor are in very close competition at the top.

We'll consider them complementary in this case.

Wow, this is great! Thank you, everyone, for those responses.

And with that, I will turn it back over to Wendy.

(0:32:34)

Moderator: Thanks, Becky. Next up, we will hear from Steven Woloshin from The Dartmouth Institute.

Steven, you're on.

(0:33:11)

Steven Woloshin: No industry funding. I am a consultant for the National Cancer Institute. And any opinions that I express right now are mine and not theirs.

So, if you're interested in study results, it's easy to find them on ClinicalTrials.gov and start looking at the numbers. But to make sense of the numbers, you need to understand something about where they come from, so you can decide if they're relevant and whether to believe them.

So let's take a step back and think about the research that generates the results.

Research sounds complicated. So let's think about cooking instead.

Imagine you want an apple pie. What do you do?

Well, you find a recipe. You follow the steps. You buy the ingredients, the right amounts, the right order, at the right temperature, the right amount of time. And out pops an apple pie.

And if you did it right, it really represents what was imagined in the recipe.

But if you do it wrong, it can be a disaster.

So, for example, if you use salt instead of sugar or you cooked it too long. It won't be a very good pie.

Research is the same way.

Research answers a specific question. It follows a recipe called a protocol, with the design and who's in the study and so on. The researchers implement the protocol, and out pops the results.

Now, fortunately, you can get information about all these different aspects of the study on the ClinicalTrials.gov website.

So, imagine I have insomnia and I want to find research about sleeping pills.

So I go to the search page, and I put in the condition, insomnia, into the page and request studies. I want interventional studies because those are real experiments, and I want studies with results because I want to find out what happened.

Not all the trials on ClinicalTrials.gov have results. Sometimes that's because the trials haven't been completed yet, and sometimes it's because investigators, unfortunately, haven't posted them.

So, my result, my search rather, turned up a bunch of studies, 166 interventional trials about insomnia. And, unfortunately, the website isn't organized in a way with structured headers, so you can easily sort through the trials to find what you're looking for.

Instead, you kind of just have to scroll through the list, which I did.

And this one popped out right away. The study of eszopiclone in people with insomnia. And it popped out to me because I know that this is the drug Lunesta, and I remember the advertising campaign with the lunar moth.

So before I jump to the results, of course, I want to take a look under the hood and look at the recipe, the research that generated the results.

So, the website has a nice summary of these things. For example, there's a brief summary explaining what the study is; the purpose of this study was to evaluate long-term safety of this drug.

So immediately I would know that it's not going to answer my question. I'm interested in how well the drug works; does it help me sleep longer. Safety is of course crucially important, but the main thing I'm interested in is the efficacy of the drug.

So if I was doing this in reality, I would stop here.

There's also a nice description of the trial. It's a multicenter, randomized, double-blind trial, and it's clear in this table who's in the trial and other relevant details.

There's a lot of fancy words here. So it would be great, I think, if all the different terms had links to a glossary — and that would be a nice feature to add.

This page also explains in detail what happens to each of the study groups, so four arms in this study. And one thing that jumps out right away is that every single group includes the drug.

What that means is that you can't really answer my question then about how well the drug works because everyone in the study got the drug. There's no one to compare it to.

So again, if I were doing this for real, I would stop. This trial is not going to be able to answer my question.

Now let's go to the actual results. And you really need to put on your seat belt here because it gets kind of overwhelming. Good, but overwhelming.

The results section of the website starts with a detailed description of the study flow. So it shows you how many people started this study, how many dropped out, and why. And this is crucial information because if there are a lot of dropouts, here 10–15% in each arm, it's a big red flag about the liability of the study.

So now, finally, let's get to the actual numbers.

First, there's a table that describes all the different outcomes, so the things that were assessed in the trial, which is very, very nice. The problem is when we actually want to look at the numbers, it gets pretty daunting.

So if you expand these things, you get pages and pages of these detailed tables with all sorts of words and numbers, and it's very, very hard to get through them. At the bottom, I found an outcome that I was particularly interested in, which was do you sleep longer if you take the pill?

And what this one shows you is how many people were analyzed, how long they slept at the data trial, 314 minutes on average, and how much longer they slept at the end of the trial. Here, 63 minutes longer. And it does this for each of the study groups.

So I want to just make three points from this table.

First of all, as I mentioned, you can't learn what happens if you didn't take the drug at all, so it doesn't answer my question.

Secondly, this is a minor thing, but it's kind of awkward the way that the numbers are presented. I mean, people think in hours, not in minutes, and you have to divide it out in your head.

And it's a pain in the neck to look at all the other outcomes to get a full picture of what happened because there's no way to display all these things on the same page at all. And that includes harms. Because any time you think about the benefit of a drug, you should also think about the harms.

It is possible to organize these things in a table that's much more accessible.

This is an example of doing just that. It's called the drug facts box that Lisa Schwartz and I developed, and this is a box that summarizes the results of another trial of the same drug, Lunesta.

This one is a comparative trial, so you can see how well it worked because they tell you what happened to patients randomized to the drug or to a placebo.

And the way the box works, it organizes all the benefits together, so you can get the big picture, and all the harms together. And these are all next to each other, so you can weigh the benefits and the harms and decide if it's worth it for you. And the way that the results are actually presented, it uses numbers in a way that's a little more accessible to people.

So did the drug help? Sure.

People slept 37 minutes longer through the drug, and it has columns which tell you how long people slept with and without the drug.

So, things to keep in mind: Probably the most important message is that just because you see results doesn't mean you should believe them.

Lots of things can go wrong.

Right, you might have asked the wrong question, so it's the wrong kind of pie, you might have a bad recipe, you might not have followed the recipe. And if that happens, you don't want that dessert; you don't want that pie.

It's the same thing for research.

If it's the wrong question or a bad design or wasn't implemented well, then you don't want to bother to look at the results.

So if you're looking at results on ClinicalTrials.gov, or anywhere, there are a few things that you should keep in mind.

First of all, is it the question that I'm interested in? Is there a good design that can answer the question? And are these the outcomes that you care about?

And only if these things are true, only then do you want to look at the results.

And, finally, you want to be careful about just looking at the results and acting on the results of one trial. That would be like deciding to hate apple pie because the one I baked was bad.

Especially if the stakes are high, you really want to look at all the evidence, and the best way to do that is by looking for things called systematic reviews, publications which summarize the totality of the evidence.

And it would be wonderful, I think, if ClinicalTrials.gov included links to places where you can find relevant systematic reviews, such as the Cochrane Library.

So, thank you very much.

(0:42:47)

Becky Williams: Thank you, Steven. I was having a little delay on unmuting myself.

I really appreciate those insights and especially the last point about some of the challenges related to looking at the results of any single clinical trial and thinking about other sources where there may be the totality of the evidence available.

You really hit on some of the key aspects of the site in that there's a range of studies that are required to be listed, and we list all of those. And so, as a researcher or other person needing to look at that information, you may have different needs and requirements in terms of identifying the studies that may be of most interest and of most use to you.

So, in taking a pause here to think about another poll question, we're sort of interested in where our own audience looks for information related to a clinical trial.

Again, we're giving you the option to choose more than one and are curious sort of where you go, and many of these are sort of interconnected.

So we've got ClinicalTrials.gov; PubMed or PubMed Central; journal publications; or sort of the media, newspapers, magazines; and other.

I know I sometimes hear about results of a study from a magazine or a newspaper first and then end up going to the source.

That's great. Well, it seems clear winners, and obviously this is perhaps a biased audience, but with ClinicalTrials.gov being, of course, central interest, but PubMed and journal publications right up there as well.

And so with that, I will turn it back over to Wendy. Thanks.

(0:44:41)

Moderator: Thanks, Becky. And I will welcome our final panelist of the day, Stephen Rosenfeld from the Secretary's Advisory Committee on Human Research Protections.

Stephen?

(0:44:54)

Stephen Rosenfeld: Thank you.

So, I'm sensitive to the time. I'll try to talk quickly.

I do have to make the usual disclosures. I'm listed as the Chair of SACHRP. That's because that affiliation is probably the most relevant to what we're doing today, but I don't speak from SACHRP, and my thoughts are my own.

And second, while this meeting is about improvements to ClinicalTrials.gov, I did want to acknowledge the tremendous resource that it is already and thank the staff who've worked so hard to keep it that way to date. So, thank you.

A little bit about − let's see how long.

So my use of ClinicalTrials.gov, I've always thought of it as a niche perspective. I was for many years a full-time IRB chair. And I used ClinicalTrials.gov routinely for several things.

One was to assess the context of a study intervention in a proposed trial we were reviewing, including status and results from earlier studies in the same and different conditions, to give an overview of the research landscape for the study condition, what other things were being investigated.

For disseminating results to the board.

So, as Steve Woloshin showed you, reading results can be − well, it's certainly time-consuming.

And yet, the IRB; there's no regulatory requirement to give the result of the study back to the IRB, but everybody who sits on that board is essentially a research professional, and I feel there's almost an obligation to tell people how a study turned out. So I would read the results and summarize them.

And then the last thing was to periodically scan ClinicalTrials.gov to see if there were changes to studies that hadn't been reported to the IRB.

I was far too busy, I chaired typically three meetings a week, to do all of this manually. And I think that's what my — the substance of my message will be about visualizations.

What I could do is record the NCT numbers with the study, and I built tools that would automatically or periodically scan the database, retrieve results, and build visualizations.

So, most people don't think of this kind of work as being in the purview of the IRB, and I would make the argument that it is.

So there's been a debate about trials that are essentially uninformative. And a lot of that debate has been about trials that didn't post results. And so you never knew if they worked or not.

That's obviously not the most relevant thing to an IRB, which is looking at studies before results are available.

And so what we're concerned with is what's been recently − the framework has been proposed, scientific validity and scientific value.

And I think everybody on an IRB knows about scientific validity; it's the statistical soundness, whether you're enrolling a sufficient population, whether the design can answer the question.

Scientific value is a subtler point.

And it really is whether that question is worth answering and whether this study can do it, beyond its actual design.

And so many people, actually − there's a debate in the IRB community about whether this is our role or not.

IRBs are empaneled to look at human subject protections. They have very specific review criteria, and scientific merit or scientific value is generally felt to be, by many, outside the IRB's purview. On the other hand, one of the critical determinations an IRB has to make is that the risks we're asking people to undertake in the name of science are justified by the importance of the question we're trying to answer. And without making that determination, it's really impossible to determine whether the risk level is appropriate or not.

So, in the long-term structure of research oversight, I would have no compunction to say there are other people better equipped to answer the scientific value question than a sort of general-purpose IRB. On the other

hand, since there is no mandate for such a thing, I feel like the IRB has to take it on.

So, this is just an example of one of my visualizations.

And I wish I had chosen an intervention that I found easier to pronounce, so if I struggle with that I apologize, but this is a graph of studies of pevonedistat, which is an NEDD8 antagonist, so what that does is the intended mechanism of action is to promote apoptosis in cancer cells, particularly in hematologic malignancies.

And this is just the bottom part of this graph.

So, what you see here is a list of studies. And it extends much higher, but I cut it off to make it legible.

The size of the circles is the enrollment target for the study, the color of the circle indicates whether it's open to enrolling, which is green; whether it hasn't started yet, which is blue; whether it's closed to enrollment but ongoing, the yellow ones; or whether it's completed, gray.

And the clock hands indicate the phase. So a clock hand at 1 o'clock is a phase 1; a clock hand at 3 o'clock is a phase 3.

Oops. Sorry, I inadvertently closed my − put my screen to sleep. Hopefully that hasn't affected my connection.

Okay, sorry about that.

So you can see from this graph, if you can read it well, that right away there are problems with it.

So again, as I said, this is data taken right off ClinicalTrials.gov.

If you look at, there's a whole section in the center that deals with diffuse large B-cell lymphoma, and that has at least four different ways it's described.

They're all together here, so that actually works okay.

But if you look at acute myelogenous leukemia, that's actually described in what we can see in this graph in three different ways: as acute myeloid leukemia, as leukemia myeloid acute, and as acute myelogenous leukemia. And that kind of lack of standardization basically is an intrinsic flaw of this kind of visualization.

Now, I can go through and, in a limited dataset like this, I can pull those together manually. But if the point is to have visualization tools that are easy to use and don't require that kind of effort, that doesn't work.

So, here's some additional − that was an old graph.

I've been tracking COVID studies for a variety of reasons, and I want to share some exploratory data that may be more immediately relevant.

So, this is just the scope.

I looked at the database for these graphics, on the 22nd of April. And I started with all studies. And there were 795; 495 of those were interventional. And 115 of those interventional trials had sites in the United States.

So that's the basic sampling.

Then I looked at what the interventions were. So the 115 interventions listed 232 interventions, about right. Of which, 139 were uniquely described.

So that's immediately a problem.

Either that means we're looking at different things in every trial, which seems unlikely, or the same thing is being described in different ways. And that makes it harder to know what you're looking for.

So the ClinicalTrials.gov, the site, has been wonderful, in that they have this link that gives you all the COVID trials.

If you try to search them manually, you start to get into trouble with how things are described. And so, manually looking at those 139 descriptions, I came up with actually − let's see, 49 unique interventions.

So I'm going to go rapidly through the next couple of slides.

So, this is what this looks like.

So, I know you can't read this.

The depiction on the left shows what it looks like if you don't actually group interventions by what they are. And the graph on the right is what a curated set of interventions creates.

And zooming in so you can see the consequences. So this on the left, this is the original data from ClinicalTrials.gov, and on the right the same data manually grouped. And you can see right away the thing that pops out is

that big group in the middle, not so big on the left, much bigger on the right, of hydroxychloroquine trials that were called all different things.

And so, by not grouping them you were missing a large proportion of those trials.

And right above that, you can see IL-6 receptor, IL-6, IL-6 receptor antagonist, so I grouped those together because it doesn't really matter which one you were using, if you're looking at the efficacy of that intervention, and you can see, suddenly you see a bunch of trials together that you would have thought were disparate before.

So, what's the bottom line here?

And I like to think of it as building with stones versus bricks.

So if you take − if every trial is taken by itself, you end up with a bunch of stones. They can be really solid, heavy, and dense. But you can't build much more than a wall with them.

If you build trials − if you design trials knowing that they are contributing to a foundation of knowledge, you design trials as bricks. And each one can be entirely different; some can be better weight-bearing than others. Some can be different colors.

But they'll all fit together, and they'll be part of the structure you're building.

And that's basically — I understand as scientists we're often not trained to think like this, but every study is a brick in a sort of knowledge structure that we're building. Nothing stands alone, and we need to start taking account of that when we design and approve studies and when we report studies. That's the first step.

If you don't describe them similarly, it doesn't matter if they're stones or bricks.

I don't have time — I'll let you read the quotes by yourself, but this is, basically, captures that idea that no research study stands alone.

Anyway, thank you.

(0:56:47)

Becky Williams: Thank you, Stephen. That was really excellent.

And I think you really brought to light some of the challenges that we see when trying to balance some of these issues around structure, but also

flexibility and highlighting some key areas that also came up in the RFI comments themselves where there are further opportunities for standardization and normalization. I think you really gave people great insight into sort of what value that can potentially deliver, especially also thinking about the unique context of the work of the IRB.

So we thought that some of the visualizations that Stephen was showing were great because they can help you see a story kind of quickly.

So, we're using our upvote tool down in the pod here, where you can just type in words.

And we're sort of curious what types of information would you find most useful to appear in data visualization.

And remember that you can vote for other people's responses, just to the right of their +1, or plus however many, to add your own votes to that.

I'm seeing study results, interventions, conditions, yeah.

Really being able to see the study design of the study, the design of the study seems a theme.

Great. I'm going to let people keep adding things for a little bit. This is really useful.

And I'm really impressed that everyone is still hanging in there and engaged with us as we close our 3 hours of this meeting.

So thank you for continuing to participate.

This is great. People are still commenting, so I'm going to just let it run a little bit longer.

All right, well, while that's running, I'm just going to start transitioning to closing out the meeting and some of the next steps that you can expect from us.

I really do hope from today's discussion that you were able to get a sense of the modernization project overall.

I'm behind on my slides here.

And I guess, let me just pause and say thank you to this panel, Alissa, Seth, and Steven, and Stephen, for your contributions; it's really been great to have all of your unique insights. It's been really helpful to me, and I hope for our audience as well.

In terms of next steps, today we were able to cover an overview of the modernization project. As we stated, this is really a multiyear effort that's informed by engagement throughout the entire process.

And as you can sort of hear and see from many of the themes that we heard today, we are really focused on establishing a modern infrastructure that will continue to support us in the long term.

When you think about website functionality, the way to really simplify it is people want information that is easy to find and use for their own particular uses.

And in the context of submission, there were kind of two themes around simplifying the submission process to really improve that experience for submitters and make it easier in the context of their own work and then enhancing the quality control review process that goes alongside the submission process itself, really thinking about how there can be more just-in-time help or other things to make sure we're getting the highest quality data the first time.

I shared our timeline for engagement over the course of this fiscal year, in the government that's of course how we think and operate, that's our funding lines. But I really just want to reinforce the fact that this is the beginning of a multiyear effort, and through that entire effort we will continue to engage you in events like this and other one-on-one meetings and other ways that we can continue to get your feedback throughout the entire process.

And so, one of the things that we're particularly interested in is how you would prefer to continue to be informed about modernization activities moving forward.

We have another poll here that you can respond to.

We've listed some options around email updates; we have a newsletter called Hot Off the PRS! that we currently use to target our submitters. And informational blogs, other training or information sessions, a lot of those will probably be done virtually these days.

Meetings in person or again sort of teleconference, again updates to our own website, and other options.

While you folks are continuing to respond to that, I just want to give you a sense too — we will − just because the RFI closed, it doesn't mean that we are done taking feedback from our users and stakeholders.

We always encourage people to provide comments and suggestions when they think of things, and we are happy to receive that information at this point in time.

And in terms of how long it will be before you can actually see changes that matter to you, there'll be things that are in different timeframes.

Some of these things we haven't them done yet because they're hard, and we will take time to figure out how to do them and how do them well in a way that meets your needs.

But there's other things that are sort of easier and lower hanging fruit, if you will, that will be easier for us to sort of begin incorporating sooner rather than later and don't require many significant updates to the infrastructure of the system itself.

So we're hoping that we can give you a combination of things that you can see sooner and a combination of things that you can see later.

And our goal is to be able to share with you sort of a longer-term roadmap, in terms of how we're going to be going about this work, what those priorities will look like, and we'll be continuing to get your input on these types of information.

And so, just a reminder about some of the different places where you can see information related to modernization. We do have a webpage available under the About Site section of ClinicalTrials.gov, in which we are posting all things ClinicalTrials.gov modernization; that is where you will find the RFI report summary that we posted, as well as the original comments, and where you will also be able to eventually access this meeting recording and presentation within the timeline we said.

We do have an email newsletter called Hot Off the PRS! Hot Off the PRS! is obviously a take on our submission system, so it's primarily targeted at submitters, but everyone is welcome to join.

And you can subscribe on our website; you probably can't activate that link there.

And then, finally, as I mentioned, we always take suggestions and comments; our email address is register@clinicaltrials.gov. If you were paying attention, that's also the same email address you'd use to request one-on-one assistance with results information, if you need it.

And with that, I really just want to thank everyone for their contributions to the RFI, and your contributions to this meeting today and taking the time to be here with us. It really means a lot to everyone here and with the program.

And with that, I will turn it over to Wendy to close us out.

(1:05:14)

Moderator: Thanks, Becky. Yes, I agree this has been a wonderful meeting full of insights, and all of the different perspectives have just been amazing to hear. So thanks, everyone, for your engagement.

We have one final, wrap-up poll question.

It's a two-parter: So did today's meeting meet your expectations? We would love to hear some comments.

And we'll leave this up for a few minutes as we close.

And that's it. Thank you so much.

[End of Program]