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HEALTH RESEARCH

MONOGRAPH

ONLY ELLIGO ACCELERATES CLINICAL TRIALS THROUGH HEALTHCARE

Elligo Elite Learning Series Monograph: Solve Clinical Trial Enrollment Struggles With Better Utilization of Healthcare Data

Only Elligo provides direct access to known patients with their trusted physicians and research practice management solutions to streamline your research.

SOLVE CLINICAL TRIAL ENROLLMENT STRUGGLES WITH BETTER UTILIZATION OF HEALTHCARE DATA

Real-world data (RWD) and electronic health record (EHR) data hold vast potential for reforming clinical trials, from using EHR data to accelerate patient enrollment to leveraging RWD down the care continuum for the benefit of patients, physicians, and sponsors.

Michael Ibara, Pharm.D, Chief Data Officer at Elligo Health Research®, presented an Elligo Elite Learning Series roundtable with Xtalks, entitled, "Solve Clinical Trial Enrollment Struggles With Better Utilization of Healthcare Data." This roundtable was a deep dive into using RWD and EHR data in clinical research and featured industry experts TJ Bowen, Chief Scientific Officer and Co-Founder, Deep Lens; Riley Ennis, Chief Product Officer, Freenome; Jeremy Brody, Head of Global Strategy, Cerner Enviza; and Mitra Rocca, Dipl.-Inform. Med., FAMIA, Senior Medical Informatician, FDA

The roundtable's first section found Mitra providing a detailed background on the FDA's Real-World Evidence Program and its guidance on the use of RWD in supporting new indications for approved drugs and satisfying post-approval study requirements. Next, Riley and TJ discussed how RWD and EHR data are already revolutionizing clinical research as well as the exciting possibilities they hold for accelerating and increasing diversity in clinical trial enrollment, streamlining protocol design and implementation, enabling precision medicine, and delivering postmarket value.

INDUSTRY EXPERTS

MICHAEL IBARA, PHARM.D.
Chief Data Officer,
Elligo Health Research®

JEREMY BRODY
Head of Global Strategy,
Cerner Enviza

TJ BOWEN, PH.D.
Chief Scientific Officer
and Co-Founder, Deep Lens

MITRA ROCCA
Dipl.-Inform. Med., FAMIA,
Senior Medical Informatician,
FDA

RILEY ENNIS
Chief Product Officer,
Freenome

The following section featured Jeremy explaining and expanding on the challenges of using EHR data for research, specifically that since EHR data was not created for research purposes, it's often inconsistent in quality and sample size and therefore requires significant time and effort in cleaning and validation. Finally, Michael led the group in a Q&A focusing on actionable solutions and innovative ideas for overcoming EHR data challenges so we can better utilize this data for the benefit of patients, physicians, and sponsors.

Ayesha Rashid

Good day to everyone joining us and welcome to today's Xtalks roundtable . Today's talk is entitled, "Solve Clinical Trial Enrollment Struggles With Better Utilization of Healthcare Data." My name is Ayesha Rashid, and I will be your XTalks host for today. Today's roundtable will run for approximately 60 minutes. This presentation includes a Q&A session with our speakers. This roundtable is designed to be interactive, and roundtables work best when you're involved. So please feel free to submit questions and comments for our speakers throughout the presentation using the questions chat box, and we will try to attend to your questions during the Q&A session. This chat box is located in the control panel on the right-hand side of your screen. If you require any assistance, please contact me at any time by sending a message using this chat panel. At this time, all participants are in listen-only mode. Please note that this event will be recorded and made available for streaming on Xtalks.com.

At this point, I'd like to thank Elligo, who developed the content for this presentation. Elligo Health Research accelerates clinical trials through healthcare with access to known patients and their HIPAA-compliant healthcare data, IntElligo® Research Stack technology, and hybrid enrollment model, PatientSelect. Coupled with the largest known patient access network, Elligo's site solutions enable healthcare practices and research sites to participate in clinical trials. By adaptive engagement of known patients and physicians, Elligo accelerates the development of new pharmaceutical, biotechnology, and medical device and diagnostic products.

Now it's a pleasure for me to introduce our speakers for today's event. Dr. Michael Ibara has more than 20 years of experience in clinical research and development. Throughout his career, Dr. Ibara has sought to improve healthcare by bringing together healthcare data and digital technologies. His interests include regulatory and policy implications for digital healthcare, exploring the factors needed to allow interoperability of healthcare data for all stakeholders involved and implications for the use of big data, machine learning, and natural language processing to improve the ability to perform regulated clinical research. Before joining Elligo, Dr. Ibara was the head of digital healthcare for the clinical data interchange standards consortium (CDISC). There, he led the FDA eSource project and healthcare link efforts with registries clinical trials and mobile health to enable use of real-world data from healthcare for regulated research and decision making. Prior to CDISC, Dr. Ibara was head of business development, coordination, and innovation and also head of pharmacovigilance innovation at Pfizer, where he worked for 15 years in various positions, leading implementations of global systems and large-scale technologies.

Dr. Bowen brings a diverse... a diverse set of skills to the team. Prior to joining Deep Lens, Dr. Bowen's career spanned from cancer research to software development and strategy and management consulting. His research focused on pathological identification of tumor differentiation in breast cancer is derived from P53 braca one to ATM and other mutations. Following his graduate work, Dr. Bowen worked as a strategy consultant in the biotechnology, pharmaceutical, and medical device space for LTK Consulting, where he helped with M&A strategy and operations for dozens of global organizations. Dr. Bowen has also held operating roles as the General Manager of the world's premium biology and pharmaceutical patent search software at CES. More recently, he was a founding leader of the software innovation team at Fuse by Cardinal Health, where his teams developed innovative products for healthcare providers, pharmaceutical companies, and patients. Dr. Bowen was a Regents Scholar at the University of California San Diego, where he received his doctorate in biomedical sciences and graduated with honors from Pepperdine University with a Bachelor of Science in Biology.

Mitra Rocca joined the Food and Drug Administration in 2009 as the Senior Medical Informatician responsible for developing the health information architecture of the Sentinel system. She serves as the lead for the FDA CDE, our health information technology board focusing on the use of health IT to enhance regulatory decision making. She serves as the lead for the FDA CDER lead to Health LevelSeven, or HL7, responsible for the review of HL7 draft standards. Prior to joining the FDA, a Mitra served as the associate director of Healthcare Informatics at Novartis Pharmaceuticals Corporation, focusing on the reuse of the electronic health record in clinical research. Mitra has served as co-chair of the Health Level 7 clinical interoperability counsel from 2012 to 2018. She holds an advanced degree in Medical Informatics from the University of Heidelberg in Germany.

With the knowledge and skills he gained as a biotechnology entrepreneur, Riley is helping to make Freenome's vision of a cancer-free world a reality. As the company's co-founder and chief product officer, Riley heads the clinical and commercial development of Freenome's non-invasive tests for early cancer detection and treatment selection. A Thiel Fellow, Riley developed a cancer vaccine and founded his first biotech company, Immutacon, while still in high school. While earning his degree in molecular biology at Dartmouth, Riley co-authored several publications and worked as a visiting scientist with Novartis. In addition to his work as a scientist, Riley worked as an analyst at Morgan Stanley and an associate at Bridgewater, where he observed the positive impact of a strong organizational culture firsthand. Riley's previous biotech experience includes work at Foundation Medicine, Cirrus Pharmaceuticals, Adam Mab, and Emergent BioSolutions.

Jeremy Brody is the Head of Global Strategy and a member of the executive committee of Cerner Enviza. Jeremy's primary responsibility is to lead the growth of the business. Areas of particular focus include real-world evidence, advanced big data analytics, clinical research, patient-centric applications, and digital health. Jeremy received a Master of Science and Health Policy and Management from the Harvard University School of Public Health, and a Bachelor's of Science in psychology from New York University. Jeremy is based in Israel and keeps his entrepreneurial spirit alive by interacting with startup companies located in the startup nation's famous silicon Wadi. When not at work, Jeremy enjoys spending time with his wife, six boys, and granddaughter who always keeps things exciting. And now without further ado, I'd like to hand over the mic to Dr. Michael Ibara as well as the panelists. You may begin when ready.

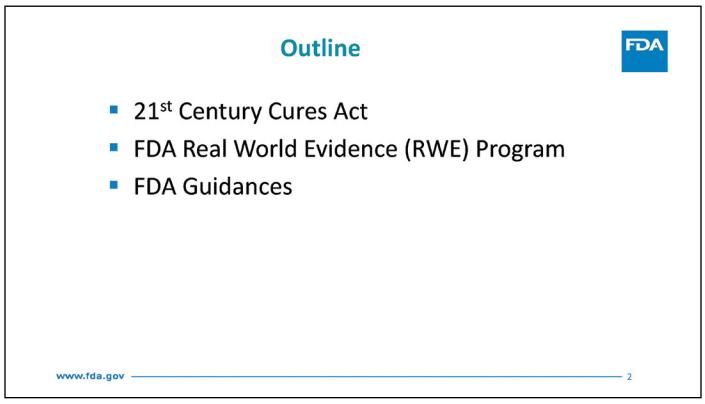
Michael Ibara

Thank you very much, Ayesha, and welcome, everyone, to this roundtable. I'm delighted to be here with several old friends and my colleagues on the panel. And we hope that we can provide an overview for you and then get into some specific discussion. So, the way we'd like to start is, I'll be asking a question of each panelist to get their perspective. And then we'll... we'll open it up for Q&A and for broader discussion.

The first question I'd like to direct to you, Mitra, as a representative of FDA. Could you describe for us the regulatory developments that the FDA has pioneered in the use of the electronic healthcare records and how that might impact with real-world data? And I understand that you have some slides that you'll be able to go over with us to give everyone background for that.

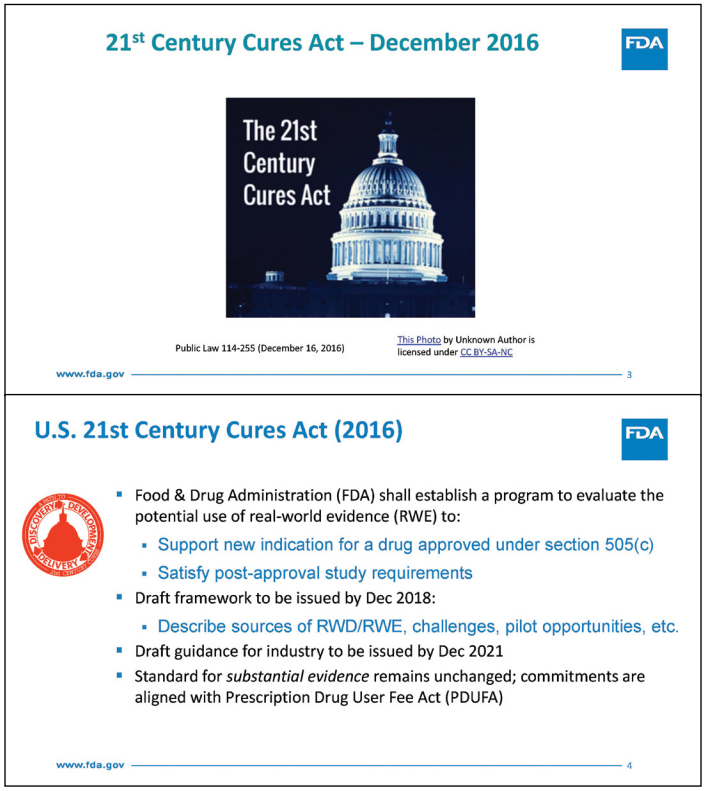
Mitra Rocca

Yes, thank you, Michael. So I'm going to answer your question in the slides that I have prepared. So I'm going to provide an overview to FDA Real-World Evidence Program and answer Michael's question on guidances.

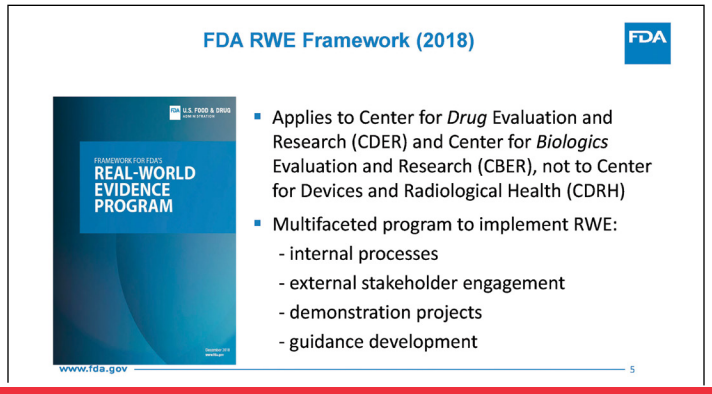


So the 21st Century Cures Act mandates FDA to that. We will establish a program to evaluate the potential use of real-world evidence to support new indication for a drug approved under Section 505. C, and also satisfied post-approval study requirements. FDA will develop a framework by December 2018, and describes the sources of real-world data, real-world evidence challenges, and a series of pilot demonstration projects.

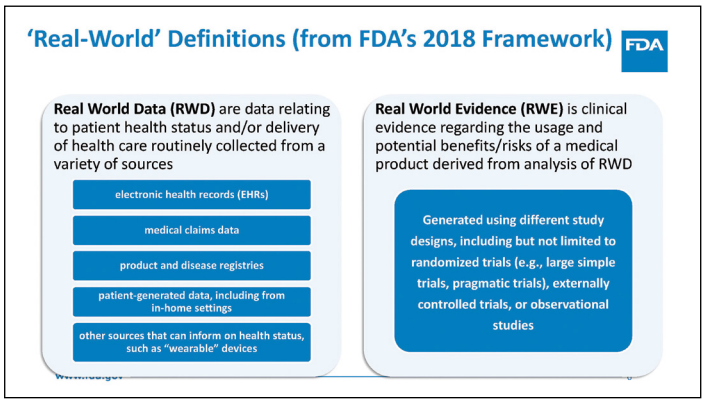
We develop a suite of guidances by December 2021. And what is important is that the standard for substantial evidence remains unchanged. So commitments are aligned with PDUFA (Prescription Drug User Fee Act). Next slide please.



So as I mentioned, one of the requirements of the 21st Century Cures Act is that FDA shall develop a real-world evidence framework, and this framework was published December 2018. And it applies to two centers at FDA: the Center for Drug Evaluation and Research, where I work, and a Center for Biologics Evaluation and Research. See that it does not apply to CRS Center for Devices and Radiological Health. It is a multifaceted program to implement the real-world evidence. It

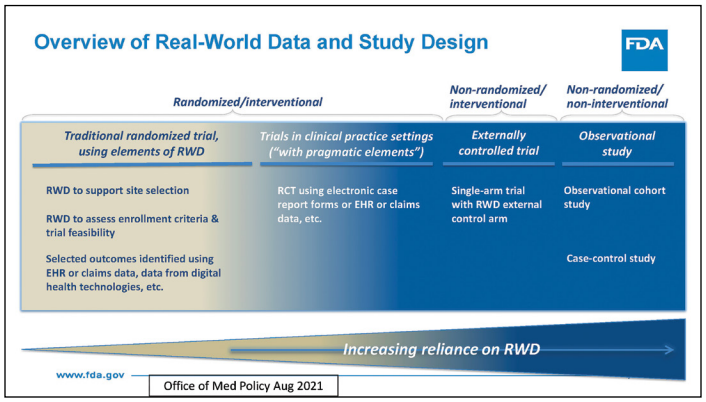


addresses internal processes or how to engage with external stakeholders, a suite of demonstration projects that are in the appendix of this framework, and a suite of guidances that we have developed and are… they are still in development. Next slide, please.

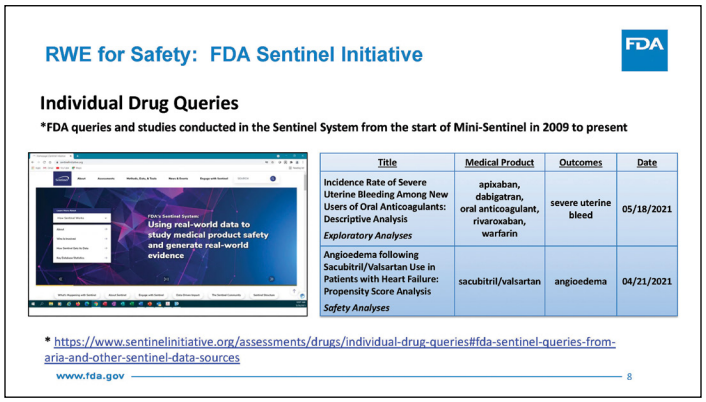


So this framework also explains or defines what is real-world data and real-world evidence. Real-world data is the data related to patient health status. This is data collected at the point of care, and examples of real-world data or electronic health records are administrative claims, product and disease registries, and patient-generated data —for example, the electronic patient-reported data. And then also data from digital health technologies, wearable devices. Real-world evidence is the evidence that is generated from these sources of real-world data. And that will help us with the usage and potential benefits or risk of the products. Next slide, please.

So here you see an overview of real-world data in study design. Real-world data can be used in different types of clinical trials: randomized, interventional, non-randomized interventional, non-randomized, non-interventional. And as you will hear from the other panelists, real-world data can support the site selection. They can help with patient recruitment, enrollment criteria, trial visibility, with selected outcome identifying using EHR claims, and also data from digital health technologies that could be used by patients participating in clinical trial. The real-world data can be used in clinical trial execution. And I have an example of a project that we're leading at FDA, where the electronic case record called or directly auto-populated from electronic health record data and multiple sites, then externally controlled

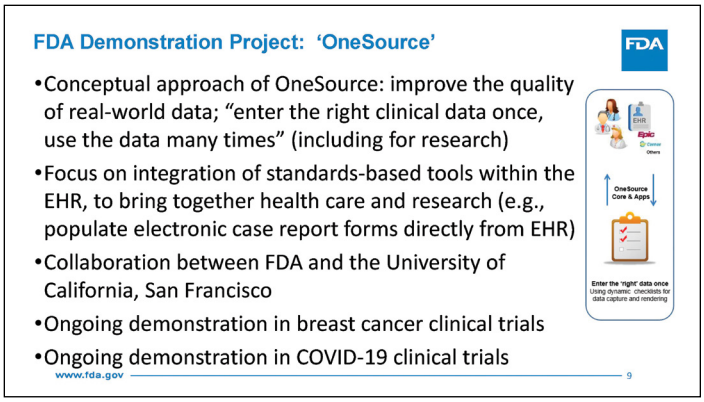


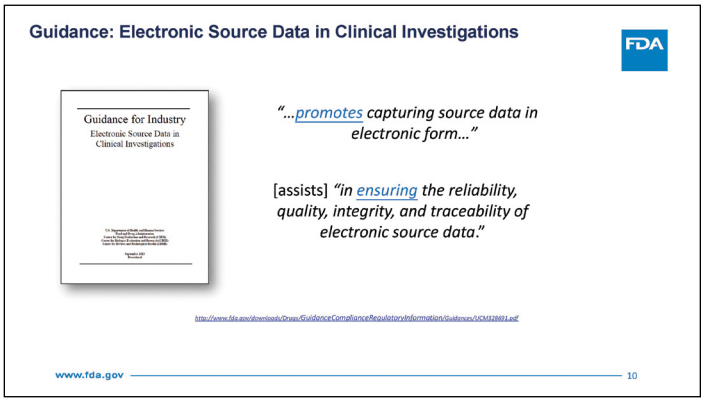
trial, which is a single on trial, where the real-world data is used as external control. And then observational studies variable data can be leveraged both in cohort studies and case-control studies.



So as you see, there is increasing reliance on real-world data in clinical trials. Next slide, please. So two examples of projects are one focusing on postmarket and one on premarket. This project is the FDA Sentinel Initiative. This is our national system that is focused on postmarket surveillance and looking at safety of medical products. And on the right side in the table, you see two classes of medical product where we use Sentinel and sources of Sentinel system to analyze. Those look at the safety of those classes of medical products. And next slide, please.

So this is a project that I lead in collaboration with University of California in San Francisco. The project is called OneSource. This is focusing on premarket. And here the goal is to build a case report form directly into the electronic health record system of the University of California, and not only the University of California in

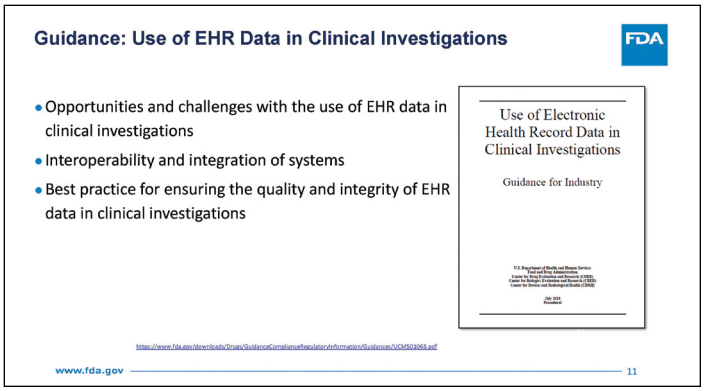




San Francisco, but the University of California and also other hospital academic medical centers. And we collaborate with...we leverage electronic health record systems Cerner and Epic, and populate the case report form directly from the electronic health record system, both for a breast cancer trial. These are adaptive trials for breast cancer. And then, when the pandemic started, we also are leveraging the same platform, OneSource for COVID-19 drug, clinical trial not for vaccine, for drugs. And the goal of OneSource is to collect data once and reuse it many times.

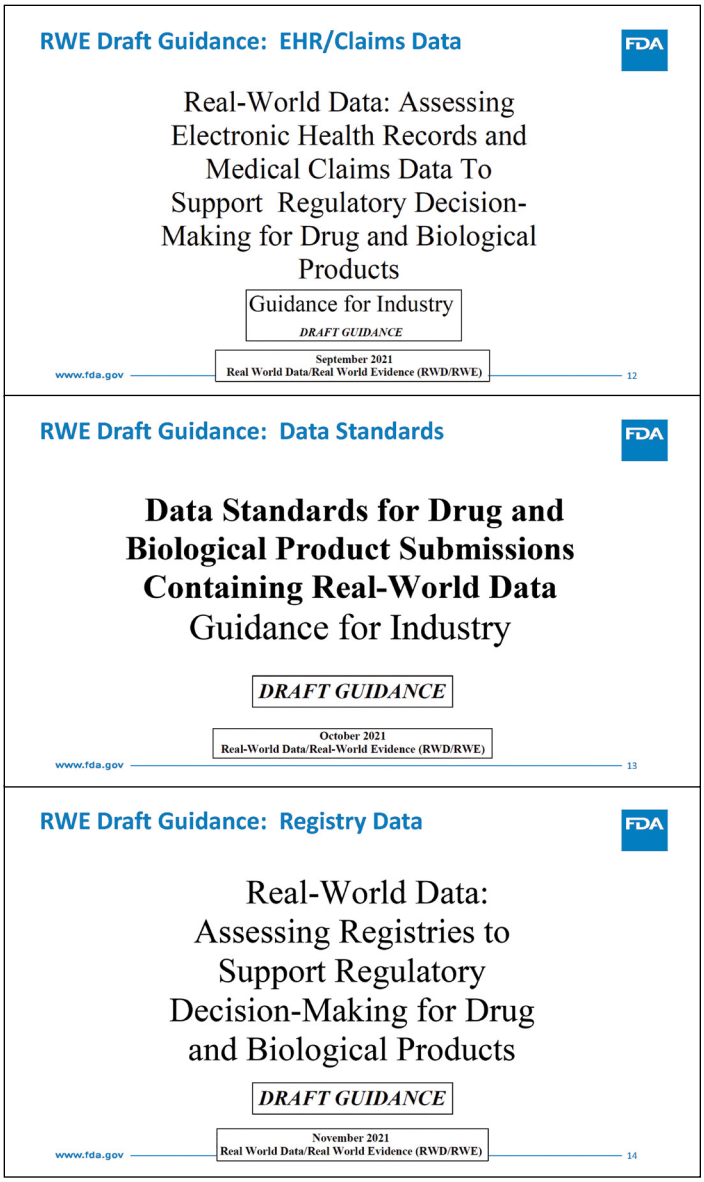
So now I'm going to answer my first question about the guidances that we have developed. The OneSource project is a working example of two of the guidances that we published. The first one was published in September of 2013 and is called Electronic Source Data and Clinical Investigation. It is a guidance that promotes capturing source data in electronic form. And with that said, it assists in ensuring the reliability, quality, integrity, and traceability of electronic source data. Next slide, please. The guidance use of electronic health record data and clinical investigation was published July of 2018. And in this guidance, we focus on opportunities and challenges: where the sites, the biopharma industry, the sponsors would like to use electronic health record data and clinical investigation, what are the interoperability challenges, and also integration of healthcare and clinical research systems. And then this guidance provides best practice for ensuring the quality and integrity of EHR data in investigations. Next slide, please.

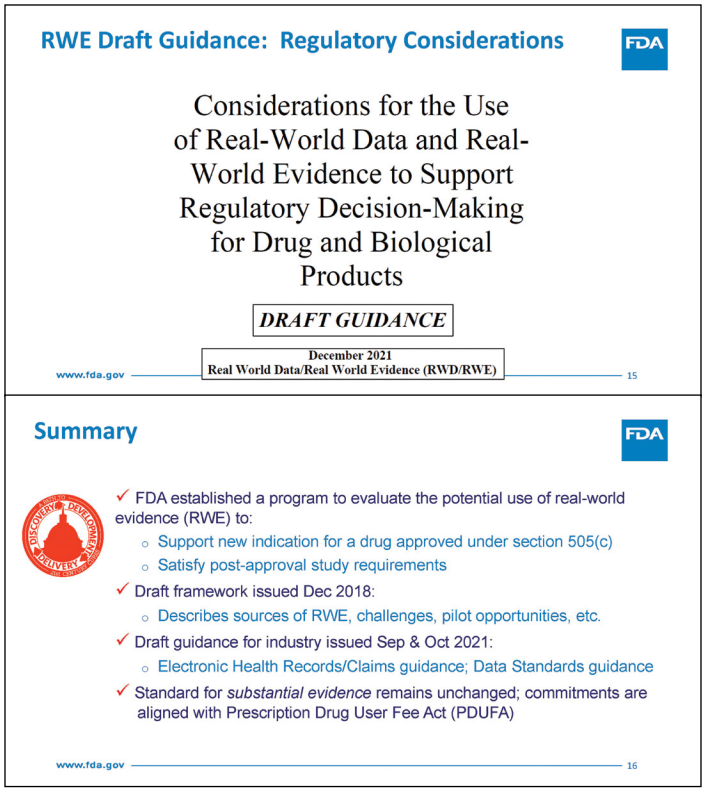
So as part of the real-world evidence framework, we have published several guidances, and those have been draft guidances. And currently, we are addressing the comments that we have received. The first guidance we published last year was September 2021. This focuses on assessing electronic health records and medical claims data to support regulatory decision making. And this is for drug and biological products, not devices. Next slide, please. A data standard guidance that we published October 2021. This guidance focuses on data standards that are needed for drug and biological product, or when the sufficient use real-world data. And that one that was published, and we are addressing the comments currently.



Next slide, please. Registry data... this is both a disease registry and product registries. And how you can use registry data as a source of real-world data to support regulatory decision making, also for drugs and biological products. This guidance was published November 2021. Next slide. And the last guidance was published last

year, and there are still some guidances in development, in regulatory consideration. This was published December 2021. And this is consideration for the use of real-world data and real-world evidence to support regulatory decision making, also focusing on drug and biologic products. Next slide. So in summary, we have established the program to evaluate the potential use of real-world evidence. And we developed the framework that was published in December 2018. And we have developed a suite of guidances in past fall, and the PDUFA requirements...are the commitments are aligned with the requirements. Next slide. Thank you very much.





Michael Ibara

Thank you very much, Mitra. And I can... I can say as a frequent discussion, as these were being developed, often with you, and as somebody that's working in the space trying to apply some of this... it's, it's a real credit to FDA, I think, to be contemporary with this work and put out these guidances, which are very timely and help us while we're in the midst of trying to figure out how to do it all. So thanks. Thanks very much for that. So we're going to move now to sponsor perspective. And Riley is Co-Founder and... and CEO of Freenome. You're clearly qualified from this point of view, I want to ask you, from a sponsor's point of view, how valuable do you find real-world data or EHR medical records data and the work that you're trying to do or that you want to do? And what are... from your point of view in development, what are some of the greatest challenges in employing it?

Riley Ennis

Absolutely. And I would say that we've all experienced firsthand how COVID has transformed and really accelerated some of the opportunities around real-world data. At the start of the pandemic, we started looking very closely at EMR scheduling. And we saw that colonoscopies, which usually there 1,000s, occurring every week in the United States, went down to around over... I don't know, around 100 per week. And we saw that drop as we were enrolling in our pivotal trial for our Colorex cancer screening tests. We saw very quickly, from a leading indicator, that colonoscopies were going to have a huge backlog and that enrollment into our study would be near impossible.

So we actually had to use real-world data. Tt became a requirement to monitor and look at how COVID was spiking in different geographies and change your study operations so that not only could we reach people in any ZIP code through more of a virtual trial and incorporate telemedicine and other aspects into our study operations, but we also could help our clinical partners, where we have about 200 clinical sites as part of our pivotal trial. We saw a lot of information from real-world data that helped people really look at referral patterns from screening—some of the challenges and barriers from a health equity perspective that were preventing individuals from getting screened.

So not only did real-world data allow us to find individuals for the study, but it also allowed us to provide value back to our clinical trial partners and provide insights into their active screening programs today. So the value was there. And it created a level of flexibility and adaptability throughout the pandemic and allowed us to publish with a lot of our partners, just showing the opportunity that with real-world data and those insights, we actually could increase enrollment in some of the Black and other communities that were traditionally not well represented in clinical trials. So I'd say that real-world data become a necessity in the pandemic.

But a lot of the work at the FDA and Mitra, especially with your leadership and others across groups like CDRH, as well, we've seen tremendous opportunities to not only help in the clinical study phase, but postmarket, continue delivering value, improving our existing devices, identifying new populations, and really building evidence. But that comes with a lot of challenges. It's not easy. And we found that a lot of the foundational infrastructure...and it sounds like the work that Mitra is doing with UCSF, really speaks to a nice case study where we're missing the ability to handle heterogeneous data. And that infrastructure from a data perspective also requires cybersecurity and a level of privacy, given the trust that any subject and any patient is really giving to us as part of a clinical study.

So we see that there are a lot of opportunities, but still a long journey ahead in building those foundational pieces to ensure that the data is handled well. It's clean and normalized and can be leveraged to really maximize the impact in patients' lives. But I'd say the nuances that with real-world data at the front and center of these clinical studies, it's important that sponsors also give back to the clinical sites. And I think that's something that, you know, we're starting to see more and more. But I would definitely encourage anyone who's running clinical studies to really think about how can you leverage real-world data to help the patients, help the nurses, help the principal investigators really gain additional value and insights from ongoing studies.

Michael Ibara

That's really interesting. Thank you. Thank you for that perspective, Riley. And as somebody that's waded into it, it's interesting that you can see the promise and it sounds like it's foundational to your development program as well. So thanks for that perspective. So, next question is for you, Jeremy, as somebody who, you know,... Cerner Enviza, one of the EHR vendors, which originally was meant to do a few things is, and now is asked to do a million different things. I'm wondering about your perspective. And specifically, the question is, from the point of view of a company managing the EHR, and generating the real-world data that we're all using, what are the some of the challenges, and also some of the misconceptions for those of us trying to do the research about the use of that data for clinical research?

Jeremy Brody

I'll start with the misconceptions. On the one hand, I think that there are a lot of people out there who feel that real-world data represents just a panacea of opportunity. That it's, you know, available, easy to use, and so forth. And therefore the use cases are never ending. On the other hand, there's a group of people out there who feel the exact opposite: that in fact, only randomized clinical trials can provide any evidence towards, you know, marketing, authorization, and FDA decisions and so forth like that. And I would say both of those, you know, are misconceptions, and both extremes that exist out there. And as with many things in life, the reality is, you know, somewhere in between.

And so where does that somewhere in between take you... take you, it takes you into the real world of real-world data, and in the real world of real-world data, the data are not clean. They're inconsistent. They require validation, there are parts of the data that are better parts of the data that are worse. Sample sizes, you know, vary dramatically from one data set to another, as does the quality. The ability to link those data sets varies from one data set to the next. And so the devil is in the details in terms of being able to go ahead and

take what has tremendous potential, has the ability to do all the things that Riley mentioned— very practically to do all the things that Riley mentioned in the great examples that he just gave.

If, in fact, you go ahead, and you spend the appropriate time and effort in order to be able to make those data usable and valuable for these particular use cases. Because in fact, these data were not designed for this purpose. These data existed as part of clinical care, existed for billing purposes, and so forth. They were not created originally for research purposes. Again, tremendous potential for turning them into wonderful research data, but requires significant time and effort in order to in order to be able to do that. And if you're in fact successful, then indeed many of these challenges can be overcome. And the utility of these data is tremendous.

Michael Ibara

That's great. And it's... we really appreciate— all of us who have worked with the data, —appreciate your description of the misconceptions. I often in the past, and sometimes still talk to my colleagues about the fact that the EHR is not a big bucket of data. And it's usually quite surprising when people who haven't seen it before actually get into it. So your firsthand experience is well received, I think. So. Next panelist is TJ Bowen working at Deep Lens. TJ, in our conversations, you know, we've talked about the fact that you guys are on the front lines, in a sense. So it's... it's very interesting

to hear from people doing what we often, a lot of us, talk about or write about, from your perspective. What do you see are the challenges in… in enrolling these patients using real-world data, specifically on oncology? In order to get them into clinical research, both working with the site and with the sponsor?

TJ Bowen

It's an important question. I think following these panelists, you've heard a lot of the reasons why this is challenging. You know, the data is not clean. The data is not consistent. Things like COVID have really impacted the ability to even capture the data. But I think I think it actually starts more fundamentally than that— it starts with the science. You know, over the past 20 or 30 years, the movement to precision medicine has been super important for patients. It's really improved the quality of care they're able to get and the access to those game-changing therapeutics. But that also is increasing the burden on the practitioners because the volume of data required to find patients that qualify for specific treatments is really hard. So, it's great for patients. It's hard for practitioners, which

I think Riley said it almost makes real-world data mandatory that you can't find patients anymore, unless you're leveraging real-world data. Because especially in clinical trials, which is where we focus, you know, the inclusion-exclusion criteria are getting so specific. It's really impossible to just go out and find a patient with breast cancer and find the right trial. You'd have to know so much about their molecular information, their treatment histories. The list goes on and on.

So I think it starts with that, which is where there's challenges. We spent a lot of energy focusing on harmonizing and normalizing the data as well. And as Jeremy said, you know, a lot of these systems are initially billed as billing systems. So if it's not something that gets billed for, there's not a whole lot of emphasis in normalizing the data. So you know, we dive into pathology records, where you start looking at stages in grades of tumors. We focus on oncology, but, you know, it can be applied across the board. And so when you start getting into that, you have to do a lot of things with natural language processing machine learning to really create your own normalization across disparate systems. I think the stats say that almost 50% of new therapeutics have some sort of precision component. And in oncology, it's close to 80%. So it's not… it's not resolving itself, right; it's just the data is continuing to pile up.

So when you're a community practice, that's trying to get the best therapies for your patients and there's this notion of CRACO, or clinical research as a care option, which is becoming really viable, you really have to be in in control of the real-world data that you have access to it those practices. And historically, it's really only been possible at large academic medical centers. But we all know, as Riley mentioned that, you know, the patients need to be given access to this stuff where they're treated. You don't get a diverse patient population enrolling in studies unless you go to where those patients are being treated. And so you know, the mission is really to give access to the real-world data that they're collecting, where they are. That's the biggest challenge and something that we're trying to tackle.

Michael Ibara

Thank you very much, TJ. And you're really somebody that's… that's been on the front lines, as you're discussing things, and you pointing to the future, as well. And adding ending my two cents to this discussion, with everything that's been said, I just want to point out to

you that, despite the challenges, we're all in the same room now. And that's because after 21st Century Cures and the adoption of the electronic medical record, we do have, whereas our fight used to be to find the data. And we would pay people to get it.

Now we have a tremendous amount of data. And so of course, the focus switches to how best to use it. I would say that I am guilty of this idea— 10 years ago, maybe— thinking that just getting all the data would get us a long way to solving our problem. But as those of you that have been working on interoperability for the last 10 years, now, it didn't. And everything that's been talked about here is evidence of that. And not only from the data point of view, but when you were talking about finding patients for trials, I just want to remind everyone that we're now talking about doing this across sectors. We've got patients in Healthcare that we want to bring into regulated research, which is a different sector with a different business model— different concerns that do overlap. But we also need to do that as per the regulations, which is, again, is a different sector.

And anybody that's been in any of these knows that these are all their own universes. I think I was in a meeting with Dr. Califf before his first-time round, when he said, you know, he, his interest was in bringing together the two universes of healthcare and regulated research. And this is not an easy thing to do, not only because of the technical aspects of it, but because of the cultural differences, literally, in the concerns that have to be met. So in order to go into healthcare, and bring those patients into regulated research, we have to go there to where they live, as TJ, said and bring regulated research infrastructure to them. And it varies tremendously.

When you get outside of academic medical centers, you have sites that are focused on treating their patients, that don't have an informatics group, that barely have a group that manages the EHR, and certainly don't have a data scientist on staff. So that ability to enable them to do that, enable them to provide their data, I think is a key challenge of getting the data that we want in order to find the patients. So this initial discussion is meant from a varying perspective.

What I'd like to do now is just ask an open question to the group. And that is, we're talking about the use of the data that we can generate. Now, it's real-world evidence largely is often from the medical record, the EHR directly. And the challenges there. And we're talking about using that to put patients in clinical trials and some of the challenges there. A slightly provocative question from your point of view or your direct experience: What would you say as a panelist about if you had to give advice to the way that we do that today, that our traditional method of finding patients for trials and where it's coming up against the use of real-world evidence, either specific examples or general recommendations or that thing that really you think we need to fix in order to make it more effective?

So from your point of view, what is it about the way that we enroll patients or the way that we start up clinical trials today, that could be made better in terms of a process that would better allow us to take advantage of the clinical trial data that we're using? Open question for anyone.

TJ Bowen

Yeah, so I think what we see a lot is it's two sided, right? It's all... it's a sponsor issue, and it's a provider issue. So I think sponsors of studies, you know, put a lot of energy into making their clinical trial inclusion-exclusion criteria more uniform. We see them doing things that are really shortcuts for them that don't really help the practitioners, like saying a patient can have had a prior PDL1therapy.

Well, what they don't think about is that you have a clinical research coordinator, working on the ground that now has to go through and figure out what all of those therapies are, because nothing's recorded as a PDL1therapy in the EMR. So there's things like that on the sponsor side. I think it would really help a lot if they could sort of harmonize and provide things digitally...

would be super helpful, so that...so that as people are trying to use digital solutions, the source is also digital to make that connection easier.

And then I think on the provider side, some of it's a little bit, you know... if we're going to take accountability as technology providers, making the UI better for the physicians, I think a lot of times we see them taking shortcuts. You know, they'll do things in the clinical notes instead of in a field location, just because the application's too challenging or not clear enough on how they need to do that. And that makes it really challenging to find the information you need to really kind of pair that patient with the right study. So I think just from my perspective, there's a couple of things that would be a good starting point.

Michael Ibara

TJ, the first comment you were making about on the sponsor side, are you thinking in terms of at the level of the protocol development. Being able to get that better, so that, because by the time you get to finish protocol, that could be one of the key reasons that you're not finding the patients?

TJ Bowen

Absolutely, yeah, the protocols are... are really challenging. And, you know, they change all the time, which I understand. I mean, they have to modify, update. But when you put very vague terminology into the protocols, somebody else has to interpret that. I think making it as explicit as possible for an end user will help you find those patients that you want to qualify for the study.

Jeremy Brody

Yeah, actually, I was going to make similar points to TJ. But then just one other thing, in addition to add is just that it's critical that the latency of the data, you know, also be as real time as possible. Because often what happens is that you go through that entire effort that TJ just described, and you work through the inclusion-exclusion criteria. You identify the sites. You identify the patients, and then, lo and behold, it comes time for actual recruitment. And situations have changed because people are human beings, and their lives change and their circumstances change. Their clinical data changes, and so forth like that. And therefore, a group of people who you thought were going to be great candidates for your trial are no longer great candidates for your trial. And vice versa: People who were not eligible for your trial are now eligible for your trial. And so keeping that latency to as minimal as possible in order to be able to make all that hard work and effort that TJ just described, actually produce, you know, patients enrolled in a trial at the end of the day... it's a critical piece of the equation.

Michael Ibara

Absolutely. Well, I've had the personal experience of looking for patients at a point in time, and then the protocol actually doesn't kick off till four or five months later. And you've lost a lot of them, as you're saying. Something else I've experienced, talking about the process by which we find patients and the world we're in, I do think there's some dissonance that we experienced because things have changed so fast.

And we mentioned, you know, the FDA deserves a lot of credit for trying to keep up with regulatory aspects of this. I wonder how well we're doing, keeping up with the aspects of the way that we initiate trials. I have a colleague that talks about going fishing, and he said, the traditional model is you put out your fishing pole and you wait for the fish to come by. So you stand up a site, and you put out your pole, and you wait for the fish to come by, meaning you wait for that site to do... find the patients over time. And it's not that you stand up all sites at once. You stand up sites over a period of time. By the time you're done, you've got all the sites up and running, but you've taken up a whole lot of time getting those sites up and running. And you don't know which ones are going to have the patients for sure. So you inevitably end up missing your recruitment timelines.

And given the fact that we can search for the patients so readily now, at least at a higher level, and try and enroll them in a more precision way, I feel like sometimes that's coming up against our traditional model, because there's so much involved in changing that process. That even though we understand there's a lot of patients, we end up hamstringing ourselves. Because we still do the same thing that we did in the past. We stand up at these individual sites and sort of wait around.

I think, Riley, what you described, you went through a quickly, but it's already a different model, I think, or how you guys have been working. I wonder if you can just compare that to what I was talking about to how you're really recruiting patients these days?

Riley Ennis

Yes, no, it's been tremendous. And I would say, I've never seen a clinical study where we were ahead of schedule in terms of enrollment. We initially were targeting 14,000 for the Colorex scan screening trial. And we're now at 35,000, completed subjects, meaning blood draw colonoscopy, and it's covering such a diverse population. And we decided to upsize our study just given the rapid rate of enrollment.

But really following a similar model to what Mitra spoke about with OneSource and UCSF, it's investing in your sites. And I think the concept of recycling and leveraging not only proprietary data, like our multiomics data to help, you know, TJ, find these very, you know, specific inclusion-exclusion criteria, but being able to invest in sites and build an infrastructure for them. While understanding what the pain points are, specifically around some of the quality measures, we found that simply by helping folks identify and improve their screening adherence today, they can hit HEDIS, and STARS, whether it's on the provider, the payer side, and that brings tremendous value to the site. And then when we, you know, progress to some of our multicancer studies, we've now built all that foundational infrastructure. We've helped improve their existing screening workflow, and they see us as a long-term partner that's enabling them to deliver better care.

And really, it's about listening. It's about sitting down with the nurse practitioners, with the clinical site coordinators, and understanding the challenges they face. And I think to TJ's point, you really must understand those operational burdens on sites and find ways that we can invest in and support these sites to be able to perform, you know, the best research. But I still think there's a gap in the industry, where we have tremendous data now on 35,000, individuals with longitudinal follow up and tokenization in place.

And those data can help support so many other clinical trials out there. And I think we tend to silo data a lot of times, especially as companies, and I think it's time that we find ways and leverage the data that's been

generated. So we can recycle... we can use them to improve outcomes and improve clinical studies across the board. Especially when there's no competition, you know, on the screening, diagnostic side versus therapeutics, we can play a huge role as we first engage the patient at screening and help leverage that data down the care continuum to not only help providers and sites but also sponsors.

And I think that's one of the biggest opportunities, and the companies that can help bring us all together as sponsors... I think it's going to make it much easier to identify patients and solve unmet needs today, and help sites build that infrastructure that they can run trials, where they don't have the IT, they don't have the funding or support, but they really do want to deliver on better care. And I think that's going to be the future is, you know, really delivering the value today, and then also coming together to share our data so we can enable more efficient trials.

TJ Bowen

Yeah, Michael, I think picking up on that, to what Riley just said, and kind of extending your metaphor about the fishing, right. So I think one thing we see a lot with sponsors is they tend to go back to the same fishing holes, without much evidence that that fishing hole is going to produce fish for their new... for their new study. I think what we really need to focus on is making sure we have data from a lot of the fishing holes that nobody's fishing it, right?

And I think, Riley, you said that you guys have done that a lot lately, and I think this whole equity issue is really important. You know, as we start getting more and more precise treatments for people, we really need to understand from a compliance perspective, if those patients are all going to benefit by, you know, race, ethnicity, other sort of socioeconomic status. And if we're going to the same fishing holes over and over again, we're really being homogenous with where we're sourcing our patients. So I think there's something we need to consider as an industry on how we democratize this access to data across all of the different fishing holes.

Michael Ibara

It's a really interesting idea. And I'm assuming from some conversations with you, Jeremy, it's not dissimilar to the approach that you know. Because Cerner Enviza has such a large repository of data, you have the same goals of being able to use and reuse that data for clinical research in similar ways, I would think.

Jeremy Brody

Yeah, no, that's absolutely true. And to TJ's point, one of the unique things about the Cerner footprint is that yes, there's a presence in the academic medical centers and some of the larger healthcare systems. But in addition to that, Cerner also has a tremendous presence in community hospitals all around the United States and many underserved populations.

And so when the FDA speaks about the idea of diversifying, you know, clinical trials and bringing in additional patients, you know, from hospitals and health systems that perhaps have not traditionally participated in clinical research, in many ways, that is the Cerner footprint, and we're very proud of that. And really, what we'd like to be able to do is bring clinical trials into everyday healthcare, and then to Riley's point, you know, beforehand, being able to bring that data back into the hospitals and health systems and ultimately, to the doctors and patients in order to be able to impact that same everyday healthcare. But this is what TJ and Riley were just speaking about. It really hit home for me and really speaks to many of the things that we're trying to accomplish right now.

Michael Ibara

So this is tremendous. We have a question that's going to take us right back to our fundamentals. And we've

all talked about some of this. And FDA has been looking at it from their perspective. Everybody looks at this, but the question is, we're so dependent on healthcare clinics and if their staff puts data in the right fields, and scan that result incorrectly from another clinic.

The first part of the question is, what are some thoughts and solutions that are being put in place to clean up real-world data for clinical research? I remember starting on an answer to this question years ago, and I still haven't answered it. But I'd love to hear everybody's perspective. Certainly, from the EMR vendor to Jeremy.

But the second part of the question is, how are the research sites getting back into the healthcare sites' patients' EMR? So I think the general idea here is, how is it a good idea? And are we able to bring study data back into the EMR, both for patient care and just as a technical solution? So anybody interested in commenting on either of those questions?

Mitra Rocca

I can comment on both of them. So for the first part of the question... so one of the things I work on, because there are so many data elements in clinical research that are not in the EHR system. So I collaborate closely with the Office of National Coordinator for Health Information Technology, and I push the data element needed for clinical research into their future EHR certification.

So for example, the adverse events actually sometimes are not in the right place in EHR. Sometimes it's allergy intolerance. Sometimes in unstructured text, you need to apply NLP to get the adverse event. And then for the research side for the project that I am... we're collaborating with UCSF. We will have... you have been working with EPIC to do a write-back. So the data from clinical research are written back to the EPIC, and then the next phase is to collaborate with Cerner on the same rate by capability.

So then the healthcare provider knows that this patient participating in this clinical trial had adverse events, so they know that their subject might have some adverse event happening to them. So this way, the clinical investigator knows what happened to the patient—if they went to emergency room and was seen by regular healthcare provider and yet, also the opposite, like healthcare provider. And here's what happened to the subject and can contrast.

Michael Ibara

That's a scalable solution, and tremendous, Mitra. I think it also goes back to your general point, Riley, of giving back to sites. I do. I will note here, too, that we are in a world where I coined the phrase, "The future is here, it's just not well distributed yet." I've seen these solutions. I've also seen sites where we need to supplement them with a study coordinator. And it's the only way to try and get them to input some of the data into the field. But other comments or perspectives on this— on these two questions?

Jeremy Brody

Well, the EMR obviously needs to continue to improve and, you know, be that much more user friendly, to enable, indeed, better data to come in on the front end. With that being said, the EMR will, I believe... will continue

to be not designed for research purposes, right... So that will not be the fundamental reason why people will be entering in data in it. And therefore, there's also... when sites do agree to participate in clinical research, and, you know, they're being compensated, you know, for that activity and so forth, there is a quid pro quo, that is, indeed, you know, going on there.

And I think there's an education that's required. And it's really on the... on the sponsor, on the sponsors, partners who are working with them on that trial, in order to be able to educate the physician, the staff, and so forth, about the type of data that are being collected, why it's being collected, how it needs to be collected, and so forth. And to go ahead and reduce some of that friction that exists, you know, around the data that are being entered into the EMR versus the data that are required for the study.

Ultimately, however, I do believe that there will be some amount of cleaning always, you know, required on the back end. Data abstraction, you know, taking place will leverage technologies to the best of our ability to be able to do some of that work. But today does require also, you know, human beings to be involved. And so they'll always be sort of that element, as well. So I think that's with regards to the first half of the question.

And then on the second half the question, it's critically important to be able to, once all this effort has been done, to go ahead and get really good clinical data that's usable, and leverageable, and not an unstructured data and so forth like that— for that to indeed be fed back into everyday healthcare. And this is definitely one of the things that we aspire towards and are working towards right now. And when maybe the ways that Mira just referenced.

Riley Ennis

Yeah, couldn't agree more. And one thing I just want to add is that a lot of times in the early protocol development phase, we focus a lot on, you know... for example, our lead site is Kaiser. And Kaiser is very different than a lot of the other sites of the 200 sites that we work with. But we spent a lot of time in the communities understanding, from a data perspective, what are the challenges, where are the blockers and really co-develop and have an advisory board, that's not always the key opinion leaders, but also really working with sites before we lock a protocol to make sure that the burden is as little as possible, but also that we can understand what some of the barriers and challenges they're facing, and clinical questions that they're interested in, such as some of the issues in health equity and social determinants around cancer screening.

So that partnership and co-development is something that we found sites were very surprised by, especially, you know, very rural and other sites that don't traditionally participate in clinical studies. And they felt motivated, and they saw the short-term benefits their practice, as well as how this investment together as a team could allow for much more and better care long term. So that working relationship and not being in the helicopter approach, or just coming in using the site and moving on, but really getting on the ground and helping understand those operational data challenges. Because a lot of times when there is an issue of data quality, if you can understand the source and the root cause and do that, in the beginning phase of designing a protocol, that can improve the data quality. It really builds trust with sites, and you can find them the clinical questions to then deliver data back to sites to help them in real time with existing clinical care.

So there's a lot of that work upfront. I think we rushed to get into the protocols lock, get role... you know, enrollment started, but taking that time at the beginning, pays dividends. And you know, I think we've really appreciated it and are actually humbled by how much we've learned by getting in the communities, in the neighborhoods, and just understanding what those barriers really are.

And then publishing, we had a great poster with Morehouse, at ACG, where we were hearing that African Americans have members of the Black communities did not want to participate in trials. And that was fundamentally not true. And we jumped on that

opportunity to say, "Why is that the perception?" And we had amazing leaders on the ground who helped us really identify what the barriers were. And then we were able to make changes to the study operations, which allowed us to beat U.S. census around enrollment in the Black communities and with African Americans. And that was so motivating and meaningful because those are individuals that we want to serve and want to help.

So there's so much learning, and I think you have to go locally. And you... we can still operate globally and operate, you know, systematically. But we need to understand a lot of those issues upfront if we're going to maintain data integrity.

TJ Bowen

Some of those... some of those soundbites about, you know, certain ethnic groups not wanting to participate— I think that's almost becomes a scapegoat. And it's... it's a little bit that there's an endemic problem and where those patients are being served, that people don't want to address. Right, it's like getting access to them, which is what we see in our network is the first thing, and then once you get access, we see that a lot of people want to participate. Once you explain kind of what the opportunity is. So I think... I think it becomes this... this easy kind of broad brush to use to kind of basically avoid the reasons that they're not getting the right enrollments. So I'm glad to see that Riley and Freenome are addressing that head on. That's great.

Michael Ibara

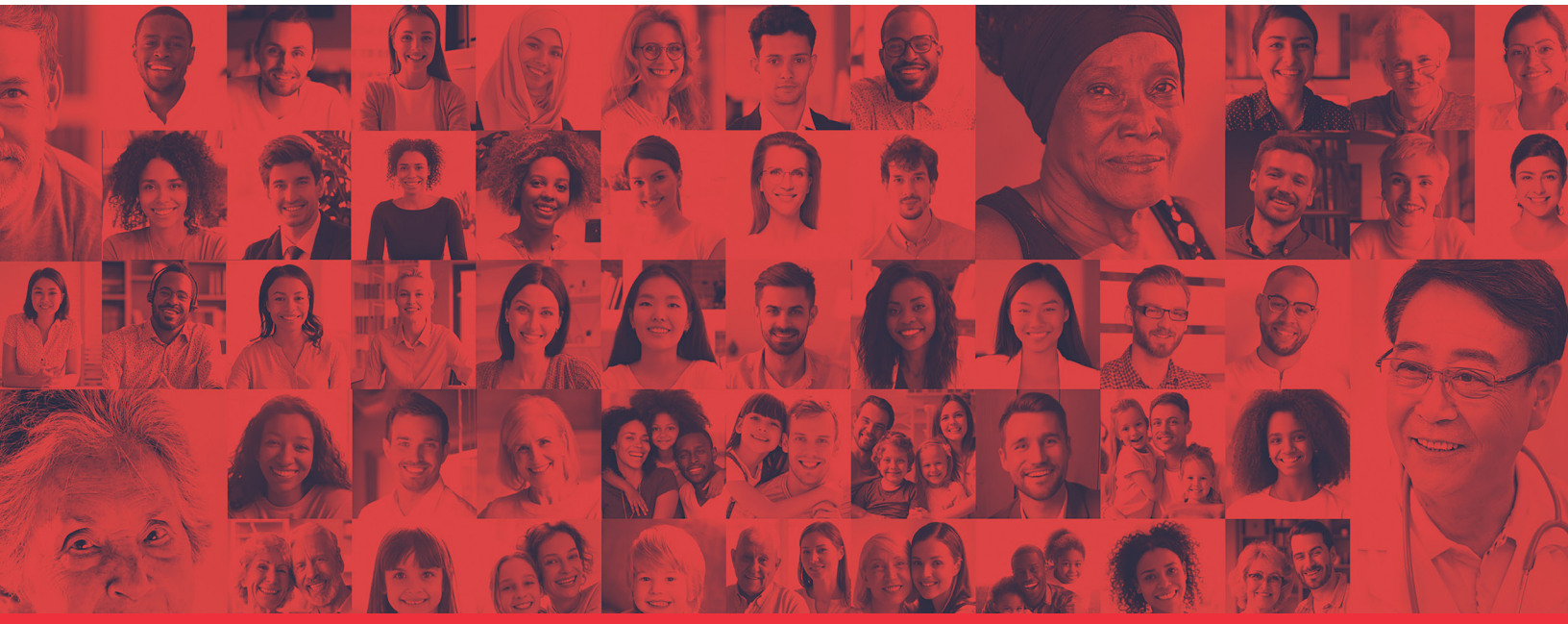
These are... this is tremendous — tremendous discussion and lessons. In the last few minutes, I just want to summarize a couple points that we just were touching on that really, I think, go across the whole discussion here. And the first is in terms of, you know, as usual, when we're talking about how do we get more patients in our trials, one of the lessons learned is start further upstream.

So we're talking about, don't finish your protocol, and then wonder why you can't find the patients. Co-develop your protocol. And with the amount of data that we have today, then, really, it's sort of repurposing the term feasibility, which traditionally has meant "I've got a protocol. How many patients do you have for it." Feasibility now becomes part of the modeling process in creating your protocol, so that you can have a much better chance of hitting the right population downstream.

And then the second thing that... you mentioned it, Riley, you know, the famous phrase, "think globally and act locally"? This idea that— and really, you guys are also living proof of this, TJ— you often get a hold of molecular data that you put together and sort so that you can offer back to sites that don't have the same ability to see what you're seeing. So you're actually able to organize the data and give it back to them. Jeremy, you're doing the same thing now with your Learning Health Network. And you guys are doing this for your protocol development rally.

So I think all of you are representing this part of this new model, which is the organizations that are expert at gathering and organizing the data can also then give back to the sites and help them augment what they're doing in order to then have them help bring the patients into research. So I think it's tremendous. I think it represents a good model.

When you ask the question, how do I get more patients into my trial? These are really the answers, I think, that you're all… you're all demonstrating. And on the regulatory side, Mitra, and your discussion of the OneSource program— I think it's fits in the exact same vein. And it's…it shows that throughout all the sectors, even though they're so different, there's actually a common model that I think is emerging. And that's… I think that's very exciting. So I think we're right at time, personally. First, I'd like to just thank all of our panelists, TJ, Mitra, Riley, and Jeremy. I talk and work with you outside of this, too. So I really appreciate you participating in this. And I really liked this discussion. Absolutely. So thank you very much, all of you, for participating. And thank you. Thank you. Thank you.



Ayesha Rashid

Well, thank you very much to our speakers for the very insightful presentation and discussion. We have reached the end of the presentation. If we couldn't attend to your questions, the team at Elligo Health Research may follow up with you. Or if you have any questions, you can also direct them to the email address that is displayed below.

Michael.Ibara@elligohealthresearch.com

I'd like to thank everyone for participating in today's roundtable. You will be receiving a follow-up email from Xtalks with access to the recorded archive for this event. A survey window will be popping up on your screen. Your participation is appreciated as it will help us to improve on our roundtables. Now I'm about to send you a link in your chat box where you will be able to view the recording for this event. And you can also share this link with your colleagues when they register for the recording here as well. So I do encourage you to do that.

Now please join us in thanking today's speakers, Dr. Michael Ibara, Dr. TJ Bowen, Mitra Rocca, Riley Ennis, and Jeremy Brody. We hope you found this roundtable informative on behalf of the team here on Xtalks. Thank you for joining us. Please take care, and bye for now.

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