Introduction to Innovation in Medical Evidence and Development Surveillance (IMEDS): The Research Resource Webinar
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Transcript

Opening Remarks
Carla Rodriguez-Watson, PhD, MPH, Reagan-Udall Foundation for the FDA

Dr. Carla Rodriguez-Watson

Hello. Welcome. Thank you so much for joining us. I'm Carla Rodriguez-Watson. I have the pleasure and privilege of serving as a director of research at the Reagan-Udall Foundation for the FDA. For those of you who have not heard those words strung together, we are the nonprofit, non-government organization created by Congress to advance the mission of the FDA and help it do more to protect and promote the public's health. On behalf of the Foundation, I'm pleased to welcome you to this webinar where we're going to share information about the Innovation in Medical Evidence and Development Surveillance program or IMEDS as it's known. We'll also have a panel of experts who work regularly with the IMEDS program and we're also delighted to welcome to the virtual stage Dr. Jacqueline Corrigan-Curay from the FDA will deliver opening remarks.

So now on to today's agenda. In just a moment, FDA's Dr. Jacqueline Corrigan-Curay will provide a keynote speech to set a foundation for our discussion. Then my colleagues, Dr. Claire Huang and Georgia Peeples will present an overview of the IMEDS program. Once we learn about what IMEDS is and what we do, we'll spend some time talking with our panelists, all of whom are IMEDS collaborators. And then finally, Susan Winckler, the Foundation's CEO, will close our meeting with some final thoughts. And now it is my pleasure to introduce our first speaker, Dr. Jacqueline Corrigan-Curay. She serves as the Principal Deputy Center Director in the Center for Drug Evaluation and Research (CDER) at the U.S. Food and Drug Administration (US FDA).

Keynote
Jacqueline Corrigan-Curay, JD, MD, Center for Drug Evaluation and Research, FDA

Dr. Jacqueline Corrigan-Curay (02:16):

Yes. Thank you. And thank you for inviting me here for this really important meeting. I'm just really pleased to be here with everyone. IMEDS is a public resource that arose out of FDA's Sentinel Initiative. And for those who are perhaps not as familiar, it really dates back to 2007 when Congress passed the Food Drug Administration Amendments Act of that year and tasked us with starting a post-marketing real-world data system. We launched what we called the Mini-Sentinel Program in 2009, and by 2011, we had reached the distributed database of a hundred million lives, and that was a benchmark from the original congressional mandate. We then move forward to what today is a Sentinel system in 2016, and

it continues to grow and evolve serving FDA's post-market surveillance needs. It's a unique federated data system linked by a common data model and has a suite of reusable programming tools for routine queries.

(03:20):

However, it was also clear to leadership as we really understood the value of the system that we needed to create opportunities to allow parties outside of FDA to leverage this government funded resource. And it is our partnership with the Reagan-Udall Foundation and their innovation and commitment to achieving this goal that has really led to the success of IMEDS. So, since its inception in 2013, the Innovation in Medical Evidence and Development Surveillance or IMEDS program has supported the use of real-world data in each step of the research process. Pilot studies, feasibility assessments, drug utilization monitoring protocol development, statistical analysis plans, result interpretation or preparation of final reports, IMEDS can be used. It really does play a critical role in supporting our goal to make the Sentinel tools more widely available and to help organizations maximize the benefit of those tools through their deep experience and engagement in regulatory science with the agency and other interested stakeholders.

(04:28):

These are trustworthy analytic tools. And what I mean is they were developed by FDA Sentinel. We understand these tools and that really helps ensure the relevance and reliability of results when you're using them. The Reagan-Udall Foundation for the FDA's broader portfolio of regulatory science projects, convenings, and public-private partnerships bolsters the ability of IMEDS to support organizations to make the best use of Sentinel tools for their regulatory submission. As you'll hear, IMEDS is made up of nine Network Partners, all of which are either Sentinel data partners or Sentinel collaborators. And the data in the IMEDS Network is expected to be geographically representative of the commercially insured U.S. Population. And there's some wonderful graphical representations of the data on the Reagan-Udall Foundation's IMEDS page. The IMEDS Network includes investigators with expertise in their native source data and scientific expertise in their field of studies, which is so critical.

(05:30):

And of course, like Sentinel, IMEDS uses the federated network approach. And why is that important? Because we really think it promotes data protection and privacy, very important as we use real-world data. It fosters partner autonomy and central coordination and contracting. So we are so pleased at the progress made to date in the IMEDS program. A testament to the leadership of the program and the Regan-Udall Foundation. And we look forward to the continued growth and use of this important resource. And I want to thank you for your attention and I will turn it back to Carla on the exciting agenda.

Overview of IMEDS

Claire (Hsiao-Ching) Huang, MPH, PHD, Reagan-Udall Foundation for the FDA
Georgia Peeples, MPH, Reagan-Udall Foundation for the FDA

Dr. Carla Rodriguez-Watson (06:08):

Thank you so much, Jacqueline. Always really pleased and eager to hear your words and want to grow as is needed with the needs of the Sentinel program and the FDA. And so now I'm going to turn it over to the Foundation's Research Scientist, Dr. Claire Huang, and our Program Coordinator, Georgia Peeples, to provide you all with an overview of our IMEDS program. Claire, will you take it away?

Dr. Claire (Hsiao-Ching) Huang (06:34):

Thank you. Carla. Hi everyone, I'm Claire Huang and I'm the Research Scientist at the Reagan-Udall Foundation. My role with the IMEDS projects is to serve as a scientific and content lead on the Foundation side in overseeing day-to-day activities on IMEDS projects. And now I'll hand it to Georgia to introduce herself.

Georgia Peeples (06:54):

Hi everyone. My name is Georgia Peeples and as the Program Coordinator, a majority of my time is dedicated to our IMEDS projects where I coordinate efforts between our IMEDS Network Partners, our Analytic Center, and our Sponsors. I do that to ensure that we have deliverables that are produced at the highest standard and efficiency. A little bit about how IMEDS started. The Innovation in Medical Evidence and Development Surveillance program or IMEDS program is a public-private partnership launched in 2013 by the Reagan-Udall Foundation for the FDA. We focus on improving and leveraging real-world data to advance the safety and effectiveness of medical products, particularly for those who have high unmet need. And the IMEDS program is a distributed network with nine Network Partners, and we'll get into that a little bit more in later slides.

(07:52):

The IMEDS program leverages standard tools including a common data model and query tools developed by the FDA's Sentinel Initiative to assess the safety of approved medical products. While only the FDA can leverage the Sentinel system, the FDA encourages leveraging of Sentinel capabilities through the IMEDS program as a national resource for broader public health and medical evidence generation. The IMEDS program mimics the structure of Sentinel including a distributed framework approach to protect patient privacy. The tools used are the same as those used by the FDA. Query tools include those for quality assurance and descriptive and inferential analyses that allow for matching and adjustment.

(08:38):

And then here we have our IMEDS team. This includes the IMEDS Operations Center, which sits with the Reagan-Udall Foundation, and we have our Analytics Center. For each project we also have scientific and biostatistical leads that provide their expertise in content-specific areas. The IMEDS Operations Center is responsible for project coordination and administrative coordination. We also provide project oversight where our familiarity with regulatory science submissions can be of great benefit. We also provide our scientific and epidemiologic expertise. At our Analytics Center we use trustworthy analytical tools to design and distribute our queries to answer the research question at hand. And these are our partners. They are the backbone of IMEDS and it is built on their nine health insurance systems that are geographically representative of all U.S. States and territories. There are approximately 32 million persons represented annually and 125 million covered lies since 2000. The primary data include enrollment and demographic data and adjudicated medical and pharmacy claims.

(09:49):

A portion of systems have linked claims and electronic health record data. In addition to these Network Partners seen here IMEDS also has experience translating U.S. Centers for Medicaid and Medicare services data into the Sentinel common data model and leveraging that for evidence generation. All Network Partners have experience participating in one or more of our IMEDS network projects. A majority of our partners are also Sentinel data partners, so they are familiar with Sentinel tools, have our data and the Sentinel common data model, and are familiar with the quality assurance tools as well. A little more on our distributed IMEDS Network. We have trustworthy analytic tools that were

developed by Sentinel and vetted by the FDA. These tools ensure relevance and reliability of results. We also have a distributed network framework for data protection and privacy as well as partner autonomy. Our typical process goes something like this.

(10:50):

The operations center would distribute a query through a secure file transfer portal then all Network Partners would complete that query. Then they would send their results to our analytics center. Our analytics center would then aggregate all results and mask cells less than 11, and then the project team would receive the aggregate report. And then of course our experienced Network Partners. Our Network Partners are experienced health system partners with deep knowledge of their native data. They also provide scientific expertise in a range of topics. And then here we have some of our IMEDS population data. We collect demographic data annually through Sentinel. The IMEDS network has data from 2000 to 2023, but we are continually collecting data to present day. Our network is currently made up of over 125 million patients with at least one day of medical coverage. Of those patients, 51% are female and 60% are within the 19 to 64-year-old age range. And then here you can see the geographic data and representation of IMEDS data. And this data is specifically from our 2023 IMEDS data characterization. I will now turn it over to my colleague Claire to give more insight in the IMEDS projects and capabilities.

Dr. Claire (Hsiao-Ching) Huang (12:18):

Thank you, Georgia. So before we get into the capabilities of IMEDS, I'd like to spend a little time talking about the role of the real-world data in research. So you are looking at a figure from a study published in 2022 that discussed different roles that real world data can take in different phases of research. On the left side we have the randomized interventional studies. In the randomized interventional studies, real world data can be utilized to identify enrollment criteria, trial site, and outcomes. On the far right side is how real world data has been most commonly used, which are observational studies. So IMEDS is a distributed network that utilizes administrative claims data that can use real-world data to produce real world evidence. Like how this figure shows, IMEDS can be utilized for a project of different phases to help produce the real world evidence.

(13:24):

So in particular, IMEDS has done and continues to conduct post-marketed requirement studies. We have conducted PMRs across many therapeutic areas including cardiovascular, immunology, osteoarthritis and oral contraceptives. So, on the screen are screenshots from our website for details on three current PMR studies that [involve] IMEDS. The PMR studies with IMEDS can utilize our distributed network and work with all or selected network partners based on the objective of the PMRs. With IMEDS, sponsors can expect scientific, epidemiological and administrative support. If you're interested in the details of any of our current and past IMEDS PMR studies and how you can engage with IMEDS, you can go to our IMEDS website for more details.

(14:23):

So, one important highlight of IMEDS is our pregnancy data. IMEDS has and continues to conduct projects that are related to pregnant women. IMEDS utilizes Sentinel tools for the mother-baby linkage. So a little bit about the Sentinel's mother-baby linkage. This linkage is using an infant ID with the first year of life with deterministic match. The more detailed linkage information from the Sentinel tools can be found on the Sentinel website. With that in mind, we are now showing the distribution of linked and unlinked deliveries in IMEDS by mother's age. So, as you can see from this figure, IMEDS has around 4.2 million deliveries among women aged 20 to 44 years old, and 78% of them are linked across all the historical data. These are the data that can be utilized for a pregnancy-related project.

(15:26):

So a little bit more on the pregnancy data. Here is a figure that's showing the number of deliveries in the IMEDS network by calendar year. The linkage rate as the figure show has been consistent since 2006, which is around 75%. The drop of the data in 2022 and the 2023 is due to the incomplete data since our data partners have different data refresh dates. All the data presented including this figure and the figure from the last slide reflected the live births only. So having the linkage of the live births is an important first step to be able to conduct studies in pregnancy. Both these data [points] show that IMEDS has rich pregnancy data that can be utilized to studies that focus on pregnant women.

(16:23):

So now we'll want to talk a little bit more about projects beyond the PMRs. So, like *I* mentioned earlier, IMEDS has the ability to interject in projects of different facets using the regular epidemiologist tools. While there are real-world evidence generation within the PMR, we conducted real-world evidence generation outside of our ties to the regulatory submissions. Beyond the PMR, IMEDS can also be leveraged to do descriptive studies, utilization studies, hypothesis generation and safety and effectiveness studies. We can support the full spectrum of activities from feasibility assessments, protocol and statistical analysis plan development, utilization monitoring, data analysis, interpretation, and writing reports. On top of that, the IMEDS network is often invited to engage with the Foundation projects such as the regulatory tool projects. Here on the right side we have two examples: Pregnancy ACE-IT and QCARD projects. We will go into a little bit detail on the ACE-IT project and how IMEDS engages with this project.

(17:44):

So the algorithm certainty tool, what we call ACE-IT, is a collaboration between the Foundation with the University of Massachusetts to develop a tool that helps users to determine whether an algorithm of an endpoint in the safety study is fit for use. We created and tested a framework to support users to determine whether a published algorithm is appropriate for their specific use case. This tool is a 34-[question] questionnaire that included prompts to consider population, internal ability and generalizability to their use case. The original ACE-IT tool was conducted using a major adverse cardiovascular event as a use case. And we're now in development of a revised tool that focuses on a pregnancy use case. More than one of our IMEDS Network Partners participated with this project. As you can see from the right side, there are a lot of different clinical areas of interest that we're showing. We're planning to expand this project into other therapeutic areas, as well. If you're interested in the project and would like to know more how you can get involved, please don't hesitate to reach out to us. So, that concludes the overview of IMEDS. I hope our overview helps you understand a little bit more about IMEDS and I will now turn back to Carla to introduce our panel and facilitate today's discussion with IMEDS collaborators.

Panel Discussion

Moderator: Carla Rodriguez-Watson, PhD, MPH, Reagan-Udall Foundation for the FDA
Ryan Kilpatrick, PhD, AbbVie Inc.
Cheryl N. McMahill-Walraven, MSW, PhD, CVS Healthspire Life Sciences Solutions
Kristin Palmsten, ScD, HealthPartners Institute
Darren Toh, ScD, Sentinel Operations Center, Division of Therapeutics Research and Infectious Disease **Epidemiology (TIDE),** Harvard Medical School & Harvard Pilgrim Health Care Institute

Dr. Carla Rodriguez-Watson (19:19):

Thank you so much, Claire. And we're getting some interesting questions in the chat and I think this is all towards the future of what we want to talk about. There was a question in the chat about whether IMEDS is engaged in long term follow-up of gene therapy studies. I think this is the question of the day. These meds are just rolling out and I think some of our partners are geared up/have the ability to do that opportunity to do that, but I think more has to be done. And the larger work of the Foundation is around focusing about how to answer those questions.

(19:51):

And with that, it's my pleasure to welcome to the virtual stage our panelists. So, we have with us Cheryl N. McMahill-Walraven, Dr. Darren Toh, Dr. Kristin Palmsten, and Dr. Ryan Kilpatrick. Thank you so much to our collaborators for joining us. I'm going to ask a question of all of you and through that question we want to give an introduction and I'm just going to tick right down the line for who I see on my screen here. You all have worked with IMEDS in different capacities. Can you briefly introduce yourself, your role, your organization, and just quickly what brought you to IMEDS and what keeps you engaged? So one minute. Let's start with you. Dr. Kilpatrick. Ryan.

Dr. Ryan Kilpatrick (20:42):

Yeah. Great. Thanks, Carla. So first off, thanks for having me. It's really a pleasure to speak here at the session. Gosh. My name is Ryan Kilpatrick, as you said. I am the head of epidemiology at AbbVie. As you saw from the earlier presentations, we do have a couple of really key studies ongoing with IMEDS. Principally looking at pregnancy safety for one of our products was in Risankizumab across a number of different indications. What brought me personally to IMEDS? I think going back to the really nice overview of the history of IMEDS and really Sentinel and Mini-Sentinel. I remember years ago when Mini-Sentinel was underway, which was really the pilot that preceded the rollout of Sentinel proper. Just really being amazed at what ... I mean, this is a really ambitious project and I know I probably have 20 seconds left, but this is a really ambitious project to create a federated model that allowed for a shared protocol and a centralized, if you will, development of a study that then is pushed to individual data partners to execute against a common data model.

(22:06):

I think it was a very ambitious undertaking and the fact that it was successful I think is an incredible triumph for pharmacoepidemiology. So I was always fascinated by the concept and really impressed at what was able to be done there. And obviously when we thought about where certain studies would best, where it would be fit for purpose to utilize IMEDS capabilities, I jumped at the opportunity to reach out and see if there was an ability to partner on those. So that's very briefly what brought me there. I think we'll talk more about what keeps us interested in a later conversation. Again, pleasure to be here and thanks.

Dr. Carla Rodriguez-Watson (22:49):

Thank you, Ryan. And Kristi, same question. Name, role in your organization and what brought you here and what keeps you with us?

Dr. Kristin Palmsten (22:58):

Sure. I'm Kristi Palmsten. I'm a senior research investigator at Health Partners, which is an integrated healthcare system based in Minnesota and I'm a perinatal pharmaco-epidemiologist. So what draws me to participate in IMEDS as a network partner investigator is the opportunity to be involved in interesting post-marketing safety studies on medication use during pregnancy. So we have an opportunity to participate in projects through IMEDS that we wouldn't otherwise be able to be involved in. And I also

want to acknowledge the programmer analysts internally on my team at Health Partners and they tell me that they stay engaged in IMEDS because the more they use our data within the Sentinel common data model, the more they understand and can improve our data across all of our projects.

Dr. Carla Rodriguez-Watson (23:50):

Thank you, Kristi. I love that. Learning and continuing and passing it on. Cheryl. Dr. McMahill-Walraven.

Dr. Cheryl N. McMahill-Walraven (23:58):

Hi. I'm Cheryl. I'm the executive director of safety surveillance and collaboration at CVS Health. I have been the site PI to the Mini-Sentinel initiative here at Aetna. And, then I'm also the site PI for the other Sentinel initiatives including the Sentinel program and the BEST program and the NEST program. I have been the IMEDS site PI since IMEDS' inception in 2013. And Aetna became a network partner back then because we care about our Aetna members and the community as a whole and the health of both. Through our Aetna data, both the medical and pharmacy claims, we're able to assist in all these wonderful projects. Through our IMEDS' participation and leveraging that electronic health data, we're able to aid in the safety surveillance monitoring and the investigation about the outcomes throughout the U.S. and in the end helping the world's health.

Dr. Carla Rodriguez-Watson (25:18):

So the higher mission is the calling for you. That's great to hear.

Dr. Cheryl N. McMahill-Walraven (25:22):

Absolutely. Absolutely.

Dr. Carla Rodriguez-Watson (25:24):

And, last-- but not least, Dr. Darren Toh, my partner in crime. Will you pick up the mic?

Dr. Darren Toh (25:32):

Darren Toh. I am a professor here in the Department of Population Medicine at Harvard Medical School and Harvard Pilgrim Health Care Institute. I've been involved in Sentinel since 2009 when the concept of Mini-Sentinel pilot was conceptualized. So right now I'm the principal investigator of the Sentinel Operations Center. For our discussion today I also serve as the director of the Analytic Center for the IMEDS program. So the reason why I am involved in this program is mentioned already, which is that IMEDS is really a living example of a national evidence generation system envisioned by the FDA when they set up the Sentinel system. So through the program we are able to use the data and the tools that are being used by FDA to answer questions that matter to other stakeholders, including the sponsors.

Dr. Carla Rodriguez-Watson (26:48):

Thank you so much, Darren. And now I'm going to turn to our first set of questions to get this discussion started. I'm going to turn to first Ryan to answer the question, but if anybody else wants to chime in, totally welcome that. So Ryan, we've heard a lot about how IMEDS helps people achieve a mission of being able to protect the public's health, to look at long-term safety, how using and leveraging larger information that we're gathering and working in and regulatory science can be applied in IMEDS. I'd like to ask you, can you tell me a little bit more about what's unique about working with the IMEDS program compared to other CROs or in your experience?

Dr. Ryan Kilpatrick (27:39):

Yeah. Absolutely. Yeah. So I think it's three things. One has already been described. The data is really ... It's an amazing resource. It's an amazing public health resource. Access to the data and also the infrastructure, the analytics center and all of the work that was done to create a fit for purpose, again, public health surveillance program, the algorithms. It's an incredible tool. I think it's really unique. And still I believe serves as the gold standard across really globally for what can be done in terms of a real-world data public health surveillance tool. So that's one. I think number two is the opportunity for collaboration. So, through the Network Partners and through you as well Carla, the ability to think scientifically about where the field needs to go, to think about how to apply and how to evolve to meet expectations in terms of data quality, in terms of methodologic expertise and methodologic innovation. I think we obviously all have the public health front and center. We're here to continue to improve our ability to understand how drugs perform in the real world and to have that evidence be high quality and decision grade. So I think that's been wonderful.

(29:16):

I will say also related to collaboration and we have an amazing group of scientists as I know many others do across industry. Amazing group of epidemiologists and pharmacoepidemiologists and biostatisticians within the organization that also our leaders in evidence generation and the opportunity to collaborate within the IMEDS framework is I think is really quite unique. I think one of the things that really drew me to it initially during initial discussions was understanding, look, we are scientific partners, we also want to be part of designing the right research, thinking about the future state. We want this research to be aligned with the mission and vision of IMEDS leadership of the FDA to be honest as well. And, so this, I think has really been a platform that continues to enable that. Some of the work that was already described, ACE-IT, some of the other work, which I think is really foundational to where we want to go. And to do it in this forum, which is also highly transparent. It is transparent, visible. I think it's just really a unique space between the data, the collaboration, the scientific expertise. I think it is a unique place to do really good pharmaco-epi work.

Dr. Carla Rodriguez-Watson (30:49):

And it is a two-way street. You're right Ryan. I think through our work together on our post-market safety studies and in more of this regulatory tool development like ACE-IT, we've really benefited from the expertise within your group and other scientific groups across industry. And I think some of the challenges that some of our post-market studies before have really pushed the development of our tools. Right. Darren, I think we talked about how the work that we're doing with you on Risankizumab in pregnancy really pushed forward the timeline a little bit on our pregnancy tools and expanding those tools. I don't know if you want to say something about that Darren?

Dr. Darren Toh (31:33):

Yeah. Sure. I think Ryan's point is all excellent. So I think the more people that are using the tools and the data, the faster we can make improvement on the gaps that are identified. So that has always been the intention. Like having a community or ecosystem that could help advance the field of real-world data or evidence generation. And to answer your initial question, Carla, I think that the higher-level coordination offered by the operation center of the IMEDS program at the Foundation really freed up time for us at the analytics center and the research partners to focus on the science and the data. So I see that as another strength.

Dr. Carla Rodriguez-Watson (32:31):

Lifting that burden a little bit to make space because we can all use a little more head space to think about these heady problems. I just want to tap you again Darren and continue this thread. We've been working together a long time. What would you say makes our collaboration so unique and what challenges do you see us facing in the future?

Dr. Darren Toh (32:59):

I think that the Foundation has reached that we don't have. For example, we are an academic institution just trying to do research and to answer questions that people care about. So, the Foundation and the IMEDS program has the ability to engage multiple stakeholders with different priorities and perspectives. And by working with IMEDS or the Foundation, we have the opportunity to work with different stakeholders of funders. So I see that as a strength. Another one is the one I just mentioned. That the overall programmatic oversight that the Foundation is offering frees us to do the science and the data because you take care of the other things that are equally important for a project to be executed successfully.

Dr. Carla Rodriguez-Watson (34:06):

And you mentioned some of our partners, so I'll just turn now to Cheryl. Cheryl, as you've explained, you're involved with a lot of different networks. So what makes your work with IMEDS so special, near and dear to you ... And what could we do differently and where could we expand? I think a question came into the chat or to the Q&A that I might pass to you. Can you think of a concrete example of how IMEDS data is used for a specific question and specific type of data that we leverage and why is it better than what would happen without IMEDS?

Dr. Cheryl N. McMahill-Walraven (34:50):

All right. You're absolutely correct, Carla. The Aetna data is a part of the Sentinel initiative both in the Sentinel program, the BEST program, and in IMEDS. Each of those collaborative research networks provide some wonderful opportunities for us to assist the community in safety surveillance. IMEDS network truly, and I think Darren mentioned this, opens the door for participation with research projects and of course the Foundation staff and the wonderful expertise that is within those walls. It allows CVS and Aetna to use our vast data sources that include primarily the Aetna data being medical claims, laboratory results, pharmacy claims, and our research experience to assist in those shared protocols, to be able to assess all of the specifications that come out and marry our expertise and our experience with Sentinel into the IMEDS program.

(36:27):

And then I think the other question was what makes the data so special? I think what really makes ... I guess it's a couple of things. The collaboration among the data partners in the Sentinel initiative and specifically the IMEDS program is the vast number of people that we can identify across the nation and throughout time. You have multiple large national data partners as well as integrated delivery systems. And by all of us answering that exact same question within our population, you are harnessing many more lives than you could if you used a different data source. And then the other unique part of that data is that you can actually get back down to the patient or the provider if needed. Because each of our Network Partners as a part of being of the Sentinel initiative is we have to be able to re-identify if need be, go down and get that medical chart and look at that for validation purposes. So I hope that answers the question.

Dr. Carla Rodriguez-Watson (38:06):

Yeah. No. Terrific. And I think as you said, Cheryl, we have three of our Network Partners on the stage, but there's six more out there and they are a mix of both claims, administrative claims only from health insurance systems, but some of them also have integrated electronic health record and are part of a healthcare delivery system, so they can have that more granular data. And importantly that we leverage the Sentinel common data model. So we've taken away ... A lot of the work has already been done in the integration and harmonization, which any data scientist at a health system knows is like 80%- 90% of the battle, then designing the study. We like clean data when we design studies. But this is the real world so as close as we can get to harmonization, we still have to deal with practice variation. And so having I think your expertise, Darren's, Kristi's, and the team at AbbVie and across our Network Partners as well, having that knowledge of working so long in real world data and in health system data and understanding what you get from one source versus another source and even within the same source practice variation is going to impact the data that we're using and how we treat those data.

(39:36):

We saw that example I think. And speaking to your point about being able to leverage new tools and roll with it is when some of the work we did with one sponsor, Novartis. The summary is on our website. They initially wrote a protocol in an EHR-based system network and needed to expand that population because it's really to look at the increased risk of serious angioedema in patients with heart failure. But wanted to see it specifically in a black population what that increased risk was in blacks and in non-blacks. You are on that study. The first thing we struggled with was when it came to the IMEDS Network is that we had to adapt an EHR protocol to one based on claims. So through that process, like you said before, Kristi, we've learned a lot about our data and also I think our partners that we were collaborating with and the cardiovascular research network, which is the EHR-based systems, they learned a lot about their data too.

(40:51):

And again, the purpose of those data. Care delivery versus administrative claims. And what we've been using our data for in Sentinel, in IMEDS and Sentinel to look at really safety of the medication versus some level of adherence to the medication, that created differences that we saw in how the algorithms themselves were created. In learning, that we adjust and we make space. I was just on another call talking about really understanding what's the lowest common denominator and what people have in the data and talking in a community of scientists and experts to talk about what is reasonable and how do we come together and align appropriately understanding that we all bring different strengths with our data and our expertise. So really appreciate that. I hope that also answered one of the questions in the chat. Something came in also about natural history studies.

(41:56):

Yes. To natural history studies. That's really some of our early work in the IMEDS program is to describe the population. And we do more in the Foundation to also enhance the data that we have to be able to do those natural history studies. And so I want to turn to Kristi, unless somebody else has something to say on this point because Kristi, we've been working together on the ACE-IT program, which is the Algorithm CErtainty Tool Kit. And I get really excited when we do this work together and other work that we've done in collaboration with FDA when we get to apply these regulatory science tools into IMEDS and really move forward on some of the real world evidence framework. Can you talk a little bit about how you see that work that we've been doing impacting IMEDS?

Dr. Kristin Palmsten (42:54):

Sure. So first just to mention, I learned about the Pregnancy ACE-IT tool project through IMEDS and being a perinatal pharmaco-epidemiologist, I was thrilled to participate in the Pregnancy ACE-IT project

because it gave me an opportunity to be involved in a hot topic in my field and collaborate with others in my field. So yes, I think the tool will be used to guide the development of protocols for post-marketing studies of medications and vaccine use during pregnancy. And I see it being used within IMEDS to assess which safety endpoints we can address in pregnancy safety studies and also what algorithms are the best to use given the data. And also just a side note to bring up that Network Partners are involved in the development of the IMEDS protocols so we can contribute our methodological and substantive expertise along with expertise on our own sites data. So I think a challenge of using the tool is the time involved, it's time-consuming to implement. However, I think really, you can view it as an investment, as an worthwhile investment to help ensure an appropriate pregnancy post-marketing safety study.

Dr. Carla Rodriguez-Watson (44:16):

That's so helpful to think through and present information about how our partners engage. That's just a little bit on the structure that Georgia had presented. We have a scientific leadership team within the IMEDS Network and we don't always have the same organizations participating in that. But from one of the partners, they might be the biostatistical lead, with Harvard Pilgrim often as our analytic lead, but we get the scientific expertise from across the Network. So fortunate to have you, Kristi, engaged on a lot of our pregnancy studies as well as Dr. Susan Andrade at Harvard Pilgrim. I think that it's been really fortunate for us to harness that expertise across the board. Darren, if I could ask you a question that came into the chat. With this network or any network like we have with these tools developed by FDA, what do you see as the main distinction between a network like IMEDS and HIEs- like health information exchanges? How would we be different?

Dr. Darren Toh (45:40):

We might not be as different as we thought. So there's been some work that has been explored within the Sentinel system to see whether HIEs could be helpful to FDA at some point to monitor medical product safety. I would try to answer this question in a different way, which is that the nice thing about distributed networks like Sentinel or IMEDS or other networks is that it can be scaled pretty easily. So if there is a data source that will be fit for purpose or could be useful to answer questions, you can add the database on top of what you already have. So it's one additional site or one additional data partner. And we have experience converting the data into a data model. So it just often is Sentinel data model. It doesn't have to be. So the new data partner could just be added on and expand the network. So if HIEs or another data source will be useful to IMEDS, I don't see a reason to not include that because we know how to do it.

(47:02):

So, one example that I would also mention is that in another IMEDS project we started out with a number of Network Partners and it turns out that we did not get the simple size that we expected. So we expanded it and we included the Medicare data fee-for-service data and Medicaid database to get to the sample size that we needed for the study. So that was another example to show that it's actually possible and feasible to include additional data sources into the program because of this distributed neural architecture that we have.

Dr. Carla Rodriguez-Watson (47:49):

Super helpful because HIE is very encompassing in specific regions and allow for that kind of integration and sharing of data, but also the purpose being different. Like the purpose there for the managing care actively and for IMEDS and specifically those tools really maximize for evidence generation. But like you said, I think part of it is thinking about how we include HIEs and also so that we can do, ask these kinds

of questions, leverage these tools that have been developed both for querying the data to understand the relevance and reliability for a specific question that we might have for it, but also in being able to produce for those data to inform results that are transparent, relevant, reliable, and minimize bias.

(48:52):

So that's a huge opportunity there for us. I love the example of how we really pushed ... We had a sponsor that pushed us to think through how we incorporate a new partner like CMS Medicaid and I remember a lot of conversations about what's the right source for that Medicaid data and translating it to the Sentinel common data model so that we could leverage it. I think it's a beautiful example of adaptability. So thank you for that.

(49:24):

All right. And so I think if we ... I'm seeing other questions popping up. I'd like to end this with our last brief question about the future. So in 60 seconds or less, can each of you tell me what are some ideas for the types of future activities that you'd like to engage our network in? Deep breath and I'll start with you Cheryl, since you perked up.

Dr. Cheryl N. McMahill-Walraven (50:01):

I've got two suggestions on where IMEDS should go next. One would be additional validation studies, and that would include going back to the medical charts to validate topics such as negative controls and re-evaluation of claims algorithms that were created in the pre ICD 10 era. I think both of those would be pretty important. I would also think that for post-approval safety surveillance of medical devices is in IMEDS' future. We've been waiting many, many years for the UDI, the unique device identifier to become a part of the claims-based system. And once that is actually is starting to come in, I think IMEDS should extend their drug and biologic PMR portfolio and experience leveraging the Sentinel tools to include medical advice, safety, surveillance, and health outcomes. Was that 30 seconds?

Dr. Carla Rodriguez-Watson (51:22):

Dr. Kilpatrick the future for you? What would you like to see us do?

Dr. Ryan Kilpatrick (51:28):

Yeah. I think picking up on a lot of what already was said about the strengths, I think continuing to double down on the strengths of the network. It's always great to think about incorporating additional data partners, incorporating different types of data. We think about oncology, I think about more biomarker data, perhaps more opportunity to do nested studies, deeper nested studies, whether they be nested cohort or case control studies that would allow us to do things like validation, but also perhaps other work I think would be excellent. And there's a lot of pre-competitive questions that could be answered. So I think that could be a really great source of ongoing collaboration.

(52:17):

I believe that there are a lot of demonstration. There's a lot of demonstration work and I like, again, what ACE-IT is doing that could really help to implement or to show how good pharmaco-epi safety can be done and provide tools. Really I think the value in providing new tools and resources has been hugely helpful and will continue to be. Like…as you said, Carla, yourself -- the learnings just from what we need to do to demonstrate benefit-risk translate into innovation around developing new tools. Yeah. I would say that's where I think where things could go data. Thinking about novel sources of data, perhaps deeper data, molecular data, thinking about opportunities to do more deeply characterized studies, whether they be nested, case control, or nested cohorts within certain centers or certain providers I

think it would be great. And then just doubling down on what you're already doing, the vision, which is really to provide valid tools and continue to build up the resources that are available to pharmaco-epidemiologists to better serve public health.

Dr. Carla Rodriguez-Watson (53:44):

Thank you Ryan. Kristi, and then Darren 60 seconds. Quick.

Dr. Kristin Palmsten (53:48):

Yes. I'll second about validation studies, but I'd like to extend it further to pregnancy type validation studies. And also just note that it can be challenging for our researchers to get grant funding related to validation studies. So we're really interested in other venues like through IMEDS to do this type of validation work.

Dr. Carla Rodriguez-Watson (54:10):

Great. And Darren.

Dr. Darren Toh (54:11):

Well, I agree with everything that's been said. I think pretty competitive activities. I would group validation activities in that bucket as well, especially if it's independent of any treatment. I think it's an underappreciated activity, but important for many, many people. And another thing that we could think about is whether there's additional methods development work that would be useful just taking on the pregnancy discussion we have. So the best pregnancy algorithm in claims data is still to wait for the pregnancy to end and then look back. So we've been trying to see whether prenatal indicators will help us identify pregnancy faster or more accurately. I think that there's work that can be done. There's work that needs to be done to figure out how to best analyze linked data. And I think that at some point we're going to get into that in IMEDS. Right now is still a lot of claims supplemented by some EHR, but I think there are some questions that can only be answered by linked claims EHR or linked claims registry data. And there are some issues that we just have to figure out if we get to that point.

Dr. Carla Rodriguez-Watson (55:34):

Right. Figuring how to do all that is the pre-competitive space and rising tide lifts all boats. So we are committed to doing that and that rounds out this panel. But before we go, I really want to hand the mic over to our Foundation CEO to provide some closing remarks. Susan, will you pick up the mic please?

Closing Remarks

Susan Winckler, RPh, Esq., Reagan-Udall Foundation for the FDA

Susan Winckler (55:55):

Absolutely. And thanks so much to everyone who spoke today. It's always great in my role to learn even more about what it is that we're doing at the Foundation. I get a sense and then I so enjoy the opportunity to hear and learn more from our collaborators. So I want to thank everyone for joining today. There's a quick list here of what it is that we provide through the IMEDS resource and what a great opportunity to continue to learn more about the performance of medical products, drugs. And Cheryl, I'll have to say, really excited about the prospect of devices in the real world. So with that, I want

to thank everyone for joining us today. Thanks to the IMEDS team and to all of our Network Partners who work with us on a daily basis to explore these important questions about the safety of products in their performance. And we look forward to helping you solve some of your research problems. Take care and have a great rest of your day.