Drug Repurposing: Considerations for Selection Criteria and Prioritization

Hybrid Public Meeting
Wednesday, August 5, 2026 | 10:30 am – 5 pm (*eastern*)

Transcript – Morning

Welcome

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

Susan C. Winckler:

[00:00:30] Look at that brilliant timing of quieting down just as we started the meeting, thank you. So, good morning and welcome. My name is Susan Winckler and I serve as CEO at the Reagan-Udall Foundation for the FDA, and we're thrilled that you could join us for today's public meeting on drug repurposing considerations for selection criteria and prioritization. For those of you who are new to the foundation's work, we are the nonprofit non-government organization [00:01:00] created by Congress to help the FDA do more to protect and promote the public's health, and today's meeting is part of that work. We're bringing together experts and interested parties to talk about an area of importance to the agency and the public at large, thinking about how to explore opportunities to expand treatment options for patients by identifying new uses for approved drugs. To be clear, today we're talking about drugs that are already on the market and those predominantly [00:01:30] in what some of us would call the small molecule world or those regulated by the Center for Drug Evaluation and Research.

Now, this is a meeting about shared learning. So, we are all here to both provide information and to gather information. It is not a meeting about specific regulatory actions or individual products, the foundation does not engage in regulatory decision making. So, I have a few housekeeping notes before we get into substance. Those of you who are in [00:02:00] the room know that we have about 60 folks gathered here to participate in person, and then we have a few hundred attendees online. Because of the size of the meeting, the virtual attendees cameras and microphones will be off with the exception when we turn to the public comment period for the last section of the meeting, and I will have detailed and exhaustive instructions about how to do the public comment period when we get to that portion of the meeting. If you have a question and are attending virtually, please use the Zoom [00:02:30] Q&A function.

If you're here in the room and have a question, please write that on a note card. The staff have them if you don't, and hand it to one of the staff members. I will get to as many questions as I can, although I believe we've planned every minute except for about 37 seconds of this meeting, but we can weave in questions as we go throughout. We are recording the event and we will post the recording and a transcript after the meeting. The slide deck is already available at [00:03:00] our website, reaganudall.org. One final request for those of you who are in person, we ask you to embrace the in-person dynamic and not log in virtually. It creates what we call audiovisual chaos if you do so. So, join us

and embrace being here. Now, I thank each of our speakers for investing their time and preparing for and participating in today's event.

Also, thank our colleagues at FDA Center for Drug Evaluation and Research for their partnership and [00:03:30] support in planning this public meeting. So, let me just do a little bit about the agenda. Today's agenda, what's important about it is it's a mix of both presentations and discussion in the structured part of the agenda. And then, at the end of the day we have time set aside for public comment and that public comment will be on three different topics. I'm pleased that we're able to offer a comment slot to all who requested, so we'll be hearing from about 40 members of [00:04:00] the public at the end of the meeting. That will be time limited. And again, I'll have instructions for that when we get to the end of the day. So, one other part about the public comment, the foundation will accept two pages of written comments via electronic submission through August 21st.

So, if there's something that you hear today that you want to provide additional insight on, two pages. We don't have a font minimum, but two pages of written comment [00:04:30] would be welcome. Additional information about submitting written comments can be found on the foundation website.

Opening Remarks

Brian Fahey, Senior Advisor, Immediate Office of the Commissioner, FDA

With that, I'm going to turn to the first speaker of the day. And so, we are thrilled to have Brian Fahey joining our meeting this morning. You are senior advisor in the office of the commissioner at the FDA, and working to advance FDA's top legislative priorities, which are often many. So, come on up to the stage. Welcome you to the meeting.

Brian Fahey:

[00:05:00] Thank you, Susan. I see some familiar faces in the room, which is great. On behalf of the FDA, I want to thank the Reagan-Udall Foundation for bringing us together. And thank everyone for joining us online and obviously in person, from federal agencies, clinical and research communities, [00:05:30] patient organizations, and other partners. Today's subject begins with a very practical question, how can we make better use of medicines? We already know to address medical needs that patients still face. Drug repurposing offers a compelling opportunity by building on what is already known about an approved drug, including its safety profile, manufacturing, and clinical experience. [00:06:00] We may be able to identify effective new uses and move promising options to patients more efficiently. But let me be equally clear, repurposing is not a shortcut around science. A new use must still be supported by rigorous evidence or safety and effectiveness. The advantage is that we are not always starting from zero.

This work is directly aligned with the department's Make America Healthy Again agenda. [00:06:30] HHS has established a unified strategy centered on addressing chronic disease, advancing gold standard science, empowering patients and improving affordability. More specifically, the Make Our Children Healthy Again strategy calls on NIH and FDA to work together to strengthen the use of repurposed drugs for chronic disease and to examine collaborative clinical trial approaches that can support [00:07:00] FDA approval. And I know just as an aside, FDA and NIH have embarked on this for quite some time, including or dating back to 2019. So, we're happy to be able to continue the conversation and obviously

work collaboratively with you all in the room, but more importantly, across government to try to identify real solutions.

Drug repurposing also has a clear home with FDA's new public health pillars, particularly [00:07:30] the third pillar, increasing access to affordable medicines and medical products. And again, as an aside, if people have not viewed those pillars I would encourage everyone to do so. These were developed in partnership with every one of the center leaders, FDA leadership, reviewers, and I think it lays out a pretty strong vision for what the future looks like at FDA. Pillar three is about [00:08:00] removing barriers that delay or limit access to safe, effective, and affordable products, modernizing regulatory frameworks, improving efficiency and predictability, and reducing unnecessary burden while maintaining strong safety and efficacy standards. Repurposing can put those principles into practice. In some cases, an older or widely available medicine may have credible evidence supporting another use, yet there may be limited commercial [00:08:30] incentive to pursue a supplemental application or update the labeling.

That can create a gap between scientific knowledge and the information available to patients and to prescribers. Closing that gap when the evidence supports it can expand treatment options, promote more informed clinical outcomes or decisions, and potentially improve affordability. In May, FDA issued an RFI that was designed to [00:09:00] help us better understand that opportunity. It sought input on priority disease areas, potential candidates, particularly approved drugs for which there appears to be little commercial interest in pursuing a new indication. The RFI also recognized that candidates may be at different stages. Some may already have evidence capable of supporting a new use, while some may have promising clinical signals that require additional study.

Others may emerge from preclinical research, [00:09:30] high throughput screening, real world data, or artificial intelligence. That's why today's discussion matters. We need transparent and scientifically grounded approaches for deciding which candidates should move forward. We need to consider unmet clinical need, the strength of the evidence, disease burden, potential public health impact, feasibility, and the practical barriers that prevent promising candidates from reaching the next stage. We also need [00:10:00] to identify where FDA, NIH, and CMS and other federal partners can each contribute while preserving the substantial evidence standard that protects patients and sustains public trust.

Success will not be measured simply by how many candidates we identify, it will be measured by whether we develop a credible, reproducible, and patient-centered framework for moving the strongest candidates toward evidence, labeling, and access patients need. I'm grateful to [00:10:30] the Reagan-Udall Foundation and to all of today's participants for contributing your expertise. We look forward to a candid and constructive discussion. Thank you.

FDA's Drug Repurposing Efforts

Marta Sokolowska, PhD, Deputy Center Director for Substance Use and Behavioral Health - Center for Drug Evaluation and Research (CDER), FDA

Susan C. Winckler:

Great. Thanks so much, Brian. I think many of us who've been in the FDA ecosystem know that to drive an initiative like this, the collaboration between the relevant centers and the office of the commissioner is one of those things that makes things happen. [00:11:00] So, thank you for being here today. I'm going

to turn the podium now over to Dr. Marta Sokolowska, who serves as Deputy Center Director for Substance Use and Behavioral Health within FDA's Center for Drug Evaluation and Research. And I think it's fair to say, Dr. Sokolowska, that you have been thinking about this repurposing work quite a bit. And so, if you would provide some of the framing for FDA's activity, we'd appreciate it.

Dr. Marta Sokolowska:

Well, thank you very much, Susan, and thank you everybody here in the room, the virtual room and the room [00:11:30] in here. I'm really grateful for you participating and joining the conversation. I wanted to start with thanking Susan, Reagan-Udall Foundation and the repurposing working group at CEDR who've put plenty of hours of work to make it happen. So big, big thank you to the team. I'll provide a brief overview of our current thinking on FDA Drug Repurposing Framework for the Unmet Medical Needs, service slides. And I will cover a range of [00:12:00] topics from background, our ongoing activities. I'll touch on MODERN Labeling Act, as well as provide a quick overview of the proposed FDA repurposing framework and the goals for today's meeting. So, these are my disclaimers. This presentation reflects my views and I have nothing to disclose. As Brian had mentioned in the opening remarks that drug repurposing is not only a new initiative, but it's also aligned with the broader public health [00:12:30] priorities.

And what's important to call out is that these priorities really call for collaboration across the different agencies as part of our government, because I think together we can really accomplish much more than separate. So, the objective is not simply to encourage off-label use or circulate promising observations, it's to create a pathway through which strong scientific hypothesis can be evaluated, and rigorously, and supported and reflected [00:13:00] in FDA approved labeling.

But as I mentioned and Brian mentioned, we are not starting anew. This is not a new initiative and I do not want to present it as such. We are building on a substantial work that was completed before. I do want to call out the 2019 meeting that was hosted by Reagan-Udall Foundation for FDA and NCATS participating where we really [00:13:30] covered in the meeting the research and regulatory challenges of the repurposing of patent drugs. I also want to call out Duke-Margolis because they have done extensive work in this space as well. They examined repurposing, the incentives for genetic drug repurposing, regulatory policy and pathways of repurposing and across different repurposing models. And it's really helpful to actually see the different [00:14:00] perspectives. But I would be amiss if I wouldn't mention advocacy groups who have helped to really maintain the momentum of repurposing, especially one to call out rare disease community.

Because many have highlighted that even when patients and clinicians would benefit from clear or more current labeling reflecting the state of evidence, when there's limited commercial interest in updating older genetic [00:14:30] labels, there is no progress and we don't have incentives to do it. So, they've been asking for the path forward. How can we help them to reach the goals? How can we help them to get the treatment that they need? And also within the government, we have a number of initiatives related to the purposing. So, I wanted to call out a project renewal from Oncology Center of Excellence, that when they recognized new uses [00:15:00] of all generic drugs, they created an initiative to summarize the evidence and work with the sponsors on updating the label. We'll have more on that later, as well as a CURE ID collaboration between FDA NIH as a platform to collect more of that information.

And not only that we have good initiatives, we also have good success stories. We already have repurposing label updates within [00:15:30] the countermeasure space. We have on the timeline three projects to do project renewal. And more recently leucovorin calcium label update, which is also another example of drug repurposing. I wanted to call out MODERN Labeling Act, which provides an important statutory pathway for updating certain generic drug labeling. [00:16:00] If you look at the law, and I'll try to summarize to my take what's in the law, it really represents the six steps. But I want to focus on six steps for the drug label updating. But I really want to focus on the first three, definition, identification and selection, because they are most pertinent, most important to our discussion today. The pathway begins with the FDA approved drugs. When we are thinking about [00:16:30] the definition of the covered drugs, the pathway starts with FDA approved drugs with no unexpired patent or exclusivity for which relevant approval has been withdrawn for reasons other than safety and effectiveness.

But there also must be a meaningful labeling gap, and updating the label must provide a public health benefit. The labeling may involve new scientific evidence for a new and or existing condition of use. It may involve labeling that no longer reflects [00:17:00] the current content or format requirements, or it may involve an accepted clinical use that is not reflected in approved labeling. The central question is whether the label is out of step with the available evidence or current clinical context in the way that matters for public health. The second gate or the second point is identification of the covered drugs. It may identify drugs for which labeling updates could provide public benefit. Importantly, FDA does not [00:17:30] have to rely on information generated within the agency. FDA may use cooperative agreements or contracts with public or private entities to review scientific evidence. The FDA might also seek input from public meetings, from public more broadly, from public dockets or other mechanisms, and this is a great example.

This creates an opportunity for clinicians, for the public various stakeholders to really provide the very important information. The [00:18:00] third one, it refers to selection for updating the labels. And I think it's important to identify that when we are thinking about identification, this identification establishes that drug may fall within the statutory scope. But the selection requires a further determination that the available scientific evidence must meet the regulatory standards for adding, modifying and supplementing a label. So, nobody wants to lower the standard. [00:18:30] It's really critical to emphasize. So in other words, public health lateral events is not enough, the existing approval standards continue to apply. After selection, FDA would notify the approved generic applications holders, there would be notice summarizes supporting evidence that states the additional modified supplemental labeling that FDA is requesting. And each abbreviated new drug application NDA holder would have an [00:19:00] opportunity to have a conversation of FDA if they do not agree with the labeling.

And following that conversation, FDA would issue a decision if they believe that the label needs to be updated. So, that's the general overview of my take on MODERN Labeling Act, and what I wanted to really highlight is that FDA has not been waiting. And we just recently, in June of this year, issued first label modification [00:19:30] utilizing the authorities from MODERN Labeling Act, and a second one was issued just recently as well.

So with that, I want to very briefly focus on what is the FDA drug repurposing framework. What's in the scope of eligible drug candidates? Referring back to the previous slide. What we are considering is that FDA approved drugs for which there currently appears to be no commercial interest, a limited commercial interest [00:20:00] in adding new use through supplemental application, and this is a really important point. The criteria for new use include the information that there is compelling scientific evidence to do so, that it's within the dosage form and route of administration of currently approved

use, and that there's a comparable safety profile for the patient's population for the new use as for the approved use. The reason [00:20:30] why I stress that is that there are a variety of different definitions of repurposing. So, first and foremost we wanted to stress that if there is commercial interest in adding new indication to already approved drug, we have a pathway for that.

We strongly encourage sponsors to come in with these applications. This discussion is not about that. There are also definitions related to reformulating, reformulation of repurposing. Again, we have a pathway for that, this is not this discussion. There are a lot of conversation [00:21:00] regarding drugs that are shelved and repurposed through that. Drugs that are not approved by FDA would not be candidates for this pathway. So, this is our high level vision. Once we solicit the public input for repurposing candidates, just like through RFI we will have a candidate selection discussion. Again, this is topic of today's discussion. When we have that, we will review [00:21:30] these candidates. We'll evaluate the data that there is available. We'll work with our NIH and other partners to further compliment the information. Once we have FDA review, the final packet, FDA will review them. If there's substantial level of evidence of effectiveness, the label update will proceed.

But that review, FDA review of the evidence would also be critical for working with professional societies to potentially update labels, work of our partners [00:22:00] to potential update compendia or formulary decision. That's why I'm so glad we have CMS as part of this discussion today. So, we already have the RFI that is out to select the public input. I won't go into the great detail. We have Carla who will be talking about it in a second. But we already asked regarding the priority areas and candidates and the approaches to identification of new products. This is our meeting, I'm really looking forward to hearing more. This is a really exciting time, and thank you very much [00:22:30] for your interest.

Session 1: Snapshots of Repurposing Efforts

Mitra Ahadpour, MD, Deputy Director, Office of Translational Sciences, CDER, FDA

Matt Hall, PhD, Scientific Director, National Center for Advancing Translational Sciences

Heather Stone, MPH, Health Science Policy Analyst, Office of Medical Policy, CDER, FDA

Susan C. Winckler:

Great, thank you. So, with that understanding of the current policy framework and what it is that we're thinking about and want to gather insight in this discussion, we want to turn then to presentations, a quick set of presentations about ongoing efforts. So, what are some other examples of things that are happening? So, our first presenter is Dr. Mitra Ahadpour, who serves as Deputy Director [00:23:00] of the Office of Translational Sciences within CDER at FDA. Yep, there you go.

Dr. Mitra Ahadpour:

Good morning. More than 30 million Americans have rare diseases, most have no approved treatment. This is Noah, he is four years old and has Kabuki Syndrome. His mother is a former FDA colleague. [00:23:30] 52 diagnosis, and at only eight days old he had open heart surgery. He communicates through a combination of sign language, word approximations, and assistive technology. I am sharing his story to remind us this work is about real lives, children, adults, [00:24:00] and families who care for them. More

than 10,000 rare diseases, most with no approved treatment. 80% have a genetic origin. Half of those affected are children.

Advanced AI now allows us to ask of [00:24:30] the generic drugs with established safety profiles, which ones might work for rare diseases with no treatment? To explore that, we have entered into a research collaborative agreement with every cure, a nonprofit organization that has created an AI platform called MATRIX to evaluate [00:25:00] biological relationships between generic drugs and diseases. We are using this collaboration to better understand how AI can support repurposing decisions for rare diseases. So, how does the platform work? On the left, you see the biomedical knowledge graph. This is a database of biological [00:25:30] relationships. Drug mechanisms, gene to gene interactions, protein to protein interactions, disease pathways, phenotypes, clinical trial outcomes, real world evidence. In the middle is the machine learning models that convert that database into a mathematical map. [00:26:00] On the right, every disease and drug becomes a point. The closer together means more similar biology.

So, that proximity becomes the score. Drug A is close to disease X, so we'll get a higher score. That's not a conclusion, that just tells us where to look. Next comes the scientific [00:26:30] and clinical validation. So, Marta mentioned this. This is we first find a candidate, that is great. That is a start. Next, we have to ask the question, what regulatory authority does FDA have to act on it? Under the MODERN Act, FDA can update the labeling of generic drugs [00:27:00] when the brand version is no longer protected by patents and exclusivity, this includes additions to the labeling when it is supported by evidence that meets FDA's approval standards. MODERN gives FDA a new tool, a useful tool. It was done [00:27:30] in the ACT/PAS in 2020 for repurposing. This is my personal vision. If I was given the opportunity to build one thing at the FDA that would advance this work, it would be this. So, some of the building blocks are already exist. They're there. So imagine [00:28:00] a system that continuously updates, and automatically updates, as new drugs become generic. New genetic and phenotypic data emerge. New clinical evidence is published. Patient-reported outcomes and natural history outcomes, all that data is taken in [00:28:30] into this system. External nominations are submitted, and internal FDA data strengthens that evaluation. At every step of the system, it will screen for those candidates that are eligible, that do not have patent or exclusivity protection.

[00:29:00] At the end, it is having this automated evaluation that surfaces all these different types of repurposing opportunities, including generic drug combinations tailored to each patient. So, that vision is where I like to end up. But what is [00:29:30] possible today? So today, it is possible. Why should we try AI matching? This is for Noah and every patient waiting. Generic drugs may have untapped potential for rare diseases with no approved treatment. Not a promise, a direction worth taking. Thank you.

Susan C. Winckler:

[00:30:00] Thanks so much, Dr. Ahadpour, for reminding us why we're here and then presenting an opportunity and description of ongoing efforts. I want to turn now to Dr. Matt Hall, who is scientific director at NIH's Center for National Center for Advancing Translational Sciences.

Dr. Hall, welcome to the podium. You're behind me.

Dr. Matt Hall:

[inaudible 00:30:27] Trying to make the button.

Susan C. Winckler:

There you go. Fire away.

Dr. Matt Hall:

[00:30:30] Thank you. I'm a researcher at the National Center for Advancing Translational Sciences, where it's an incredible privilege to work at the world's greatest biomedical research institute. I'm also a motivator and an agitator of other researchers who cannot advance slides on his own.

Susan C. Winckler:

[inaudible 00:30:46]

Dr. Matt Hall:

There we are. And it's really great to be between Mitra and Heather because what you just heard about came out of a program called Translator at NCATS that I'll touch on. And Heather, of course, [00:31:00] works very closely with NCATS for CURE ID. So the ecosystem that you refer to, Susan, exists. And it's a real privilege to be part of such an incredible effort. We all know that the pathway from disease to treatments is complex and we need to be open to all possibilities, and trying to solve all of the challenges that come with each of those. And NCATS itself, within NIH and that ecosystem, bridges that gap between understanding of disease and the trials we need and the evidence we need to generate to treat patients.

And so that's the translational [00:31:30] science space that we live in. We, of course, do that through enabling and funding the entire extramural biomedical community and through the research we do here at NIH. In the labs that I lead, which is the first part where I'll give you a couple of vignettes, we have an integrated pipeline for drug discovery and development, and we're open to all possibilities. So, it looks more like a biotech than a traditional research lab. And everything we do is a collaboration with a scientist out there somewhere in the extramural community. That is our job. We do have [00:32:00] a lot of success in only 14 years of partnering with people to get 65 INDs and five drug approvals to patients. And hopefully, the yellow circle will enlarge over time. But the goal is that every new medicine we get is a new drug repurposing opportunity instantly, and eventually a new generic drug repurposing opportunity as well.

And Martha sort of touched on the blob, what you see here, the array of four possible repurposing opportunities that we're regularly met with when we talk to scientists or through things we discover [00:32:30] ourselves. And the red box, of course, covers things where there's total freedom to operate. An advantage, of course, of having total freedom to operate is that because there is not a commercial opportunity or commercial interest, there is sometimes an absence of motivating forces to generate the evidence necessary for those patients, usually for us rare disease patients. And so, that is why we exist. That is what we do and what we work together to do. But of course, you can imagine a lot of those stories that come along and the things that we have to tackle are regularly patented things [00:33:00] with market exclusivity, where we don't have freedom to operate and we see amazing opportunities.

And so the kind of vignettes I'll give you as an example, a lot of them come out of our repurposing screening. So, we have a library. Literally, a physical collection of every approved small-molecule drug in the US, Europe, and Japan. Different regions is something we may not talk about today. There are just under 3,000 in total. That's what is available from a small molecule point of view. The majority, of course, are generic. And the first thing we do with any rare disease project is we go to this library and try to remove [00:33:30] those chevrons of time and funding to get treatments to patients as quickly as possible and generate new therapeutic hypotheses. So physically, this is a really great way of doing things.

Repurposing can be really complicated. This is an example on the top right there of a formulation molecule that is safe in humans. It's used in formulations. It isn't an approved medicine, but it was shown to be to offer incredible potential value for patients with Niemann-Pick disease, a rare heritable disorder. But we had to start from zero with this safe molecule [00:34:00] that no one had market exclusivity over, and that was safe in humans. We had to work, and thankfully within the amazing One NIH ecosystem that we have, NCAT's partnered with investigators at Child Health and Human Development and the NIH Clinical Center to go through all of the work to conduct a natural history study on those patients. We need that evidence to exist and understand those populations, to do all of the preclinical development and the regulatory work that was needed, and then the clinical trials that were necessary. And then thankfully, there's some really nice data that's come out of it. Of course, [00:34:30] that's why I'm showing you this example.

And there's an NDA with the FDA at the moment for this molecule that did not have any ownership, no market interest about patients. We saw a great opportunity. Another in the cancer space, we have a cancer drug librarian. And while I don't have a laser pointer today, which is the instinct of every scientist is to be waving a laser pointer around constantly, you will just have to cast your gaze to the top right of this slide, where you can see that after working with NCI investigators on glioblastoma and a genetically defined [00:35:00] subset of glioblastoma, we were looking for drugs that may be useful, there are only six that killed a large set of cell lines with the same mutation. One of them did have commercial interest, but we were able to go to that company, make the case for a clinical trial with the National Cancer Institute for those patients, and it's now received fast track designation because of the nice positive effects we've been seeing in patients on the bottom right.

Thankfully, Mitra really did a nice job of explaining the underlying science behind Translator. Dr. Christine Colvis will be on a panel later, and [00:35:30] she really conceived and drove the development of this AI-based tool for mining all biomedical data and knowledge to try and predict generic medicines that may be useful for individual diseases and for many diseases. That's the goal and the dream there. And if I can go back, I would add that that QR code in the middle, it's available. You can go to the page. You can use Translator yourself. You can mine this data, look for those solutions, whether you're a scientist or a member of the public. The funded community, this is a nice example at UAB for SHINE [00:36:00] syndrome: no treatments, very little research.

But the Translator program for SHINE was able to make connections across literature that you and I wouldn't make even if we stayed up all night on PubMed, and identified a number of repurposing opportunities including guanfacine that you see down the bottom. And we love these two colored in pieces of paper of a child on the left, before and after treatment with guanfacine out of this Translator program. You can see that the coloring in, and is amazing. My director Joni Rutter [00:36:30] likes to say, "Peppa Pig never looked so good." And it's just one example, an avatar of the huge potential that could come out of these programs. Scientists are taking up this open platform, DeSanto-Shinawi syndrome.

Again, very little known about it. There are QR codes for you, so I don't have to go into this in great detail. But again, investigators at the Mayo Clinic found Translator predicted treatments that are generic and could be prescribed to a patient, and they're showing a really positive response.

I think there are challenges [00:37:00] with this, of course. I'm going back to cell data for my final slide here to say that this is a disease called Sanfilippo syndrome, where we've been screening with our approved drug collection cell lines from multiple patients. And we have some really wonderful examples. In this case, we screened all approved medicines and found three. A physician has been prescribing one of those, we've learned, to that individual patient, and it's showing benefit. But what we know is that that individual molecule for that individual patient does not work on the other cells from other [00:37:30] patients with exactly the same disease. And so, looking for generalizable solutions, but still thinking about every single patient and what's going to be needed experimentally as we harness the amazing power of artificial intelligence and the amazing work that you've already heard about that is happening in this space is there. And so with that, thank you. I'm very proud that I finished 45 seconds early.

Susan C. Winckler:

And we'll take it. Thanks so much, Dr. Hall. To our folks who have joined us virtually, I understand you cannot [00:38:00] see me right now, but you can hear me. And so, I'll remind you that the full slide deck is available on the reaganudall.org website. And so you can follow along with our speakers, and the video feed should be restored shortly.

So thank you, Dr. Hall. And yes, we do not allow laser pointers in our session, which is okay. We are going to wrap up the session with a presentation from Heather Stone, who is a Health Science Policy Analyst within FDA CDER's Office of Medical Policy. Tell us [00:38:30] about Cure ID.

Heather Stone:

Thank you so much. It's a pleasure to be here and to be able to share this wonderful collaboration between FDA and NCATS to try to develop a tool that can really address the areas of unmet medical need. So Cure ID is a website and a mobile app that was designed to capture de-identified treatment experiences of originally healthcare providers, but has since expanded to capture the treatments from patients and caregivers as well. It's essentially a crowdsourcing tool. What are people using in the community [00:39:00] that can serve as a treatment registry of repurposed drugs that is openly available? The primary objective is to identify signals. It's a hypothesis-generating tool that can then be studied further. We're not suggesting that these are confirmatory. We're suggesting that this may be interesting and worth further analysis. But we do recognize that in cases of very rare diseases and where there may be no effective treatments, it can provide a useful source of information for real-time information gathering [00:39:30] for physicians and patients.

The ideal use cases are probably those where RCTs are difficult or impossible to conduct. For example, for ethical reasons, diseases in drug development where there's insufficient financial incentives, as we'll talk a lot about today, and outbreaks where there's a limited time for novel drug discovery and a need for very rapid access to potential agents. Cure ID began in 2012. [00:40:00] It's been a labor of love, to put it mildly, and launched formally at the Reagan-Udall FDA NCATS meeting in December of 2019. That was the precursor to this meeting. We've tried many different approaches to address this problem,

ranging from clinician-submitted cases to patients to EHR, extraction and treatment experiences with a global clinical community that's really been supported by the government as a public good. The data is [00:40:30] fully de-identified and immediately aggregated, and then it's made openly accessible to everyone for free with no limitations. And all cases are reviewed before being publicly posted.

So, I think the question is always like, when can a case report really make a difference? And we are fortunate to have one very illustrative example. So, there is a horrible infection that's caused by a brain-eating amoeba called Balamuthia mandrillaris [00:41:00] that causes severe meningoencephalitis and has a fatality rate of over 95% when it causes this presentation. There's really no effective treatment. Six or seven highly toxic drugs are used currently, and there have been less than 200 cases ever reported. So, it's an ultra-rare infectious disease. Joe DeRisi, who's a fantastic researcher at UCSF, saw what happened to a patient who had died of Balamuthia, and decided that he didn't want to see that happen again. And [00:41:30] so he set out to screen a library of drugs, like Matt was talking about, of thousands of FDA and European approved drugs. And to my surprise, he found one that looked very promising.

Nitroxoline is a quinolone antibiotic, so a very common class of antibiotics with decades of safety data that's been approved in Europe for more than 50 years for urinary tract infections, but had no known amoebicidal activity whatsoever up until this point. I should note, it is not approved in the US, so it would not be eligible for our [00:42:00] discussion today, but I think it's still useful to talk about. And the preclinical findings were published in 2018, showing this remarkable and unanticipated activity. A couple of years later, a patient was admitted to San Francisco General with seizures and was ultimately diagnosed with Balamuthia and went into multi-organ failure due to the toxicity of some of the other medications he was on. And so this wonderful ID fellow decided that, in an act of desperation, that [00:42:30] she would try this drug that only had a preclinical signal. And that meant that she had to get it from Europe and we had to help get an emergency IND because the drug was not approved. And the patient was treated and had this truly remarkable and objective recovery.

So, you can see here the huge difference in the white lesions with the decrease in nitroxoline. And this continued, and the patient was ultimately discharged alive to the community. A couple of years after that, I got a call from [00:43:00] the mother of this little girl who is dying of Balamuthia, and also is on the CDC-recommended regimen and is failing treatment. Apparently, Dr. Spottiswoode had made an acknowledgement in the article and the mother had reached out to everybody on the article, and I answered the phone. And so, we were able to help her physician also obtain an emergency IND for nitroxoline. And this was particularly complicated because [00:43:30] the previous instance, it had taken 45 days to get the drug shipped from China, and she wasn't expected to survive that long. They were having hospice discussions. And so, we were able to help negotiate with the review division for them to allow UCSF to supply a bridge supply of the drug to the hospital where this little girl was being treated, so that she was able to receive treatment within 48 hours.

And she too had a really remarkable clinical recovery, and radiologic [00:44:00] as well, and is now recovered and has been able to stop all of the medications, including nitroxoline. Now interestingly enough, we've never been able to get the physician to enter the case report, but the mother did. And I think that's part of the power of this, is that information can come from many different sources, and she actually had insights that I don't think the clinician would have had. And so for several years, unfortunate... Well, fortunately or unfortunately, Cure ID was really the only place where this information [00:44:30] was available. As of just, I think three weeks ago, the case was finally published, but they focused on neurosurgery instead. So, I would be remiss if I didn't point out that this is not a silver bullet. It doesn't work for everyone. I think the best estimate is that probably, 50% of patients

respond to treatment with this drug. But still, if we've now increased the survival from 5% to 50%, that's a statistic I'm willing to take.

I think it's important to note why the second case [00:45:00] is as important, or in some ways even more important than the first. Because we typically think about that first case report of demonstrating first-in-human activity, and that's crucial. But for example, CDC would not change their recommendations based on a single case report. They waited until there was a second case demonstrating the same activity, which makes sense, but is not something that we often think of. And so we're excited that with our encouragement, they've opened an intermediate IND so that they can now [00:45:30] house the supply of the drug in the US and be able to get it to patients within 24 hours. And they're recommending nitroxoline for all patients now with free-living amoeba infections. The response to this from the public has been overwhelmingly positive. And I say that because I think it's important to recognize that there really is a desire from the community and from taxpayers for the government to be doing things to help patients where there's an unmet need and where there [00:46:00] just isn't a commercial incentive, and the system was not set up to help them.

So lessons are that translating these basic science discoveries to clinical impact, even to a single patient, can take years. Cases can bridge the gap and open data sharing accelerates learning, but greater participation is needed. I would like to ultimately see a full pipeline like this, where we go to clinical trials and FDA approval, and I hope that you will help us turn these treatment insights into action. Thank you.

Session 2: Selection Criteria and Prioritization

Caroline Huang, PhD, Supervisory General Health Scientist, Controlled Substances Initiatives, CDER, FDA

Reactor Panel:

- **Susan Cantrell, RPh, MHL, Academy of Managed Care Pharmacy**
- **Emily Einstein, PhD, Senior Director, Quality and Science, American Society of Addiction Medicine**
- **Pam Gavin, MBA, CEO, National Organization for Rare Diseases**
- **Huong Huynh, PhD, Director of Regulatory Science, Critical Path Institute**
- **Janet Woodcock, MD, Former FDA Acting Commissioner**

Susan C. Winckler:

[00:46:30] Thanks so much to Heather, Matt, and Mitra for illuminating things that are occurring, and for helping with part of that overall illustration of what is happening today. So, let's turn now to our second session where we want to think more specifically about criteria for selecting and prioritizing candidates for repurposing. We are going to open with a presentation from [00:47:00] FDA, recapping what the agency has heard from a recent request for information. And to provide that overview, we will hear from Dr. Caroline Huang, who serves as the Supervisory General Health Scientist in the Controlled Substances Initiative team in CDER.

Dr. Caroline Huang:

Thank you, Susan, for the introduction. And let me add my thanks to our public commenters, speakers and panelists, and our in-person and virtual attendees. One of the main reasons we're here is [00:47:30] because of the feedback you provided in response to our RFI, as well as the feedback many of you will provide today. As Susan mentioned, I'll be providing an overview of the RFI, focusing on our preliminary analysis of public comments and our next steps. My views are my own and I have no conflicts to disclose.

My talk today is broken into three parts. First, I'll discuss the RFI at a glance. That includes a quick walkthrough of what's happened since we issued our RFI, a refresher on the four topics in our RFI, an overview [00:48:00] of our preliminary analysis process, and a summary of the priority disease areas on which we received public comment. Second, I'll provide a deeper dive on the RFI. I say deeper instead of deep because this is a preliminary analysis, and we want to emphasize that we have more work to do to break down the complex comments you all provided. But for today, I'll highlight three different high-volume topics, as well as summarize some of the barriers and opportunities that were identified in the docket. Finally, I'll close with planned next steps for FDA and current opportunities for stakeholders to continue engaging [00:48:30] with us.

So turning to our timeline, we officially published our RFI on May 12th in the Federal Register with a 30-day public comment period. The docket was originally slated to close on June 11th, but because many of you submitted such interesting and thoughtful feedback, we extended the comment period. And at the same time, we announced today's public meeting. Our public docket officially closed on July 13th, and that kicked off the analysis efforts you'll hear about today. The deadline for public comment request for today's meeting was on July 21st, [00:49:00] with questions focused on candidate selection, prioritization, and evidence gaps and barriers. And that brings us to our public meeting today. Needless to say, it's been a busy three months.

So, let's turn to a quick refresher on the four areas we asked about in the RFI. The first was our priority areas. We proposed focusing on five chronic disease areas in addition to rare diseases. And we asked you to tell us if these proposed priority areas aligned with your understanding of areas with significant unmet medical needs and high potential [00:49:30] for repurposing. Our second question was on drug repurposing candidates. We asked you about the candidates that have the greatest potential for effective treatment of specific medical conditions. In our docket, we split those up into three potential scenarios based on the level and type of evidence that exists. Our next question was on innovative approaches to identifying candidates for drug repurposing, which could compliment existing identification approaches. And our final question was on barriers to repurposing drugs, and opportunities for FDA and our federal partners [00:50:00] to address these barriers.

So now, we'll provide an overview of our preliminary analysis process, and some numbers that hopefully help contextualize the feedback we received. Over the course of our 60-day comment period, we received a total of 608 public comments. We then de-duplicated these comments at a 95% front threshold level, meaning comments that shared at least 95% of their content. And this de-duplication left us with 547 comments. In my last slide, I mentioned the four topics where we invited public input. [00:50:30] It's important to note that commenters could respond to one or more of these topics. We received 420 comments that made at least one drug candidate recommendation. So, most comments touched on our second topic. Conversely, that means that 127 de-duplicated comments did not mention repurposing candidates and instead focused on one or more of these other topics. For example, a submission identifying a need for neuroblastoma treatments, but providing no specific treatment ideas would not count toward the 420 comments. Neither would a comment focusing on sharing an AI

[00:51:00] platform for candidate identification or proposing new regulatory incentives to accelerate repurposing efforts.

Drilling down a bit further, we received 132 distinct recommendations for drug-candidate disease pairings. So as an example, if there are eight comments recommending naltrexone for treatment of long COVID, these comments represent one distinct recommendation for a drug-candidate disease pairing, but all eight would count toward the 420 comments that included a candidate recommendation. And just a few other notes, about a third of our de-duplicated comments [00:51:30] contained at least one attachment, which is important because these comments were typically more complex than text-only comments. And we also received two non-public comments from our federal partners, which I mentioned to highlight the interest and investment in our topic from federal agencies. You've heard about that a little bit already, and you'll hear more on that later in our federal partner discussion.

So now I'll summarize our review process, which we've broken into five steps. First is organizing the input by inventorying the comments and attachments, and establishing standardized review fields. [00:52:00] Second is screening and de-duplicating by using text similarity tools to identify potential duplicates or near-duplicates. Third is extracting and standardizing by categorizing input on the proposed topics and normalizing terminology across submissions. Fourth is validating through manual review of complex comments and attachments, and correcting automated classifications when appropriate. And fifth is synthesizing preliminary signals by comparing the full and de-duplicated datasets and summarizing the initial findings. To accomplish these tasks, we've been conducting [00:52:30] a manual review of the assistance of the HHS-specific version of ChatGPT. AI-assisted review has been helpful with de-duplication based on text similarity and duplicate adjacent screening, exploring potential coordinated submission campaigns and providing initial summaries of high-frequency themes. However, we also recognize the importance of manual quality control, which is ongoing.

One example is analysis of long attachments and dense technical submissions, which can over-index the counts of drug candidate disease recommendations. These kind of comments with 15 [00:53:00] to 20-page attachments are the ones that our analysis team is still in the process of reviewing. And in all cases for this presentation, the information reflects preliminary analysis and should not be interpreted as our final findings, as our analysis is subject to further review and validation.

So, let's move on to what commenters told us in the RFI in terms of priority disease areas. This graph has a lot of bars and very small texts, so I'm going to focus on some key takeaways. One, as you can see, we received a great deal of feedback across a great deal of different disease areas. [00:53:30] And we've organized this feedback by the highest volume of comments per disease area to the lowest volume of comments per disease area. Two, we've incorporated bars for all comments and all de-duplicated comments, which show you that comment de-duplication did not have much effect on the underlying priority rankings. Three, standardized categorization of diseases is an ongoing area of discussion with our FDA analysis team. As an example, complex regional pain syndrome, or CRPS, is a rare disease, but it could also reasonably be categorized into neurodegenerative or neurology or pain conditions. [00:54:00] Moving CRPS from the rare disease section to another section would reorder the rankings of the second, third, and fourth most popular disease areas. Finally, I'll spend the next few slides providing deeper dives into three high volume signals that seem to be powering the top four priority rankings. Our first high volume signal is racemic ketamine, which appears to largely drive the popularity of both the mental health psychiatry and the rheumatology musculoskeletal pain disease areas. There were 223 deduplicated comments mentioning ketamine, [00:54:30] meaning ketamine is mentioned in roughly 40% of all deduplicated comments. And across those comments, there were roughly 16 proposed uses.

So ketamine was by far the most frequently recommended drug candidate in the docket. And as you can see in the chart, it was suggested for a variety of mental health and pain conditions and substance use disorders. Depression was by far the most frequently proposed use.

Another point of interest is that a subset of the comments recommending ketamine used verbatim or substantially similar advocacy language, suggesting a coordinated effort to respond [00:55:00] to the RFI. For example, a company called Ember Health launched a call for action to encourage patients and providers to submit comments to the docket. I do want to note a few things about write-in campaigns here. These campaigns and common counts in general are a sign of stakeholder interest and indicate that a topic is salient to respondents. However, a high volume of comments from a small subset of people may not be representative of wider opinion. And in any case, the volume of comments won't determine if a candidate has sufficient evidence for a new use.

Our second high volume [00:55:30] signal is long COVID, which appears to drive the popularity of infection associated chronic conditions we saw in the priority diseases chart. There were 139 deduplicated comments mentioning long COVID, meaning long COVID is mentioned in roughly a quarter of all deduplicated comments. And across these comments, there were 23 distinct candidate recommendations. Not being a pharmacist by training, I will not attempt to say most of the drug names. Instead, I'll point out that comments related to long COVID were wide-ranging with recommendations distributed across many drug candidates, [00:56:00] mechanisms of action, and evidence types. The deduplicated recommendation counts are relatively low, even for the top candidates. Naltrexone, specified as low dose naltrexone in most but not all comments, is the most frequently mentioned with just eight recommendations. We also noted that a subset on long COVID used verbatim or substantially similar advocacy language regarding investment in prioritization of long COVID treatments. A subset of that subset also referenced the CURE ID platform, with language and framing suggesting a coordinated campaign to [00:56:30] advocate investment in long COVID through prioritization and funding for CURE ID. And of course, the same caveats about write-in campaigns from the previous slide apply here too.

The final high volume slide I'll highlight is for rare diseases. We saw a total of 93 deduplicated comments, meaning one or more rare diseases were referenced in roughly 20% of all deduplicated comments. And across those comments, 82 distinct diseases were mentioned. In the chart, we see a wide variety of distinct diseases highlighted with relatively low counts across the board. This wasn't [00:57:00] particularly surprising to us given the nature of rare diseases. We also saw a number of comments that highlighted rare disease as a collective priority area without focusing on any specific rare disease or candidate recommendation. And of note, the largest group of comments were for complex regional pain syndrome, largely tied to comments advocating for ketamine.

So now I'll shift gears and move to our summary of barriers and opportunities, which map nicely to the third and fourth topics we asked about in the RFI. I'll start with barriers first. One of the key themes we identified thus [00:57:30] far is access and affordability with a number of comments noting the lack of insurance coverage for off-label uses and evidentiary requirements for reimbursement. The topic of insurance frequently arose in comments regarding the lack of coverage for ketamine. Apologies. Commercial viability was a second barrier with commenters highlighting the lack of commercial incentives and the need to consider implications for intellectual property and exclusivity. Commenters also highlighted the need [00:58:00] to maintain evidentiary standards, as we've heard throughout the day, noting potential evidence gaps for safety and effectiveness and the need for pharmacovigilance. And finally, we heard about regulatory pathway uncertainties with commenters noting the need for clarity from FDA and federal partners.

On the flip side, we heard from a variety of stakeholders about the opportunities to innovate through adaptive, platform, pragmatic, or decentralized clinical trial designs, as well as biomarker driven trials. We heard about the potential to embrace data and evidence generation such as employing computational candidate identification, [00:58:30] leveraging existing safety data to accelerate development in real world evidence and patient generated data. You also told us about the opportunities for enhancing collaboration infrastructure by continuing to invest in existing platforms as well as developing new federal funding and incentive streams. And paralleling our barrier side, you asked for regulatory and policy clarification such as regulatory guidance and streamlined pathways.

So now I'll quickly turn to what's next before I get played off the stage like the Oscars. We'll also take the feedback shared today and [00:59:00] we plan to complete the RFI analysis, including the attachment review and the manual validation and publish that on FDA's website. We plan to hear what you're going to mention in the public comment and also from all of our panelists and speakers in connection with this meeting to develop our candidate selection and prioritization framework, which we plan to publish on our website as part of our commitment to transparency. And we'll commit to sharing additional findings and opportunities for engagement as this initiative progresses.

Additionally, we hope that some of you will submit written feedback on prioritization, selection, evidence gaps, and regulatory barriers [00:59:30] to the Reagan-Udall Foundation's website through Friday, August 21st. Please note that we're not accepting additional suggestions for drug candidates at this time. These comments are meant to support the discussion from today's meeting rather than extending the RFI. And of course, you can continue to share novel uses of existing drugs and explore what others have tried through CURE ID. And finally, you can look for the Reagan-Udall Foundation's report on this meeting on their website in the coming months.

Before I turn it back to Susan and our esteemed panelists, I'd like to thank my colleagues, Brian, Anika, Bic, Millie, Heather, and Laura. [01:00:00] We recognize that many of you in the audience shared your time, expertise, and lived experiences with us through your RFI responses. And the team is working hard to ensure that your comments are analyzed and integrated into our broader repurposing efforts appropriately. Thank you.

Susan C. Winckler:

Thanks so much, Caroline. So for any who have ever submitted public comments or evaluated public comments, it's really helpful to get that immersion into that process. So I would now welcome our reactor panelists to the stage. We want to broaden this [01:00:30] discussion about what folks have heard and provide some additional perspectives. So as our panelists are taking the stage, I will see if anyone has any quick questions for Dr. Huang based on the information that she just presented. And I'm not going to quiz you about how many comments she said were received and analyzed and deduplicated. But any questions from the panelists for Caroline or should we jump right into the commentary? [01:01:00] Commentary, it is. All right. Dr. Huynh, let's start with you. You're at the Critical Path Institute, and I hear that the Critical Path Institute was one of the contributors to the feedback that we just heard about. In your role as the Director of Regulatory Science at the Institute, what would you underscore from that recap or from the Institute's comments?

Dr. Huong Huynh:

Yes. Thank you for the invitation and the opportunity to participate [01:01:30] in this workshop. As Director of Regulatory Science, I oversee the public comments and ensure that it aligns with the Critical Path Institute's mission and goals. And so the opportunity here really aligns with how we see the role of a public-private partnership in terms of the opportunities to enhance clinical trials and drug development. So some of the things that were mentioned by Dr. Huang and [01:02:00] previous FDA speakers was that the need for a systemic framework. I think the community really wants to see how the agency could interpret or would interpret evidentiary requirements and what the standards are, how to develop and ensure that the evidence is credible.

We also recommended developing toolkits because some of us who are developing drugs would like some [01:02:30] sort of roadmap. And I'm glad that some of the presenters have presented and talked about a roadmap. But having a toolkit that identifies what biomarkers, what tools, what standards are available for use so that it can help reduce the cost and time for discovering new potential uses. And I would be remiss if I were not to encourage the use of AI, but I think also to encourage the use of model-informed drug [01:03:00] development and model-integrated evidence as well. And really take advantage of the pharmacometrics opportunities and learnings that we have to share.

And I'm glad that Dr. Stone mentioned CURE ID, not to point anything out, but I think it's time to interpret and use the real world observations and really translating that in how to generate the evidence. What are the expectations [01:03:30] coming from those EHR data and natural history data? And then also, I would also be remiss not to capitalize on the public-private partnership that C Path is by suggesting a public repository of information, of knowledge, of a centralized location that everybody can look to, and then use that in a pre-competitive space.

Susan C. Winckler:
Great. So helping us think about the structure, [01:04:00] the collection of data, incorporating patient reported information, and then exploring real world data to generate real-world evidence. If anybody's keeping a track of buzzwords, you hit most of them, but also had substance there. So thank you. So let's then think about this from the end result being for individual patients. And as we heard in the summary, a lot about the rare disease community. So I'm going to turn one person over and say, Pam, as CEO at [01:04:30] NORD, what would you want us to underscore?

Pam Gavin:

Sure. And thank you also for being here. This is an incredibly important topic that has become, as the speaker's earlier part of the day said, it's been around for a long time and of urgent interest and need by the rare disease community. The idea that we could have access to a therapy that has been approved safe and efficacious [01:05:00] for a different condition is monumental to say the least. But we already know, because we know a great deal about the pharmacology and the manufacturing, the safety of these, but that is a great, valuable place to start. But we do need to, it's not enough to remove the need to establish a drug that is safe and effective for a new use. The rare disease community has learned a lot about identifying plausible candidates, [01:05:30] that it's not the same as creating the treatment. Families have seen compelling laboratory findings, case reports, off-label experience as was mentioned also, and that those opportunities never move forward because there wasn't a structured development pathway. So I think that's kind of where my comments are focused. The gap is often not the absence of a great idea, of a great potential, but of an accountable steward, a feasible evidence plan, a pathway [01:06:00] through regulatory review and clinical adoption coverage, and ultimately sustained access.

There are about four things that I wanted to highlight that I think should be part of a prioritized framework. If not initially, given the early edict or mandate of the FDA in the beginning discussion, but eventually first, the magnitude and urgency of unmet medical need, which was discussed [01:06:30] at length. And anybody in the rare disease community knows what that looks like. The strength and relevance of the scientific and human evidence, that's also been discussed and obviously a priority. The feasibility of generating credible evidence in the affected population that we're focusing on. And the likelihood that a successful program can actually reach patients. That is further along that trajectory that I think we need to take serious consideration.

Susan C. Winckler:

Great. [01:07:00] Thank you so much, Dr. Gavin, because particularly I'm thinking about the monumental opportunity that you observed, but there's a lot to do for the path to make sure that we get to sustainable access and generating that information. So there's a regulatory role there somewhere. So let me pivot and tap the expertise of a longtime drug regulator, Dr. Woodcock. So reflecting on your experience leading CDER and then as a [01:07:30] former acting commissioner, what do you see as the challenges and opportunities? How do regulators make their way through the gauntlet that Pam just laid out?

Dr. Janet Woodcock:

Well, first of all-

Susan C. Winckler:

Oh, I need... There you go.

Dr. Janet Woodcock:

I agree with Pam. Okay. Actually, frankly, identifying candidates is the fun part. All right. And the scientists can come up with, and you can look at biochemical pathways, you can look at medical records, you can look at case [01:08:00] reports. Okay, you get all this. What is daunting is how do we get from there to into the doctor and patient's hands and into clinical guidelines? I'm skeptical, and Marta knows this, about the FDA label because they're all out of date. Most people don't look at generic labels. Let's be honest, nobody looks at generic labels. The people who look are maybe pharmacists and the insurance companies. Okay?

Susan C. Winckler:

Who are not nobody, [01:08:30] just a different audience.

Dr. Janet Woodcock:

Right. Okay. Fair enough. Fair enough. Yes, as a pharmacist. Right. Right. Well, I meant the treating community doesn't refer to those for treating instructions once a drug is generic. It's been out there a long time. So here, let me be short because I don't have much time, I think. Number one, who's going to generate the evidence? Now I agree with Pam, you could do a matrix about prioritization, [01:09:00] and

that matrix would include things like feasibility and blah, blah, blah, all these different things. But then who's going to generate it? How will it get to the agency? I don't believe the agency will do this routinely. I don't think new drugs will generate evidence and write up packages routinely. I think maybe Oncology Center of Excellence might. They have more people and their need is very urgent. But in general, I don't think they'll do this. [01:09:30] And how would they get the evidence to the agency? Once it's there, who's going to review it? The agency, new drugs people, they have PDUFA deadlines. And so who's actually going to put all this together?

Next, what are the standards? What Heather presented, so that was an N of two, but it was compelling and it was self-controlled. They were going to die and then they survived. [01:10:00] And it's against the background natural history of 80% or whatever it is mortality. So the standard depends on... But articulating that standard for these is very important. And I don't think that's happened. I think there's a reluctance to do it. In rare diseases, everybody knows, I think the agency's off on the wrong foot because you can't do an RCT. And [01:10:30] so you ought to start thinking about what else you're going to do. Okay. Then the next step is you generate the evidence, somebody reviews it, it's found to be safe and effective. Okay, what I hear is the generic companies don't want this on their label because that imposes additional burdens on them for pharmacovigilance and this and that and the other thing. So are there other mechanisms that FDA can use to declare the use safe and effective? And then [01:11:00] how do you get it onto compendia, onto clinical practice guidelines? How do you get the knowledge out there? And how do you get people to pay for it and make sure it's paid for?

So I think those are the really tough steps. And there's amazing amount... I've been working with David who's going to talk later and observing there on every cure. And there's just all these little twists and turns that block you at every doorway. It's like, oh no, [01:11:30] you can't go through this one. You have to go over here and so forth. So I do think the agency though needs to decide and make clear what is the pathway? Who's going to do this? Okay. I think outside parties will be motivated to do it if they understand what the criteria, what the standards are to develop the evidence. How would they submit the evidence? They can't submit it to a generic application. Okay. So who would you send it to and [01:12:00] how would you do that? Okay.

And then who in the agency's going to review this? Who has the signatory authority to say, yeah, this is... And then what are you going to do with it? Once you agree that the... Are you going to try to suborn the generics to put it on their label? Sometimes that might happen. A lot of times that's going to be a lot of back and forth. As Marta knows, and maybe this has been rejected, I've suggested the FDA just publish a finding. We find this safe and effective. Okay. You can [01:12:30] give that to your insurance company, publish that in a federal register. You don't have to put it on the labels. There may be 10 generics out there. Are you going to argue with all of them or what are you going to do? So anyway, I'll stop there.

Susan C. Winckler:

Well, you know what's really helpful about that, Janet... Always generates that, right? I think some people are like, "Oh my gosh, we can't ever get there." But what I heard you just, instead of the abyss that we might've had between monumental opportunity and sustained access, I [01:13:00] think what you illuminated are all of the steps that need to be taken. And some of those steps still need to be built, which is the only way that we will get there. So thank you for teeing that up.

Janet Woodcock:

Always practical.

Susan C. Winckler:

Yes. It's why you're on the panel. So we have two more voices I want to weave into the conversation, payers and providers. And we had a bit of a transition there at the end of Dr. Woodcock's comments in thinking about that. So [01:13:30] Susan Cantrell, you serve as CEO at the Academy of Managed Care Pharmacy where your members think about that combination of optimal use of resources and medications. And so what does repurposing mean in that managed care pharmacy world when we're thinking about part of the access is whether there's coverage for the product?

Susan Cantrell:

Sure. Thanks for having me here, Susan. And this is a really important conversation. [01:14:00] Our members work by and large for payer organizations. And as you mentioned, they have kind of a two-pronged responsibility, looking at making sure patients get access to medicines and at the same time stewarding healthcare resources. And as I always say, they're not always the most popular kid at the party, but that's the job that you have. And I think they would look at, sum it up in four different things. One is evidence standards. And clinical evidence [01:14:30] is what guides decision making on the payer side of the benefit. And so looking at whether evidence is strong enough to support the new use would be really important to payer organizations. And they look beyond regulatory standards of evidence. They're looking for additional information on how the product works in their population, how the product works in the real world.

And [01:15:00] so that's a nice segue into the second thing, which is RWE. And I would say that that is something payers look to frequently after a drug is approved. Often, not often, but what we've seen in some cases, especially in the rare disease space, is you have a product that is approved based on very limited clinical trials, and when the product comes to market, the labeling is much broader. So how do payers manage that through utilization management? Looking at the literature [01:15:30] to see what supports uses in certain patient populations and developing guidance based on that. So RWE is really important. But one thing that we've learned, because that's been a big topic at our organization in the last few years, is payers say they want real world evidence. Companies frequently develop and deliver real world evidence, but it's not being used by payers. In fact, there was a survey done a few years ago by the [01:16:00] RWE Forum in combination with IQVIA. And what they found was that payers overwhelmingly said they needed real world evidence to support use and coverage decisions. But at the same time, they almost never used what was available.

So in diagnosing that, what we realized is there's a gap between what was being produced and what payers wanted. And so our organization, and I hope this doesn't sound self-serving, but we set about to [01:16:30] address that about three years ago and came out in 2025 with a set of standards for payer appropriate real world evidence. That was published in our journal back in April of '25. And then we also recently approved an update to our AMCP format for formulary submissions, which is often called the AMCP dossier that we'll be releasing in the coming weeks. It's the 6.0 version and [01:17:00] it incorporates some of the tenants of RWE that the payers are looking for.

And then the two other things, just real quickly, FDA labeling and the question about whether having that indication on the label will guarantee payment or not having it will prohibit payment. And the

answer is neither of those really. Having an FDA approved labeled indication is really important for payers as one step in the process and one data point, [01:17:30] but it doesn't guarantee it. And the lack thereof does not prohibit it. I could give you myriad examples of where products are the standard of care now and there's no labeled indication.

Dr. Janet Woodcock:

Yeah, you're echoing my point.

Susan C. Winckler:

Yes, exactly.

Susan Cantrell:

Yes. But that's still important, I think. And then when we think about cost and access implications, I informally polled a few of our members that manage pharmacy benefits for large populations on, well, what do you think about [01:18:00] this conceptually? And the general consensus was if we can bring new therapies to market for patients, especially in conditions where our approved therapies fall short of solving issues like psychiatric conditions and many others, or in the rare disease space where there are no treatments, and in this case, therapies would likely be affordable, that's a win-win for everyone.

Susan C. Winckler:

[01:18:30] Really helpful. And I'm thinking in the context of particularly in the real world evidence, not only... The example you give of having payer relevant real world evidence is also part of the conundrum here, having sufficient real world evidence to show the indication. Absolutely. Go ahead.

Dr. Janet Woodcock:

Yeah, I have a question about that. So do the payers want prospective observational data basically where you prospectively set out instead [01:19:00] of retrospective, we just data mined a bunch of charts and here's what we found?

Susan Cantrell:

Yeah, actually both. They use both. So not either or, but really both. Looking for broad sets, but prospective data certainly is very helpful.

Susan C. Winckler:

Yeah. And can be more challenging. Emily, you've been waiting so patiently. So let's close in our intro with the provider voice and from a sector that's underserved [01:19:30] and was mentioned in the overview. So Dr. Emily Einstein joins us from the American Society of Addiction Medicine. In your day job for senior director of quality and science, how do you think about this repurposing effort?

Dr. Emily Einstein:

So addiction is absolutely a disease state with huge unmet medical need for sure. There's only FDA approved medications for the treatment of opioid, alcohol, and tobacco addiction. Those medications don't work for everyone and more options are absolutely [01:20:00] needed. But then in an environment of an incredibly rapidly shifting drug supply, meth and cocaine contribute to lots of overdoses. Also, more and more adults are using cannabis and betting on sports. And we simply have no approved medications for the treatment of stimulant use disorders, cannabis use disorder, or any behavioral addiction. So from the clinician perspective, patients are arriving with very acute needs and they have a responsibility to treat them with whatever tools are available regardless [01:20:30] of FDA approval.

So an interesting current example is the treatment of medetomidine withdrawal. So medetomidine is a really powerful veterinary sedative that's been popping up in the fentanyl supply, and it causes such a severe withdrawal syndrome that many patients are taken to the ICU. So clinicians just had to scramble in real time to figure out what to do. And they've been administering sort of layered alpha-2 agonist medications that are delivered via different routes of administration in order to stabilize these patients. So that's fine if these [01:21:00] medications are available on formulary and if they'll be paid for.

And an FDA approval is used to make those sorts of decisions. So there's two kind of specific areas of addiction medicine that I think would be particularly helped by repurposing. And the first are criminal justice settings. So we're currently in the process of putting together our ASAM Criteria for these settings. And we've been hearing from the experts in these settings that using off-label medications is simply disallowed. So [01:21:30] this is a population with an unusually high burden of substance use disorder. And when they're incarcerated, it's an opportunity to treat them and improve public health. So having an FDA indication for these medications could improve health in those settings. And then the other setting I think where these could be useful is primary care. So for years now, the number of people with addiction who seek any treatment, whether or not it's evidence-based, hovers around 20%.

And so primary care is an opportunity to close that gap a little bit [01:22:00] better. And an FDA indication for a medication that specialists use off-label all the time, like topiramate, for example, for the treatment of alcohol use disorder, that indication indicates to primary care clinicians who are less comfortable treating addiction that this is an appropriate treatment. And then I'll just say, my role at ASAM is on the quality and science team, and one of our work streams is that we develop the clinical guidance documents that come out of ASAM. So these include clinical practice guidelines and also [01:22:30] clinical considerations. And those are places where we pull together all of the existing published data, but we also incorporate what clinicians are doing right now because they have to treat their patients. And so many of the compounds that were in our response to the FDA RFI can be found in our existing guideline for the treatment of stimulant use disorder, and our existing guideline for the treatment of alcohol withdrawal.

Susan C. Winckler:

So what I'm hearing in particular [01:23:00] from Susan and Emily is the opportunity that even as these repurposing efforts are continuing, while label revision is certainly important in some very specific situations, we're also just continuing to expand the evidence base that then might be applied in other situations. So the overall evidence generation effort should be helping in these areas where we have unmet need, or at least has the opportunity, back [01:23:30] to our opportunity and sustained access. I don't want to leave you out here. Caroline, do you want to respond or provide any additional insight to our show openers from each of our colleagues?

Dr. Caroline Huang:

Sure. Thanks so much, Susan. I wanted to start by saying thank you to the panel. Clearly, we put together the right people to provide some really candid feedback. I think I hear a lot about some of the real challenges and a healthy dose of skepticism on the infrastructure there, which as someone working for the federal [01:24:00] government, I completely understand. It's really challenging to take these big ideas and then actually make it into something that's scalable, reproducible. So it sounds like that's an area where I think I agree with some of the feedback that was in the RFI and some of the items I've heard here about the need to really clearly state things like evidence standards, provide those toolkits, figure out how to appropriately use some of the regulatory guidance documents that we have to make our standards clear. And also to think about what are the infrastructure investments that we would need such as potentially more full-time employees, [01:24:30] which is a challenging thing as well, to try to think about who is going to review these documents.

I think Dr. Woodcock knows this best of anyone, some of those challenges when you try to implement these new initiatives on top of the OMUFA dates. I think I also heard a lot of interesting kind of interplay between some of the different players, things like the payer community, thinking about some of the real world evidence pieces. I think that's a really interesting insight. I'm looking forward to our panel after lunch to better think about how do you integrate some of the more traditional forms of evidence and also real world evidence. I think [01:25:00] that's an area we heard a lot in the RFI as well on how do you address some of these evidence gaps and recognizing that, especially in things like the rare disease community or for other areas where it's just difficult to provide clinical trials, you're going to need to figure out how do you move from these great ideas and these observations into actually looking at what might be needed to make fit for purpose assessments.

Then I think the final piece is just recognizing that we talk about FDA labeling a lot because we're at the FDA, but recognizing that it's really fit for purpose, and trying to [01:25:30] think about what is really needed if we're saying that something's important for patients. And I think going back to Mitra's observation about seeing the patient in front of you and really having some of those, the children, the adults there, the families, recognizing that if you have that patient coming in the door, a label update might take years and that might not be the right option for them. So figuring out the right way to work with associations and other folks who are doing things like clinical practice guidelines is also something really important to us too.

Susan C. Winckler:

Yeah, yeah. And right, we do all kind of look at... [01:26:00] Well, the reason you're here is that each of you looks at this from your own lens, but it helps us draw that better understanding of the environment. So now, I'm going to throw a question to all of you and we'll see who leans in to answer first. And if no one leans in, I'll call on you. So we'll just take care of that. So if each of you could direct the investment of time or resources to identify repurposing candidates with the greatest potential to address unmet need, where would you direct that investment? And we heard a little [01:26:30] bit about this from Pam and Emily, but I want to give you a chance to dig in a little bit more. And this could be by disease area, by product category, or any construct, but how would each of you think about that?

Dr. Huong Huynh:

I'll take a...

Susan C. Winckler:

Go ahead. You can run.

Dr. Huong Huynh:

I'll take a jump first. And following what Caroline said, I think there's an opportunity there in terms of internal training. As a former reviewer myself, I think there's opportunity to capitalize [01:27:00] on one, the rare disease hub, and two, the quantitative medicine centers of excellence as well as other centers of excellence to not only be a hub for external and patient information, but also training opportunities for internal reviewers, because I don't think many reviewers... Well, one, they have the user fee numbers to get through and the deadlines to get through, but I'm not sure how many reviewers understand the wider application that this [01:27:30] can have from a generic product office. It's like, how do they know it's not just for another product on the market versus the greater impact of repurposing? And so having that understanding and the infrastructure can help in that way with the quantitative medicines center of excellence. Maybe there's an opportunity to sort of establish a credibility assessment, and make sure that if AI or [01:28:00] algorithms that are used, that it is credible for its purpose.

Susan C. Winckler:

So you're kind of getting at a bit the socialization within the agency and thinking about and a construct to operate under. All right, who's going to lean in next?

Dr. Janet Woodcock:

Well, I would say that the thing that would stimulate this the most is the FDA coming out with a clear pathway. Okay, clear steps. What do you do? Because the agency can't do this themselves. [01:28:30] They're not going to generate the evidence and do all this analysis and everything. But lots of people out there want to do this for whatever their disease or their problem they have. But they need incentives and they need to understand what they need to do, and then how to get that through the regulatory process. But I also agree with you. I mean, [01:29:00] first of all, I don't think that standards for rare disease are fit for purpose, I've said that. We have to stop talking about clinical trials for rare diseases. Stop. Stop. What Heather showed with the amoeba, do we really need a clinical trial with placebo amoeba patients or them on these drugs that don't work as a comparison? No. No.

[01:29:30] So we need to apply creativity and intellectual thought to, can we use modeling? How do we do this? How do we do before and after studies and so forth? But again, then that has to be socialized within the agency. And it's a broader problem than just repurposing, it applies to any given agent for a very rare disease. So I think the biggest [01:30:00] thing that could be done is to establish clarity about what the pathway forward is. And I just don't think FDA people should focus on them doing it, doing the evidence generation. I think they should focus on how are they going to handle this, review it, and then get it out there.

Susan C. Winckler:

So we started with a bit of an education and a culture, and then illuminating for the outside world what should be done. Susan, Emily, Pam. Susan?

Susan Cantrell:

So you probably invited me here [01:30:30] because you knew I would talk about cost.

Susan C. Winckler:

Yes.

Susan Cantrell:

And I think it's important to think about. Well, of course, I was really interested in the comments, Caroline, that you summarized so succinctly for us and the interest in a number of areas. Certainly unmet medical need is important and neurodegenerative diseases, treatment resistant, psychiatric conditions, substance use disorder. There's so many areas there that rose [01:31:00] to the top that would be really important. And I couldn't help but think about perhaps considering, especially if you're talking about leveraging government resources, thinking about the burden to the healthcare system of the disease as part of the decision-making process when you're targeting that. And then of course, the best options for this type of program would be therapies that are in the market and where there is a substantial amount of evidence that [01:31:30] could be leveraged to support additional indications. So unmet medical need, high burden to the healthcare system, existing evidence already, and a definite improvement in patient outcomes.

Susan C. Winckler:

So thinking about that clinical structure and cost support structure more broadly.

Susan Cantrell:

And I was really happy to hear CMS mentioned a couple of times.

Susan C. Winckler:

Yes.

Susan Cantrell:

I know you're talking about other federal partners this afternoon, but I think CMS could be a really important partner in [01:32:00] thinking through this.

Dr. Caroline Huang:

Emily?

Dr. Emily Einstein:

I agree completely with all that you just laid out about prioritizing. And I would add that stigmatized conditions should rise to the top of the list. So of course, our patient population is among the most heavily stigmatized. And we have heard from pharma executives that they do not want their medications associated with patients who have addiction. So I think for that reason, this field would particularly benefit from sort of federal assistance in getting more treatment.

Dr. Janet Woodcock:

Well, it's ironic, it's both people with [01:32:30] addiction disorders and pregnant people.

Susan C. Winckler:

Yes. Right. Right. Right. That's a crossover that is...

Dr. Emily Einstein:

Or incarcerated people, yeah, for sure.

Susan C. Winckler:

Yeah, or all three. I mean, the area where you have little-

Dr. Emily Einstein:

Unhoused people.

Susan C. Winckler:

Yeah.

Dr. Janet Woodcock:

It's like, no, we don't want to get involved in it. But I'm sorry, this is sort of portfolio management, the criteria that would...

Susan C. Winckler:

Yes.

Dr. Janet Woodcock:

How do you manage the funnel? And of course, I'm focusing [01:33:00] on that narrow part of the funnel.

Susan C. Winckler:

Right, right, but important in then thinking about, okay, so if you're going to navigate, or if you're going to build those steps and then take them, where will we have the greatest impact? Yeah. Pam, we saw the big rare disease in the chart. Yes.

Pam Gavin:

I think for rare specifically, there are three things that I would touch upon if I had a bolus of resources to invest. [01:33:30] One would be to develop a shared translational infrastructure. And I think much of what we talked about here falls under that category that helps us connect candidate identification with development readiness. So all the different elements that we've been talking about, disease severity, unmet need, biological plausibility, et cetera. But critically in that is identified stewards capable of carrying the program through evidence generation all through that process, as I was mentioning earlier.

It's important that we don't just look [01:34:00] at prevalence or volume of available data because that naturally favors conditions that are already well studied and well coded. We have coding issues with rare disease. So we really need to, I think, at least apply some part of the portfolio for high severity rare diseases where available data are sparse. But the biological rationale for pursuing it and credibility is high. A second thing I would do is invest [01:34:30] in common assets. And maybe that's not a surprise coming from an organization like Nord, where we want to invest our resources, time and treasures to elevate the water for all boats in the bay.

And that is to make programs possible while we're looking at natural history study platforms, interoperable registries, reusable protocols, endpoint biomarker development, regulatory and statistical support, clinical networks, and mechanisms [01:35:00] for drug supply and sponsorship. That's all a part of that trajectory that Janet, I believe, not to put words in her eloquent mouth, but these investments create leverage across diseases rather than going after candidates in isolated hypotheses one at a time. And the last is that I would require every prioritized candidate to have a development map. And [01:35:30] what do I mean by that is answering questions like who's accountable? What evidence is needed next? What can be learned from existing human use? What are the formulation and supply issues we need to address? What regulatory route is plausible? And what would be required for coverage and adoption if the evidence is positive? And that really just speaks to Janet's comments that the FDA can't do it all, nor should we ask that of them.

Susan C. Winckler:

[01:36:00] Right. It's a part of that evidence generation and adoption process, but is not the only piece [inaudible 01:36:07].

Pam Gavin:

But if I had that bolus of resources and cash.

Susan C. Winckler:

Yes. Well, and I'm struck too. I think you also spoke to, in your comment about the natural history and some of that other work, that there will be opportunities. If we get the steps right in laying out what's

important for drug repurposing, then how might some of those existing evidence generation platforms [01:36:30] be adapted to feed into the information needed for those steps?

Pam Gavin:

Exactly, without having to reinvest in something brand new, or really help people prioritize what they should be doing with their time and their treasures, especially from a patient and family perspective with their experience, and clinicians.

Susan C. Winckler:

Yeah, yeah. Excellent. So we have time actually for a relatively long [01:37:00] final thought in that you each get 70 seconds to think about, what is something that you want to highlight and make sure that the folks in the room and watching online are thinking about in this space? So you can underscore something that you've already said, or you can throw out a new idea. Pam, you actually get to go first here.

Pam Gavin:

Okay. So I'll just kind of...

Susan C. Winckler:

Put your mic up, there you go.

Pam Gavin:

... wrap up what I said before. [01:37:30] Selection without that stewardship is not a development strategy.

Susan C. Winckler:

She's going to win for brevity, it was almost a haiku. Well said. Janet, do you want to pick this one up next? I think Pam ceded some of her time to you.

Dr. Janet Woodcock:

Okay. Well, lesson from the drug development world, [01:38:00] which is absence of a clear pathway, you won't get much. Predictability is what drives investment. And it's going to be the same here. This may be philanthropic investment, but people have to know that there's an end to the game, that they can achieve their objective of getting these into the hands of patients. And so that's where clarity all along the line is just so important [01:38:30] about the standards, about who's going to do what. And I agree with Pam about who's going to do what is really important. Who is the developer? The problem we have is that the thought is, and look like NIH is sort of departed, but really...

Susan C. Winckler:

Oh, no, they're still here.

Dr. Janet Woodcock:

... NIH is supposed to do the basic science stuff. And they claim they do everything, but that isn't true at all. And then the [01:39:00] thought is you have the basic science and then the industry, this has been the model for 60 years. The industry picks that up and they do the rest. And it's very expensive and people criticize them because they charge a whole lot at the end of the day. But it is very, very, very expensive to do what the industry does. And there's nothing else out there. There's no translational infrastructure. We heard from [inaudible 01:39:26], they're working on it. But then he talked about, he's working [01:39:30] on developing drugs. That's not a translational infrastructure. So there isn't one. And so that's what Pam is talking about, who's going to do this? We're talking about a new model because industry doesn't want to do this because there's no money in it.

That's fine. We're doing it for the patients. It's really forging new ground because it has been [01:40:00] thought. And then the agency, FDA, it's been thought, and they're just referees and they make the standards and what hurdles you have to get over. And then it's kind of dumped into the market and then kind of leave the insurers on their own to figure out how they're going to pay for all this stuff and so forth. And that is our system right now. So we have to recognize, I think we're talking about something very different than that. And it is drug development. And [01:40:30] so it has all these pieces to it.

Question is, okay, if you do it and you put it on a generic label, you're going to stick them, say, with the pharmacovigilance. Say, what if it's a big indication for addiction or something? Are they going to want to do pharmacovigilance for addiction medicine drug? They didn't develop it for that. And they never did develop it for anything, they just inherit it as generics. So I mean, these are real questions [01:41:00] because the system is the system I described, with large industry takes over and they get a big reward at the end of the day and everything, and that's how it works. And there's no other development pathway, really, hardly. So that's what I think has to be thought through.

Pam Gavin:

And it's exciting because, just one second back...

Susan C. Winckler:

That's okay.

Pam Gavin:

... because I think, at least from a rare disease perspective, and of course, as Emily described, there are parties who are trying to invest in components of it, [01:41:30] trying to address this. So we really have momentum. And we just have to be practical about achieving those milestones because we can get there if we do it together.

Susan C. Winckler:

Right, right. But it's not only then illustrating the steps that have to be taken, but what's the infrastructure and the driving...

Dr. Janet Woodcock:

Building it.

Susan C. Winckler:

Right, building it.

Dr. Janet Woodcock:

Building it.

Susan C. Winckler:

Yeah. All right, I'm going to do Emily, Susan, Huong, and Caroline. Emily.

Dr. Emily Einstein:

I mean, I think this is an example of the important work. This is what the government is for. So [01:42:00] FDA certainly can't do this alone, but for disease states like addiction, rare diseases, there is simply not an incentive for the private sector to address it. Yeah, exactly. So I really appreciate FDA's attention to our disease area and with the steps you've taken to make Naloxone over the counter and labeling changes. We need federal partners because it won't get done otherwise.

Susan C. Winckler:

Yeah, yeah, very much so. Susan.

Susan Cantrell:

So from a payer perspective, I [01:42:30] would say that what we're talking about here improves patient outcomes, access, and affordability. It's a model of innovation that we should try to figure out.

Susan C. Winckler:

Absolutely. Yes, yes. Huong and then Caroline.

Dr. Huong Huynh:

So I think in order to go in the right direction that Janet is saying, I think we need to share data and information so that we know and be informed of which direction to go, left or right. But then also, that brings in the collaboration. I [01:43:00] think what we've heard here is that we can't do it alone, so we need to be in collaboration.

Susan C. Winckler:

Yeah, yeah. Caroline.

Dr. Caroline Huang:

I just echo, I think the focus on coordination and collaboration, and I think I'm particularly excited to build on this conversation for the afternoon sessions. I think hearing the federal partner conversation there, we're really proud to be a big part of the repurposing efforts we've seen on Heather's slide since 2012 and frankly years before that. But we're excited to be able to add this part of the initiative there and to really work with our federal partners to figure [01:43:30] out different ways of doing what have been old ideas.

And I would also say too, I think on the evidence generation and the packaging question, I think that's really the million dollar one is when you have all these ideas, you've picked your candidates, then it's getting that kind of to the finish line, picking the right tool there and investing appropriately. So we look forward to a lot of ideas on that later too, because I think Janet laid this out very well for us, that that's really the hard part. The fun part was talking about the RFI.

Susan C. Winckler:

Right, what might be.

Dr. Caroline Huang:

Maybe not the analysis of it, which was kind of a sprint in the last few weeks. [01:44:00] But it's fun when you get to talk about all the ideas that people have on how to make lives better. It's hard to actually do the work to get there, and that's what we need everyone to help us with.

Susan C. Winckler:

Right, right. Well, please join me, I could talk to these six brilliant people for hours, but let's thank them for sharing their insight. And we're now going to break. We will return at 1:15. For those of you who [01:44:30] are in the room, there are options for lists of nearby lunch options outside the room. And virtually, we will see you back at 1:15 Eastern. Thank you.