Rare Disease Framework Initiative
Hybrid Public Meeting
October 28, 2026 | 1pm - 5pm (*eastern*)

Transcript – Part 1

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

Susan C. Winckler:

[00:00:30] All right. Hello everyone, and welcome. Thank you for joining us, both here in the room and to our virtual audience online. We're thrilled that you're here for today's public meeting on the Rare Disease Framework Initiative. I'm Susan Winckler and I serve as CEO at the Reagan-Udall Foundation for the FDA. For those of you who are new to the foundation's work, we're the nonprofit non- [00:01:00] government organization created by Congress to help the FDA do more to protect and promote the public's health.

Let's talk about today's meeting. It's a meeting about shared learning, which can help inform the agency's framework initiative. It's not a meeting about specific regulatory applications or individual products. The foundation does not engage in regulatory decision making.

I have a few housekeeping notes for today. We're joined by about 200 individuals in person who are either in the room [00:01:30] or navigating security, one of the two, and more than 2,800 virtual registrants who are joining us online. Because of the size of the meeting, virtual attendee cameras and microphones will remain off throughout the event, except for those who pre-registered to provide public comment at the meeting. We are recording this event and the video slides and transcript will be posted at reaganudall.org next week. For those of you who are present in person, we ask that [00:02:00] you do not join the virtual meeting, but rather embrace the in-person environment.

Now, I thank each of our speakers for investing time in preparing for and participating in today's event, and thank our colleagues at FDA's Rare Disease Innovation Hub for asking us to work with you on this meeting and for partnering so productively.

So let's take a quick look at our agenda. We are going to begin with a panel discussion with agency partners [00:02:30] to discuss the Rare Disease Framework Initiative. We'll have a short break and then hear from Acting Commissioner Diamantis before we hear from public commenters who are joining us in person and from the virtual stage. The majority of this meeting is that public comment period. I will note that we received more than 200 requests to provide public comment. Hearing from all of those 200 would in fact defy the space-time continuum, [00:03:00] so we are not doing that, but we did extend invitations and we have 77 individuals confirmed. There have been some last minute adjustments, but

we expect to hear from about 72 individuals. I'll explain more about the public comment process when we get to that part of the agenda.

So one note for all of the virtual commenters, please make sure that your name in the Zoom meeting is the same name you used to sign up to provide virtual comment so [00:03:30] that we can find you and promote you and hear you later in the meeting. I'll also note that the FDA will accept written comments via electronic submission through December 11. The instructions for providing or submitting written comments can be found on the foundation website, and the meeting will adjourn following the public comment period.

Framework Initiative Discussion

Michael Davis, MD, PhD, Director, Center for Drug Evaluation and Research, FDA
Karim Mikhail, BPharm, MSc, Director, Center for Biologics Evaluation and Research, FDA
Amy Comstock Rick, JD, Director, Rare Disease Innovation Hub, FDA

Susan C. Winckler:

That is all of our housekeeping, and now we can get to the substance of the conversation. So I will ask colleagues from [00:04:00] FDA's leadership to join me up here at these, we call it a stage, the front of the room. Join me at the front of the room for a conversation.

Thank you for making it to the front of the room, and what an exciting time to be at the agency and to be working on rare disease policy. Just fascinating. So I want to turn first to you, [00:04:30] Director Rick. You've been thinking about the Framework Initiative quite a bit, I imagine, and it's generated a lot of excitement. So I want to make sure that we're all on the same baseline about the initiative. Would you take a few minutes to describe it?

Amy Comstock Rick:

Sure. Is this on?

Susan C. Winckler:

Yes.

Amy Comstock Rick:

All right. I appreciate that. Thank you, and I want to start though by thanking everyone who's here in person and with us online. We need your ideas and your [00:05:00] support so much. We view this as the beginning of a period of engagement with all of you and so many others to help inform this Rare Disease Framework initiative. So with that, just give me five minutes to lay out what it is, and then we'll do a deeper dive into various aspects of it.

The primary perspective of the Rare Disease Framework Initiative is for FDA to launch [00:05:30] a initiative, a effort to really transform how we look at rare disease drug development and review at FDA. We're not ripping up and throwing away what we've done in the past. We've done some fantastic

things, continue to do some fantastic things, but with the innovation of science, evolution of FDA, strong support from leadership right now, as you see, it really is time to take a fresh look and [00:06:00] begin to weave the many rare disease programs that we have together and make sure that FDA's regulatory process really aligns with what's possible scientifically and in terms of drug development with what is possible for the rare disease community and the 95% of people with rare disease who do not have a treatment.

So we're launching this initiative with some commitments that we will see. We are [00:06:30] firm and promise that we will see these commitments met when our new rare disease review framework is out, but then entering a period of months of engagement internally and externally to receive feedback from the experts in the field. That includes drug reviewers, patients, clinicians, academics, and to make sure that we are innovating in a way that makes sense for [00:07:00] the people who do the work and the patients who we hope will benefit from this work.

So very quickly, our commitments are to approach every drug with a product and a subpopulation that's intended to benefit from that product with a tailored approach, not look at it with what's infeasible. So flexibility as alternatives, which implies subpar really, but instead, to say clean slate, clean whiteboard, what is possible? [00:07:30] Part of that will be embedding the voice of those who are experts in the disease, which means clinicians, academics and patients, and embedding that voice at the right time so that everyone can benefit from that information.

Building on shared resources, this is an internal commitment so that there's stronger institutional knowledge at FDA on what we learn. The way I like to think about it is if there's a really cool [00:08:00] innovation in a small rare disease with one review team when that review team learns so much and really becomes amazing experts on that disease and that product and potentially that mechanism, because they learned it, FDA should have learned it so that someone else, another review team down the hall also will benefit from that innovative thinking. Chemistry, manufacturing and control, CMC, is an area that really needs to be looked at. [00:08:30] I appreciate, Susan, no comments in that... No questions I mean for me in that area, if you don't mind.

Susan C. Winckler:

Well, maybe to others here on the stage with us.

Amy Comstock Rick:

I respect the importance and look forward to learning, but all of this leads to really championing the cutting edge science and innovation for the benefit of patients. Next slide please.

As I've said, the engagement very quickly, the public meeting. If you're here, you already know about that. [00:09:00] Request for information, we take those comments and very seriously. I know the time is limited today, but I strongly encourage you to give us more detail and specific suggestions as you submit your written comments to the Federal Register. Sector specific feedback, we will be hosting round tables. We're thinking thematic around particular barriers and challenges in rare disease drug development, particularly the very [00:09:30] small populations. And certainly last but not least, internal engagement. We've developed some work streams to hear from and learn from and innovate and create with the people at FDA who do this work all the time. Next slide please.

Just very quickly, the effort is being led by the Rare Disease Innovation Hub with strong partnership support from CDER and CBER and the office [00:10:00] of commissioner. The four work streams I mentioned, one is focused very much on that tailored approach, that customized fit for purpose approach I mentioned. The next will be on external engagement as part of the new framework. The third will be on CMC, and the fourth actually, it's not a repeat of the second. The fourth is on engagement with all of you and so many others during the period where we're going through this thinking creative innovating [00:10:30] initiative, and all of that will inform the framework. I went over by 20 seconds.

Susan C. Winckler:

That's my job to keep track, so it's just fine. So that was very helpful, and I think actually, it would be helpful to have the slide with the commitments up for the rest of our discussion. So one thing I want to just confirm I heard from you, it sounds like this is taking the experience of the agency and the experience of the broader ecosystem to say how do we do [00:11:00] this better, and improve because we know we can do better.

Amy Comstock Rick:

That's right.

Susan C. Winckler:

Okay.

Amy Comstock Rick:

We can always improve, but I think there's been so much innovation in science and we've learned so much, including learning about barriers and challenges in rare disease drug development, that it's time to take a fresh look. This is not a rip it up and throw it away. This is a look at the whole landscape. Where can we be better? Where can we [00:11:30] admit that rare disease drug development is different and we don't have to look to common disease drug development for how to do it and then alternatives if we need to, as opposed to what's possible and not only possible, but amazing and innovative in rare disease drug development specifically.

Susan C. Winckler:

Excellent. Well, so as you noted, this is a collaboration of the Center for Biologics, the Center for Drugs and the Office of the Commissioner with [00:12:00] the hub, so I want to turn to you first, Center Director Mikhail, and learn more. How would you describe the vision for the initiative? We just got the basics and the overview, but welcome your thoughts on articulating the vision.

Karim Mikhail:

So when you think of the vision, I mean, look around, you hear the number of attendees and the number of people online and the 30 million rare disease patients who depend on us. It is a moment to say [00:12:30] we need to move from incremental change to transformational change. The vision here is

for this to be a true quantum leap, not another program, not another step, but an actual true build from scratch, all the way, bottom up with every stakeholder so that we know we have a framework that is good for every rare disease, because today, if you look at the number of rare diseases that we are really able to serve with the current frameworks, it's a fraction. It's a fraction, [00:13:00] right? It's a fraction. So this is intended to serve all the population of rare diseases and it's designed to be, again, a completely new holistic view of thinking of from the requirement to the process to the role of stakeholders all across, and it should be fit for purpose, meaning we should not be sitting again after this framework struggling with, "Well, that's really not adapted to the situation we're dealing with."

[00:13:30] It needs to be created in a way that review teams can take those rules, standards, and be able to easily adapt them to the disease and the asset and the molecule that they're dealing with, so that we can advance and not keep looking back all the time and struggling with predictability, consistency, asking questions, whether this was really in line with the precedent or not with the precedent. We just need to be able to have a clear path to move forward and [00:14:00] keep moving forward without slowing down.

Susan C. Winckler:

Okay. So learn, apply, and then say how do we do things differently, and make sure that there's some consistency as well in working across the products. So let's move from the vision to a little bit more tactical. Center Director Davis, what are the elements of the initiative that you would highlight for product developers, for drug biologic gene therapy developers?

Dr. Michael Davis:

Yeah, I think some elements, I think [00:14:30] basically the approach, the commitment for the clarity and consistency and predictability through the tailored guidance, I think this is going to be a work stream that we're launching right now. And I think for developers, what I'd really highlight that we want this to be an initiative that really stands a test of time, and so we're engaging with staff from both centers and also getting input from CDRH and the Oncology Center of Excellence for [00:15:00] lessons that they may have learned and input they can provide. And so we're really looking for a bottom up approach from the people who are doing the work and reviewing the applications and meeting with sponsors, and so I think sponsors should really think about the opportunities to provide input such as responding to the request for information, such as participating in the thematic round tables, depending on their particular topic and scope, and [00:15:30] then also be prepared that when we're done planning and establishing what the framework looks like, just be prepared that things will be different for sponsors as well.

And just for example, one major focus that we have is integration of the patient voice and the patient perspective in drug development programs. And I know a lot of sponsors are already doing this already and [00:16:00] some very well, but this is just going to be an expectation, because really, in the end, patients are the ones who are being treated with the products that are being developed, and so their voice is absolutely critical. So I would just say participate over the next few months as we're developing it. We want to hear from sponsors and have input, but then also as we work towards packaging everything up with what we want to do to [00:16:30] move forward, there'll be guidance. Nobody's going to be blindsided by things, but it's really going to be that everybody in the ecosystem is going to be doing things a little bit different to make this work.

Susan C. Winckler:

That's a great call out, Dr. Davis, to help us just remember that if we want to truly accelerate development in this space, it's not just about FDA doing things differently. It's all in the ecosystem, in the development of the data, [00:17:00] in the analysis and thinking through it. And then I also wanted to highlight that very intrigued and impressed by the intent to, again, listen to the staff who have been doing this and learn from them, as well as the elevation of the patient voice. Excellent. So now, I want to acknowledge an observation I've heard, which is that I've heard some say, "Is this just regulatory flexibility with [00:17:30] initiative behind it? Are we saying the same thing, or how would you address that question? And we'll let you take that one, Karim.

Karim Mikhail:

Sure. So we're really trying to get away from the flexibility space, because the challenge with the flexibility space is you cannot use flexibility to deliver on predictability and consistency.

Susan C. Winckler:

Their intention, right?

Karim Mikhail:

And I think in prior [00:18:00] meetings, we've had this discussion and many of us are actually quite uncomfortable with the term. And I would say on behalf of many career staff people, when that term is used, we feel like we're driving out of the highway on the shoulder and we're going to hit the concrete wall, and it feels like you're making a very big exception, but it's not an exception. It's just the reality of that rare disease. The reality of that rare disease is not going to be that simple to define a clinical endpoint. It's not [00:18:30] maybe going to be what was validated before and tried and failed probably. It will be something new, and this is where there will be a big room, I believe, for creativity of our own FDA people, is how can we work together with the sponsors and the patients to say, "Here's how this needs to be addressed. This is how these questions need to be handled," instead of just moving [00:19:00] along with how the file is constructed and then having to apply flexibility at the end of the day, which can become very, very difficult.

So the idea here is to start early, think strategically, engage and collaborate on the key milestones so that we move together in the clinical development milestone by milestone so that we arrive at our destination.

Susan C. Winckler:

So if I want to pull the thread on your metaphor, if I'm [00:19:30] thinking about you really want to think it's not just that paved road with the walls on either side that we need to take every product through, but rather thinking about there are different paths to get there and it's not trying to off-road with a semi-truck.

Karim Mikhail:

Absolutely. And the beauty is that the framework should give clear guidance as to what those different pathways are. Which one are accepted, which one are anticipated? [00:20:00] How can we work to develop them together from now so that we know we're going to be using them? We know it's challenging to use double-blind randomized controlled trials, fine, so what is going to be used instead? Can we discuss and make sure we're aligned on the options and the possibilities of what we can use in that space? That's exactly where we want to go.

Susan C. Winckler:

So maybe there's different routes that we can follow.

Karim Mikhail:

Correct.

Susan C. Winckler:

So then I want to turn to you, Dr. Davis, again for a little more of the [00:20:30] detail, and you should always jump in please, Amy. But how would you describe that the initiative will move forward? Could you provide some additional detail as we think about that?

Dr. Michael Davis:

Moving forward, well, obviously the first phase over the next several months is going to be very intensive work across the work streams with leadership oversight, with public forums on specific themes that we're talking about, and just working [00:21:00] with high expectations for moving quickly. These aren't going to be working groups with 50 people in it that go on for years and years. We're going to be very focused on reaching deliverables, which is... We have ideas. I certainly have a lot of my ideas of if it was just me designing it as a dictator, what it would look like, but it's not, and I don't want it to be that way because [00:21:30] a lot of times, I have good ideas and there's problems with it. And so I really, with deep respect for the staff here, I want to hear their creativity and just their ideas, because I know this is a topic that the staff reviewing applications, a lot of them are physicians, pharmacists, other people who are deeply committed to public health and serving patients who are really trying to do the right thing.

And there are just methodological challenges in developing treatments [00:22:00] for rare diseases, just with the different sort of possibilities available and a lot of the things we talk about, natural history studies or external controls and even newer technologies, topics that are discussed, things like digital twins and other more cutting edge types of approaches. And so I really want the experts within the centers to be able to work with that and also take into consideration [00:22:30] external expertise as we work towards what the specific deliverables will be, whether it be updated guidance documents, internal processes, templates. I think everything is really on the table here, but we just want this to be something that becomes just the norm for how staff in both centers work with companies developing treatments for rare diseases and applications.

[00:23:00] And I think also, I want to just say, echo what Karim said about the predictability piece and flexibility, that really at a high level, the way I see the value of what we're doing is I think there could be

a lot more intensive work at the beginning of a development program, laying out with the plans, discussing what the development program will look like and what makes sense for that condition. Because if an underpowered randomized controlled study, I would say that's not an [00:23:30] adequate and well controlled investigation, and so just thinking about the condition, the patient population, the nature of the treatment and the benefits it's intended to provide for patients, and just thinking about what makes sense to be able to convince review staff that there's substantial evidence of effectiveness for the treatments.

And it's just going to look differently than what might [00:24:00] be the case for diabetes or hypertension because of what's possible to do for rare disease drug development, but I think we all are deeply committed to the idea that just because a condition people have is rare and not very many other people have it, they deserve to have treatments developed for them and the patients need help and their families need help. And so with this initiative, the end product [00:24:30] is going to be I think more agreements about what the program looks like on the front end rather than finishing a program and then getting to an advisory committee and then talking about what type of... Because the term flexibility, it also can be variably defined. It means different things to different people, and so I think there's a lot of unpredictability can be related to this.

And I just know as part of the broader ecosystem, investors [00:25:00] fund development programs and patients participated, and I know predictability is so important to everybody in the whole ecosystem. And so we want to maximize that to the extent possible. I mean, there's always going to be treatments developed that just unfortunately don't work or have very serious safety considerations, and that's just the unfortunate aspect of developing drugs where it's sometimes hard to know exactly how everything will play out, but to the extent [00:25:30] possible, we want to maximize predictability.

Amy Comstock Rick:

And if I could, building on what Mike and Karim just said, predictability really does come in two different ways. One is predictability within the individual drug development program and the actually earlier, sometimes tough conversations with accountability to follow. So we hear, I think all too often, that at the late stage, there's a disagreement about what happened [00:26:00] at that meeting two or three years ago. And if we can, sometimes it's a no, but offer a little more clarity of guidance and continue that throughout the drug development process, there'll be predictability for that drug developer and presumably the patient community. But predictability also is in the broader sense of how does FDA review rare disease drugs, particularly for very small populations? And I've gotten a question of wait, fit for purpose but predictable? [00:26:30] That's a neat trick.

And so I think what we mean is greater clarity and transparency about FDA's approach and how we're going to handle fit for purpose and what we will look at and what the communication back and forth, expectations of earlier communication. If you want the customized, these are the expectations of your role in that conversation, but if there's greater clarity on the approach, then the customized fit [00:27:00] for purpose per drug development plan should not be a surprise.

Susan C. Winckler:

Yes, yes. So I'm thinking back to our original, as we're adding in the description, I'm thinking about that metaphor, and maybe it's more when we pull up Waze or Apple Maps and are like, "What's the best way

to get there?" That what we're saying here is there may be many paths to follow, but you'll know what the rules are for each of those paths and then have [00:27:30] the continuous conversation on a path. I recognize metaphors, there are flaws within them.

Amy Comstock Rick:

There's a major transportation theme here.

Susan C. Winckler:

We started down, I was going to say that road and I don't mean it as a pun. Yes, go ahead.

Karim Mikhail:

The most important part is going to be the milestones of the clinical development, because that's just a very, very unique... I mean, all clinical development had milestones, don't get me wrong. It's just that in rare diseases, a three degrees [00:28:00] non-alignment on the clinical endpoint may end up just clearly killing the molecule. So that's why agreement, alignment, milestones are very specific on the way as we are moving.

Susan C. Winckler:

And it strikes me that those milestones also then present the opportunity for the regulator and the developer and the patient community to learn and think about maybe adaptations. [00:28:30] Is there an option as you go through this?

Karim Mikhail:

A different solution. I would call it a different solution.

Susan C. Winckler:

Okay, a different solution.

Karim Mikhail:

What is attainable in that situation? There needs to be a pallet of options. There is no one solution that is going to fit for every disease. It's a question of for that disease entity and that biologic, what would be the possibilities? What could be attainable and what evidence would be necessary to establish the bar [00:29:00] that is needed for market access?

Susan C. Winckler:

Okay. So now, I want to flag a couple of things that caught my eye in looking at the announcement and the white paper. So I noticed first, there was this explicit connection of the risk-based approaches for chemistry manufacturing and controls review, I'm not going to ask that of you, Amy, and pre-approval inspections. Second, I was struck by the connection of the word innovative and statistical approaches,

like putting that phrase together. [00:29:30] I don't know that I've seen innovative statistical approaches as a phrase before. And then the intent to embed the patient voice throughout the drug development and review process. So sorry, I put a lot out there, but why don't we start, Karim, if you take CMC, Amy, if you take patient voice, and then we'll close our loop and talk about statistics with you, Mike. Will that work? All right. CMC.

Karim Mikhail:

So for CMC currently, [00:30:00] if you look at the requirements level, they're just one size fits all no matter what the disease is, no matter what we're dealing with. And you've seen with other initiatives like expedited IND, the teams did an amazing effort already to adapt the CMC requirements to a phase one study by saying, "This is really in phase one, your focus is very much on safety, so anything beyond safety may not be necessary." That's exactly the same approach that we want to apply here, [00:30:30] which is to say, all right, if you've seen what flexibility delivered, it took us from three PPQ runs to one PPQ run in the last guidance, so it took us clearly forward. The challenge is even that bar for an ultra-rare is pretty high because it means 10, 20 million still for one bar. And if the disease entity is we have only 100 patients in the US and nobody's making any profit, we need [00:31:00] to have fit for purpose CMC requirements for those drugs which are going to be very individualized if you think about it.

That's not going to be a biologic that's going to be for thousands of people. That's just going to be in the single digit or in the tens, so what would be required at that point in time? What sort of guidance will be useful for the manufacturers to say, "Oh, I can see I can do this, [00:31:30] so maybe I can help those patients"? Because for the moment, it can be viewed as a very significant barrier for even exploring whether we should help patients of that disease or not. So there is a lot of work to do. Having said that, it is a challenging space because we are committed and I'm speaking on every FDA staffer. Our number one priority is patient safety and the rigorous science and our standards [00:32:00] in terms of CGMP and other factors, so we will have to deliver on these, but we need to find what is the most logical answer for these questions.

Susan C. Winckler:

So it sounds like it's fit for purpose or risk proportionate. What's the risk there? Amy, something on the patient voice. I think it might be the biggest word in the word cloud for some of these.

Amy Comstock Rick:

Right. So thank you for that. I mean, FDA, the last 10 or 15 [00:32:30] years, everyone in this room knows that with the patient focused drug development program, the patient listening sessions sponsors have, it's a new world in terms of sponsor engagement with patients and patient voice and drug development, but it still has a long way to go. And here at FDA, PFDD, as I said, and patient listening sessions are great and what sponsors are doing are great, but really, the opportunity for the review [00:33:00] team to directly hear at the time of looking at a new product, a new application, an IND is not as tied to that process as it could be. And in fact, a common opportunity for patient voice and patient discussion on a particular application, a particular challenge, burden of disease, often comes at the ad com meeting, and the ad com meeting, [00:33:30] if there is one and there isn't always, is so late in the process.

I mean, just to put it in really human terms, at that point, most often, the review team has already made a recommendation and the ad com is looking at a particular question or two. How many of us are super good at hearing new information after you've made a recommendation on something you've been looking at and working hard and thinking about for years? God bless you if you're that open-minded. Most of us-

Susan C. Winckler:

Have [00:34:00] a little trouble.

Amy Comstock Rick:

It's just not the right time. It may be well appreciated and heard, but it's too late in the process. So what we're talking about is bringing in the patient voice, and it's a challenge because the right time might be every day. Well, that's not going to happen. So think about, and it may be a little different for every application, every drug development plan, when is the right time to bring that patient voice in to talk about risk tolerance, burden [00:34:30] of disease, to help educate about one of these very small rare diseases that a review team may not have seen before? And there's a lot of questions about living with that disease, and then that information can both inform the application as well as inform additional external outreach that the review team may need to do. So that's what we're thinking about. These are big questions, and I think we'll have to give a lot of thought to how to manage this in a way [00:35:00] that is manageable, but it is an absolute must have.

Susan C. Winckler:

And I hear you saying it's not only the opportunity for the patient voice to be uttered, but for it to be heard and considered as part of the process.

Amy Comstock Rick:

I would say impactful, yes.

Susan C. Winckler:

Okay, great. Dr. Davis, if you forgot, I'm coming back to you for the question about innovative [00:35:30] statistics.

Dr. Michael Davis:

Yeah, which is not an oxymoron. I have to say, I have a soft spot for statistics. My father is a biostatistician and he's basically retired now, but just throughout my life, he'd always talk about it. And I never went through formal statistical training myself, but I do have a deep respect for the methods and also for the team we have in just speaking for my own center, the Office of Biostatistics, [00:36:00] the team they have. And just for an example, the last RISE workshop was focused on statistical methods and they were excited to participate, and there's a lot of ideas out there that are being discussed. And I think this is an area that I'm very open to innovation. I'd encourage our staff internally to think about different approaches because sometimes the traditional study, large randomized controlled trial and statistical

[00:36:30] analysis plan, it's not going to be adequate. It's not going to be appropriate for some types of rare disease studies, and just to think about other ways of really building the evidence base for effectiveness.

And so I think there's a lot of room for innovation. I don't want to throw out naming specific types of approaches, but I've heard discussions about several going on. Just even yesterday at the NORD meeting, a [00:37:00] gentleman came up to me and said he raised a different kind of novel type of statistical approach with the team, and there was openness talking about it with the review team that they were going to discuss internally. So I think just like CMC and clinical trial design, in terms of the actual conduct of the study itself, I think biostatistics is ripe for innovation and also applying. Just like any technical [00:37:30] field, there are different thoughts and ideas and a lot of innovation going on out there, and so I just encourage external experts in this space to be able to share ideas and to dialogue with us. And I have full confidence in our team here are going to be excited to work on this and see what types of approaches would make sense for these programs.

Amy Comstock Rick:

And if I could just throw something out, the most recent RISE workshop that Mike mentioned, [00:38:00] actually, statistics can be a little off-putting for some people in terms of, "Well, if I didn't take that in college, I may have trouble understanding this," or, "My dad wasn't a statistician."

Susan C. Winckler:

Mike didn't grow up with the dinner table.

Amy Comstock Rick:

We had the highest level of participant engagement in terms of questions and comments than any RISE workshop, and that to me was an informal measure of it's time to open that door a little bit more.

Susan C. Winckler:

Absolutely. That tells [00:38:30] us that people want to engage and talk about that. Well, as we think about the second portion of this meeting, which is all about public comment, it would be great if each of you would take a minute or two to share, what insights and perspectives are you most interested in hearing? Mike, you gave us some ideas already, but as I'm sure that some folks are still adjusting their two and a half minutes of comments and could adapt [00:39:00] quickly, but remember, if you're doing that, you have to strike out words in order to add words. What would each of you like to hear as we turn to that? And Mike, you get to go first on this one.

Dr. Michael Davis:

Okay. Yeah, no, I'm really excited. This is the part of the meeting I'm probably most excited about because just how many people are here and how many folks online, and just knowing the level of thoughtfulness that went into people preparing remarks and also responding with written comments [00:39:30] to the RFI. And one thing I'm interested in hearing about is the term predictability and consistency, and just getting ideas about what that might look like. Because I know FDA doesn't develop

drugs, but I know what does develop drugs and it's investment, funding companies and funding trials and manufacturing and so forth, and I know how critical [00:40:00] it is. So thinking about what would that look like for there to be a more predictable approach?

Because I think my ideal state would be that there was really good alignment about what the program would look like and then this program's done, and hopefully the program will be positive and we'll be excited to bring new treatment forward, but sometimes it's not. And an ideal state would be that people would just be disappointed [00:40:30] obviously because a new treatment's not available, but just feel that it was a predictable and fair process and reduce the level of frustration across the board afterwards. So just those sorts of ideas are important to me.

Susan C. Winckler:

And I'm really glad you called that out because I think many regulatory affairs folks would say you get predictability from precedent, and what you're talking about here is really saying, "No, this is new, and in fact, don't get caught in [00:41:00] the precedent paradox, but rather what are these new pathways that are emerging in the framework initiative?" All right. We'll do Karim and then Amy.

Karim Mikhail:

Sure. So what I'm keen on listening to is the solutions you think we need to apply, because I think we're all aligned on what the challenges are and what the problems are. So let's use the time talking about what's your dream? How should this look like? [00:41:30] We're not going to have 10 opportunities of engaging 3,000 people as to how we need to do this, so we should not put a limit to what the solution is supposed to look like. We should set a goal of if this needs to be as accelerated as possible and if this needs to be accessible to the smallest rare disease population, how does it need to look like? What are the key elements [00:42:00] that will build that fit for purpose approach? How do we need to look at the disease? What do we need to consider there? How do we need to look at the patient population? How does the prognosis is taken into account? How does the treatment timing impact the process?

There is a lot that we need to work on if we really want to take a quantum leap, because that's what I spoke about. It's not just tweaking the process. It's making sure we see how can this work in the next 10, [00:42:30] 15 years with eight to 10 mutations discovered every week? How does this look like? It needs to look pretty innovative, pretty innovative. It should not look like something we're familiar with, if you see what I mean.

Susan C. Winckler:

Yes.

Karim Mikhail:

If it was familiar with, we would have done it and we would be okay. We wouldn't be here, so that's what we need to challenge ourselves with.

Susan C. Winckler:

So I happened to be on a panel this morning with a former [00:43:00] regulator who may have led a center here for a long time who said, "I don't know that the agency is thinking big enough." I just heard you say the agency is thinking big and you're looking now to the broader community to say what does big look like? What are those innovations that are possible? All right. Amy, you actually have two minutes if you like. That's a little off.

Amy Comstock Rick:

Okay. First, [00:43:30] I would say in looking at these outcome commitments and what we've talked about here today, if you see something missing, how did they miss that? Why is this goal, higher level, why isn't it there? We would like to hear that. But in addition, it's hard... I'm the lawyer on this panel. It's hard to get... Well, we both are actually.

Susan C. Winckler:

It's all right.

Amy Comstock Rick:

It's hard to get the lawyer, the advocate out of me. I also am very interested in your sense of the goals of what you want this framework [00:44:00] to look like that can live for 10 or 15 years, and then really please take advantage of the opportunity for written comment to give detailed solutions. We love your support. Absolutely, it's great. Tell us how it looks to you when we actually are at the tail end of the initiative and the creative part of this, because your solutions, we're human, we won't think of everything. [00:44:30] You may have something that is just spot on to what we need to think about.

Susan C. Winckler:

Excellent. So be creative, think big, and most importantly, share those thoughts.

Amy Comstock Rick:

Write it down.

Susan C. Winckler:

Write it down and submit it for the record. Excellent. Well, this has been so informative. I hope that our audience is seeing how this initiative is taking shape, so thank you for joining us. Thank you for the work [00:45:00] that you did to advance to get us to this point, to say that you want to hear input in specific places. With that, we're going to take a 10-minute break. We will return at 1:55 Eastern, so that is precisely 10 minutes from now. Thank you.

Dr. Michael Davis:

Thank you, Susan.