Wow! Or Yeow?! 2026 Transcript

Zan Fleming (00:00:01):

Well, ladies and gentlemen, it is 11 o'clock Eastern Standard Time in Washington DC, from where this gathering is emanating. I welcome our global audience to our annual 2026 Wow! or Yeow?! FDA Looking Back and Looking Forward. What a year 2025 has been. I can't wait to bring in our stellar panel to talk about it, but first I turn to my colleague and Kinexum CEO Thomas Seoh to provide some quick housekeeping information. Thomas?

Thomas Seoh (00:00:44):

Thanks Zan. A housekeeping reminder to enter any questions for the speakers in the Q&A function of our Zoom webinar platform, and the panelists will try to get to them as time allows. As usual, a link to this recording will be circulated to all registrants and made publicly available within the next day or so. Just to highlight a couple distinctive features of our virtual webinars. First, we enable the chat function for audience interaction. So just for warmup, for those of you who are willing, please say hi in the chat, your affiliation if desired and from where you're logged in. And second, we will bring the formal segment of our webinar to a close at 12:30 PM Eastern Standard Time, but we will keep the room open for 20 or 30 minutes for informal chat for those speakers and audience who can tarry. This is the virtual equivalent of speakers descending from the dais for conversation with the audience in an in-person panel. We're also planning to take a couple of polls, so please warm up your critical and decision-making faculties. I now turn the mic over to Kinexum Founder and Executive Chairman, Dr. Alexander Fleming. Zan?

Zan Fleming (00:01:54):

Well, Thomas, again, thank you very much and to go right to the program, we're going to start with our traditional approach, which goes back to our first session in 2017. Dave Fox is going to highlight what he sees as the most significant regulatory reviews and/or approvals at FDA of biologics and drugs. So Dave, please go right ahead.

David Fox (00:02:28):

Well thank you Zan. This is the boring but necessary part of Yeow or Wow where we look back at 2025, and this is mainly by the numbers. I'll get into it because we have lots to cover. So the big picture story for 2025 in terms of approval metrics and — Sorry, I'm getting a little feedback. I dunno if people can put themselves on mute. Thank you. So the big picture story for 2025 is that FDA in the therapeutics area held steady on their historical approval rates amidst a lot of Yeows that we're going to talk about today. So there are 46 novel drug approvals in CDER in 2025. Combined with CBER, we had 58 total novel approvals across the two centers, which more or less matches the 10 year average. So, across a decade the agency pumps out about 56 novel approvals a year. We had 58 in 2025, down a bit from 2024 when we had 61 approvals.

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CBER had a particularly strong year, best year in a long time. 12 approvals, 46 were for CDER. The interesting story there though is we also had a record number of CRLs or rejections. So 2025 was a high point in total volume of reviews with 81 regulatory actions. and 23 of them were complete response letters or you could say we're getting to about 30% of the novel applications in process resulting in CRLs. And we'll talk quite a bit in the program about some of the new policies of releasing CRLs, including releasing them in real time.

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In terms of the more innovative side of the innovative novel approvals, we had about 43% of the approvals. 20 and 46 out of CDER were considered first-in-class including very early in the year suzetrigine, which got a lot of attention as the first non-opioid targeting a new channel receptor, NaV1.8, sodium channel. In the orphan drug space, which Frank is going to talk quite a bit about, so I won't say too much, about one half, 50%, of CDER approvals were for orphan drugs, which is down, I should say from 2024, 56%. Probably not a large enough number of data points to say there's any kind of trend or reaction, but Frank looks geared up to talk about that. Highlights. Two for rare mitochondrial diseases including the first approval for Barth syndrome, multiple rare cancers including low-grade ovarian cancer and a new hemophilia treatment out of the orphan program.

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In terms of expedited programs, which is sort of a surrogate marker for innovation, these are the products for addressing unmet medical needs, 72% 33 out of the 46 CDER approvals involved at least one expedited program. It's breakthrough, fast track, priority review, or accelerated approval for those. Again, keeping score about one in three of the CDER approvals were breakthrough, 40% fast track, 46% priority review, and 25% or 24% to be exact accelerated approval, which all sounds quite strong. But comparing against 2024, it's pretty interesting. 10% drop in breakthrough or breakthrough in RMAT, almost a 10% drop in priority reviews and the only metric that increased was accelerated approval. Again, the numbers are small so we can't obsess here, but a slight uptick in the number of accelerated approvals, which is kind of interesting because we heard a lot about the new leadership coming into FDA having skepticism about accelerated approval.

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But this is probably, and a lot of these numbers I should say are all carryovers from the prior administration. I mean all of these programs that matured in 2025 to an approval action had been in development many years before. So hard to stake too much on the new administration. We'll get to a few of those in a moment. In terms of overall efficiency, the agency met its PDUFA goals 96% of the time. So 44 of the 46 CDER approvals were on-time approvals under PDUFA. And then a really nice number, 85% of these novel approvals were first-cycle approvals. So it shows the value of all of the upfront interactions with the agency that the applications going in for novel products, very strong in terms of at least getting to a first cycle, but again, one in three getting rejected, which is the new kind of metric to watch in terms of this is a metric that I like to watch: US first approvals.

(00:08:36):

So novel approvals that occurred first in the US as opposed to the rest of world, 32 out of 46 or 70% were first in the US, which is actually a little bit higher than historical. It's been trending upwards, been in the low sixties. I think last year is about 65%. So we're still, at least at this point, and again this is a carryover from prior years, but 2025 saw again 70% of novel products being approved in the US first. However, this requires a little bit of editorializing. The traditional, what we would think of as European-based pharma companies as opposed to more US-based pharma companies. The European pharma companies vastly outperformed the traditional US companies. I think about five European companies had multiple approvals. Only one US company I think had multiple approvals. So again, it's hard to tell because a lot of these companies are really global in nature, but that's just something to watch as we take a look at the effect of the new administration and where the investment is going in research and development. On the biosimilars side, we had 18 biosimilars approved in 2025 against 10 different reference biologics, and we saw four first biosimilars against new reference products including include a biosimilar to Perjeta, pertuzumab; Xolair; and some NovoLog insulin biosimilars. So for those keeping score since 2015 when we started to see biosimilars come online, we've had 81 biosimilar approvals against 20 reference biologics.

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So in terms of other stories within the therapeutic space, everyone was watching vaccines. There were six CBER approvals for vaccines in the first half of 2025. There were none in the second half of 2025 and lots of reporting on the pipeline for vaccines drying up. The other area of note, just again more by the numbers, but really important, cell and gene therapy and RMATs and CAR T therapies, everything down, only one vector-based gene therapy was approved in 2025. No CAR T cell therapies, no immuno cell therapies. There were three siRNAs, antisense products, that were approved. And those are interestingly enough done by CDER, not as biologics but as drugs. But on the CBER side and the pure cell therapy side, everything is down. And some would say there's been a real collapse in the CAR T space. There's been some new announcements about regulatory policy and standards for CAR T therapies requiring superiority studies, and it'll be important to watch how that affects the pipeline as well.

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But it's a fairly stark contrast to where we were. Therapeutic classes. Overall, oncology as usual dominated, multiple therapies, rare disease, metabolic disorder, very strong in 2025. Autoimmune, inflammatory diseases, strong. Infectious disease, which is usually a difficult category, better than usual with two new therapies for gonorrhea, but neurology, neuroscience, down. So in terms of any other notable approvals, I think I'm going to leave that to Frank because everybody has their favorite spots, but I think maybe some of the more interesting ones I was just going to call out was expanded approvals in the GLP-1 space. So we had the first approval for semaglutide for MASH, which was interesting, and Ozempic expanded to chronic kidney disease. So those categories just continue to just catch all the attention and represent sort of a whole new approval paradigm. So I'm going to leave with that and let—

Zan Fleming (00:13:47):

What a terrific review, and I wish we could go on, but I think Frank, you could certainly come down to orphan approvals and other drugs or therapeutics that you'd like to point out.

Frank Sasinowski (00:14:02):

Yeah, thanks. Great job Dave and thanks Zan. Yeah, I was going to talk about four CDERs and three in CBER, just to call them out. I'll start with Barth, one that was mentioned by Dave, the Forzinity. You've probably filed that in the trade press. It's had a long history, and the reason why for those a hundred boys, the reason why I'm calling that one out is to say that it's possible that if we had the plausible mechanism pathway, that it was fleshed out, maybe that's a genetic disease. The patient community is the one who came to the sponsor and said, "We heard about your mechanism. It's a lock and key with our genetic defect." Maybe if plausible mechanism were mature right now. I just mentioned plausible mechanism pathway for those. It was just announced in a New England Journal article in November. It's kind of new, it's relatively unformed, but it might give mooring for the FDA reviewers to be able to anchor themselves in review. An FDA reviewer who's being asked to make a tough decision on some of these orphan drugs.

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They're often, before we had flexibility and before we had the 1997 law, FDAMA 115, which then we had the guidances in December, 2019. So it wasn't until relatively recently, Peter Stein was the first person who publicly announced that the FDA was moving forward with confirmatory evidence. And so, we had two great systems that allowed reviewers and flexibility and then in FDAMA 115, a single study that's positive with confirmatory. We have two systems that allow an FDA reviewer to not be seen as rogue, to not be seen as coloring outside the lines when they're trying to give an approval to something that doesn't fit squarely into more traditional patterns for showing benefit. So plausible mechanism to me is that great hope, to have a third mechanism, a third framework that FDA reviewers can look at and be able to anchor themselves in something

that's solid in terms of regulatory pathway instead of bearing the burden of appearing to maybe be going rogue if they give an approval or be coloring outside the lines.

(00:16:42):

So that's why I want to call attention to that one because everyone probably followed that in trade press. Another one, Kygevvi, that just got approved in December, is a single arm trial. It again, could have benefited perhaps from plausible mechanism because it's to treat thymidine kinase two deficiency, genetic defect. It's a single arm. The basis was a single arm trial in 47 adults and then they had some expanded access. But to give you an idea of how they had to go all over the world to find those subjects, those subjects came from 20 different countries, including countries that you normally don't think of like Ghana and Costa Rica and the UAE. So I think that some of these like Kygevvi and Forzinity for Barth, those could benefit maybe if in the future, if we have a plausible mechanism pathway developed. Right now it's kind of an idea, and it remains to be seen, and that's the work of everybody.

(00:17:47):

That's the work of the people at the FDA. It's the work of industry. patient advocates. We are all involved in that process. So think about that as you move forward with any development program. The third product I was going to bring up in drugs was Yartemlea that just got approved as like a Christmas gift, December 23rd, but it was to treat transplant associated thrombotic microangiopathies, and it was also a single arm trial based upon 28 subjects, Single arm. Single arm. So again, I think this is showing extreme flexibility, but again, if I don't think this product would've qualified for plausible mechanism, but our depth, certainly the rare disease evidence principles that were announced on September 3rd, which are really for those conditions that affect a thousand or fewer Americans and are genetically based, their etiologies, this one might've benefited from that. And the last one I was going to bring up isn't an orphan, so excuse me, but I mean it is an orphan but it's not a new chemical entity.

(00:19:00):

That was another one called Vykat XR, which was the first approval for Prader-Willi. Prader-Willi is where a person's born with a genetic defect, they have hyperphasia, that is they believe that they're starving to death regardless of their nutritional status. Imagine if you think you're suffocating, what you will do to get your next breath of air. This is what these people believe, they are starving, and they will go to no ends. They will stop at nothing to be able to address their starvation condition that they believe they're in. So this is the first, is a very important drug. The reason why I'm highlighting it, even though it's not a new chemical entity, is it's in psychiatry. When FDAMA 115, that 1997 law, first, Peter Stein, first announced that the FDA was coming up with guidance to implement that in September, 2019. And then it actually, we saw it published in December, 2019.

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We now have many therapies that are approved under that statutory standard, which the FDA has embraced. When that standard first became known, there were people at FDA and like Tiffany Farchione, the head of psychiatry that said, "Frank, I know you're moving forward with this new framework in lots of other areas, I see you getting approvals in areas like neurology, but in those other areas, something about etiology, the pathophysiology of the condition, and you know something about the pharmacology of the intervention that's going to target upstream. And so in those cases maybe you can have a reduced amount of evidence, that is you don't need two adequate and well controlled positive studies." She said, "I don't think that can ever happen in psychiatry." And yet in March, 2025, Dr. Farchione approved this drug on the basis of a single trial with confirmatory evidence. So what am I saying to the world? Even if you are encountering a situation in which you might think that you aren't foursquare within kind of a regulatory pathway or framework, work the science. I mean if the science, the FDA is, as you all know, very, very, they're very intelligent, but they're also open-minded, and so work with them and you can get to an action

like we did on Vykat XR to get the first therapy approved for Prader-Willi. So now I'm going to switch to CBER. I've got three to talk about on the CBER side and so —

Zan Fleming (00:21:43):
Somewhat quickly, Frank,

Frank Sasinowski (00:21:45):
Yes. Oh, okay. On the CBER side I'm going to talk about Waskyra, which is the first drug that's approved for treating people with WAS, I'm not going to try to pronounce it, syndrome. What's important is, it was the first therapy that was approved for a patient organization. I've helped patient organizations before like the LAM Foundation do the pivotal study that led to sirolimus getting approved for LAM, but we've never had an NDA or BLA holder be a patient organization. I think that's groundbreaking. So I'm just calling attention to that. Avance Nerve Graft. I'm calling attention to that. It's not an orphan, it was approved in December 3rd. What's novel to me about that is that many people say maybe CBER is moving away from accelerated approvals. There are four indications, three of them are accelerated approvals, one of them is for traditional or full approval. So I think that's a good sign that CBER is still open to accelerated approvals. Lastly, there was the third product approved for epidermolysis bullosa, the condition that is diagnosed at birth when a nurse takes a newborn to be cleaned up and the skin falls off the newborn. That is a horrible condition, and we now have the third. This is a topical gene therapy, it's the second topical gene therapy, and it's the third therapy for these people for this horrible disease. So I think that's really noteworthy. Zan, turn it back to you.

Zan Fleming (00:23:24):
Well Frank, another Wow! tutorial. Indeed, you have provided intellectual leadership and advocacy in the field, and we thank you for that. We're going to try something new now, and that is to actually do some polling. We're going to start off with a few simple questions and so, Emma, if we could put those up. This is for the audience to give their responses to and hear. The question is, given what you have heard, and all that you now know ,how will overall approvals go in 2026 related to 2025? So just quickly vote, you just put your cursor over your choice there, and we won't wait very long. So go ahead and do it. First impressions are generally your best, and let's see what the result is, Emma. Okay, so fairly evenly split. Interesting. Let's go to the next quick one. And again, Emma put that up. Let's see, are you finding it? Yeah, there you go. Overall, and this again fits into our name, is next year going to be more Wow! or Yeow?! or mid? Again, make your quick choice and we'll soon see the results. Alright.

Thomas Seoh (00:25:21):
Zan, just to note that Yeow?! means ouch. Wow! is fantastic. But Yeow?! means something painful.

Zan Fleming (00:25:26):
Yeah, we should make that clear. Okay, and mixed. Alright, well that's very interesting. We thank you for those responses. Let's now go to the state of FDA as we get into 2026 and we'll start with Steve Grossman. Steve, go right ahead, or I can ask you what worries you.

Steven Grossman (00:25:59):
Most? I'm willing to answer the question. I just couldn't get myself unmuted. So the question is well how do you look at the agency as a whole? And what I fell back on is that I was one of the co-founders of the Alliance for a Stronger FDA. And so through that role, I spent the better part of

20 years being one of the most visible, outspoken people speaking on behalf of for the agency. And so it was always a question, what were the attributes of FDA that were most important ,that would impress Congress, that we thought defined the agency in a way that explained a lot of things, because FDA isn't NIH, it isn't CDC, it isn't a lot of things, but what is it? And the phrase we used for the better part of my nearly 20 years was that FDA was known, was known for science-based decision making and that was if you will, FDA's secret sauce. That played well.

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So I think it defined an agency that was focused on science, that was concerned. A phrase that often comes up is precedent based. The agency was very concerned that science-based decision making not only be well supported but that it be consistent over time. And so that was the metric I decided to start our discussion of overall FDA science-based decision making has a lot of parts to it. I've picked on three that I've written about some and so feel most comfortable discussing. The first is that FDA is oriented around a process and that process involves gathering information, checking that they're not just listening to one voice or one interpretation of data or more broadly one interpretation of science and its impact. So that one feature clearly of science-based decision making is the process in which the agency gathers. What's happened there in this year is that things are different.

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The commitment of this administration, starting at the White House, not all starting at FDA, is very indifferent at best to process. They come to conclusions. And so one of the things you see that process affecting FDA is things like policy by press release, a decrease in the number of FDA advisory committees, at least as classically defined. A lack of commitment to something that was a very important feature of FDA that I know Peter and others are going to talk some more about, which is bottom-up decision making. If you've ever had occasion to ask a senator, director or the commissioner can you do something about this? And pretty constantly, consistently you get the answer, we need to hear what the people who have been working on it think first, see what they discovered, what they decided. And so one of the features of the process-oriented science decision making, science-based decision making is are you getting all the inputs?

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And there's no question compared to past years, those inputs have narrowed. Whether that is objectively important or not, it's certainly a valid observation that that has changed. Second feature of science-based decision making is adherence to certain scientific concepts and seeing them as if you will, constant truths of a sort rather than things that are variable. A couple that I've written about, the obvious one that people talk a lot about is correlation is not causation. Another of these, how do you interpret scientific information? Anecdotes are not proof, you can't prove a negative. Those are the kinds of rules of scientific interpretation that have always seemed immutable and there're more, I have about seven of them that I think really are important and at this point, there's an awful lot of decision-making where you can argue whether or not the rules of scientific interpretation, if you will, are being followed.

(00:31:27):

And that is also part of, is the agency continuing to be known for science-based decision making? The third feature of that is what I would call where's the evidence? And FDA has always as part of that science-based decision making, always committed to showing its work. And in that regard, say for instance, and I know this is controversial showing Complete Response Letters isn't philosophically in keeping with that, even if it has other concerns about it that maybe you should not have done it. But I'm just saying that would be an example of is FDA showing its work? Can you look at the record and say, I might not agree, but I can see how it's based in science and why the agency came to the decision that it has. Now that's at this point I would say a mixed bag. There's certainly things that seem not to be well tied to science. I think the problems at the moment are —

Frank Sasinowski (00:32:47):

Excuse me, can I ask you as a follow up on that right, where you work, Marcus, a former FDA neurology reviewer asked in the chat whether we could say anything about the advisory committee process because you're talking about being transparent about how the process works. Can you speak to that?

Steven Grossman (00:33:04):

Well, the beauty is not solely in the fact that you've brought in 12 to 15 advisors. It's that FDA has devoted manpower and time and a lot of energy to making sure that there's a balance of opinions and experiences and specialties represented on the panel. They don't always provide good advice, but you know that it isn't affected by the agency. It isn't a narrow gotcha being formed that you're going to hear different things. And when the agency comes to a decision, sometimes they agree with the advisory committee, sometimes they don't. Sometimes the final decision isn't what the advisory committee said, but rather a response to what the advisory committee said. And those are some of the best. And so yes, the advisory committees as balanced panels put together with thought and care are extraordinarily important. They, among other things, which I think is wonderful, enlist a very broad array of scientists and researchers and clinicians so that we don't just have decisions by an advisory committee, we have a cross section and the number of people who have been involved with FDA because of the advisory committee section selection process is enormous. It's almost like its own alumni association and it's a tremendous asset. So that clearly has, and that is also, to my last point. It is part of that process of saying is the decision tied to the science? I think there are more questions right now about that in the policy areas where science is important. It is an emerging topic with pluses and minuses on the product side.

Zan Fleming (00:35:15):

Steven, beautifully articulated, we could go on and on just with your thoughts alone, but there's no better person to follow you at this point than Dr. Peter Stein who's joining us for the first time, and we are delighted to have him. Peter has been an amazing public servant, and we can't thank him enough for his service. Peter, you have thoughts that are very related to what you've heard from Steven.

Peter Stein (00:35:55):

Zan, thanks indeed. And I think I'll pick up on a few of the themes that Steven raised. Well, first I just want to say it's a pleasure to be here Zan, as you said, this is the first time I've been at one of your meetings, so I do appreciate the invitation. Let me just start by saying it goes without saying that there have been a lot of changes in the past year at FDA. I do want to just comment that we do have to be a little careful in looking sort of at the prior year because the course of drug development, as everyone knows a many, many, many year process and to see how changes at FDA impact that process, I think particularly when we're looking at numbers, I think we need to look over years rather than over a year. Not that it's not important to look at the experience we've had in the prior year.

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I mean, again, it goes without saying that there have been a lot of changes in the past year at FDA and I also have to say that the staff at FDA continue to focus on their mission. I work as a consultant now to a number of companies and I see that the guidance and the interactions with FDA have continued to be outstanding. FDA continues to provide informed, thoughtful, useful guidance and the NDA/BLA reviews that I've seen that have been put into the public domain continue to reflect extensive analysis and are thorough and detailed, which is really encouraging. I think a key point to make is, and this is really picking up on something that Steve commented on,

is to maintain the high quality of the decision making and the advice that's provided really means that to the whole process has to really be bottoms up, just as Steve framed it, and not top down.

(00:37:52):

And I think that largely remains the rule, but this is really critical to protect, as it's really what assures the quality of decision making, and that's what assures that the FDA continues to protect the public and ensure the drugs are safe and effective. It really is critical that decisions rely on the team as that's really where the expertise is. That's the way to assure that decisions continue to leverage the deep knowledge and expertise and the understanding of the reviewers and their understanding of the science and of precedent and that what are really complex issues that are challenging, whether during IND development or in the review of NDAs and BLAs are really thoroughly considered and that decisions are based upon complete thorough time-requiring analysis, multidisciplinary input and balancing benefit and risk, balancing the considerations of what's important for public health as well as individual health.

(00:38:51):

I know with staff losses, the teams and divisions are stretched, but it's also clear that FDA staff are stepping up and continuing to focus on helping companies with expert input and advice and giving really good advice and doing good reviews. I know we've also heard about potential changes in processes and approaches to the IND review process, to NDA/BLA reviews and decisions, and even the framework in which those decisions are made. I think one important point to make is that the advice and decisions that FDA staff make, as I've already said, are challenging and they have to continue to rely on deep knowledge and experience. And we also recognize that the drug development landscape has been changing. I mean there's new targets, new molecules identified, more understanding of the genetics, new platforms, I could go on and on with all the changes over the last decade or two decades of drug development, and the regulatory approach has to evolve to keep up.

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I think that's clear, and we've seen some of the key challenges that really are evolving from the changing landscape of drug development. But I also think it's incredibly important, at least from my perspective, that FDA staff on the frontline, the reviewers, the division and the office leadership are engaged and really deeply engaged in considering and advising on these proposed changes. You need to fully understand the challenges, the issues, the processes, the precedent policy, the regulatory framework to be able to effect change and when that change can be successful and where the change leads to an outcome that's the intended outcome as opposed to unintended outcomes. And so changes are important. The landscape is changing. Drugs are, the type of drugs being developed are changing. And so the processes have to change. Maybe even the policy, the regulations and the statute have to change, but it's incredibly important that the broader institution that can leverage the institutional knowledge and the knowledge of the science and the knowledge of drug development is engaged in that process.

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A top-down process in making changes here and particularly given the complexity of what FDA does is really unlikely to be terribly successful. I think it's incredible that not just in terms of making decisions about individual programs be bottoms up, but when we think about changing process and policy, that that be a bottoms up approach as well, leveraging the incredible experience that reviewers and division leaders and office leadership brings to their continuing to be dedicated and achieving their mission. I think they can be part of the change, but if they're left out, I really then do worry about what that change will result in. Again, it's a pleasure to be here today. Thank you for the invitation. I look forward to the discussion on some of these issues that we're going to have over the next hour.

Zan Fleming (00:41:54):

Well, thank you so much Peter. That was just super. Very clear summation of the opportunities and challenges that have right now. And maybe we could bring in Tim, who's an old hand at this and are also responsible for making a smile. I hope he will do that. But Tim, you have some related thoughts about institutional memory and the larger role of FDA and helping to protect public health.

Timothy Franson (00:42:37):

Thanks Zan. Thanks to all of my fellow panelists. Very interesting discussion. And thank you to all of you in attendance. I saw some very familiar names and wish you well in 2026. As Zan said, we all have concern for how well we conduct shared learning, and FDA's oversight of drug development and approved treatments does not exist in isolation. We're talking about development as a critical cog in the overall public health machinery and especially for communicable diseases, with the other cogs being surveillance and prevention capabilities. So like any complex machine, when one cog is altered dramatically, the whole process is impacted and requires contingency planning. So for this three-cog public health communicable disease machine, there are recent changes with respect especially to vaccines. And without getting into politics, just talking about policy and subsequent industry retreat from new development, at least based on recent announcements, there is a concern that that is dramatic. Likewise with surveillance changes, and we no longer have the same international radar equivalent for resistant organisms and new pathogens.

(00:44:01):

So that indicates that two of the three important cogs in this machine are not turning as we would be used to, and therefore the remaining cog that of drug development needs additional incentives as a counterbalance to any possible negative influences from those changes. Let's take measles as one example. It has one of the highest transmission rates of person-to-person spread. For every one case, eight additional individuals may be exposed, and there are certainly new surges as now vaccine use has been declining and not encouraged in some settings. The critical point there is there's no approved treatment, there's no antiviral, there is no other intervention, and the purported use of vitamin A has led to toxicity in livers as a result of accumulation of a fat-soluble vitamin at higher doses. So overall, we need additional thought about how to integrate surveillance, prevention and development of new therapeutics in order to assure that we have that critical balance for public health.

(00:45:21):

It's kind of analogous to seat belts, we're required to wear them, it's for our own good. It's not necessarily something that we find comfortable, but it does protect ourselves and others. So, overall the risk benefit in communicable diseases has been impacted. So, I would say it's not a Wow! and it's kind of a Yeow?!, but it's more like a Holy Cow! because to me it's a flashback to my infectious disease career in the sixties, seventies and eighties. I've lived through the sixties twice and that isn't necessarily fun. The 1970s were a time of learning when we understood epidemiology better, and I would reflect that if we try to relive the seventies again and have not learned well from our past experience with resistant pathogens, that would be unfortunate for public health overall. So in concert with that, I think the other concern to raise is relative to the pediatric drug development ecosystem. Certainly a number of the vaccine susceptible illnesses relate to pediatric use, and the importance of pediatric drug and vaccine development is absolutely vital as we see with evolving pathogens, the Nipah virus and its outbreak in Western Bengal in India being the most recent media example. The bugs outnumber us, and they may be smarter than us, so we need to prepare for them accordingly.

(00:47:03):

And Zan, I'll stop there. I know we have other things to discuss, and I'm happy to come back to this later if we have time in the lightning ground.

Zan Fleming (00:47:13):

We'd love to, Tim. That was so eloquently stated. We thank you for that. Let's do get down to where the rubber meets the road in terms of FDA capability and actually staffing. What about the drama that we've seen? Maybe we don't need to focus on the drama of management that we've seen at FDA, but what maybe bringing back Steven, who is a student of FDA, what are your thoughts about the state of FDA management and personnel?

Steven Grossman (00:48:04):

Okay, I think a good prelude to that would be the poll questions, if we could get those u.

Zan Fleming (00:48:12):

We can do that. Okay, thank you. So the first one is, FDA had 24 senior leadership slots in the fall of 2024, a year later. How many of these vacancies remain unfilled? So quickly make your choice, and then Emma will report out. Alright, 16 or more. And, the correct answer, Steven?

Steven Grossman (00:48:51):

Yeah, and I think somehow the question got changed a little bit, although everybody got the answer right, which was how many have new occupants or remain vacant? And the answer is out of 24 senior slots, 21 of them are either vacant or have turned over to new occupants. And the critical issue there is if you talk about science-based decision making, if you talk about precedent based decisions, the loss of institutional memory is something that I think we're all very conscious of. Every one of us here has spent time in or around the agency over many years, and we know how important it is to have a viewpoint of how do you regulate.

(00:49:41):

I made an observation that a newsletter picked up on that there was nobody remaining who actually remembered what a good day at FDA looked like, and that's a problem in a science-based organization. I think some of the others have come up in conversation, we have other ways of slicing that I thought were valuable. What happens when so many people are new? So many people have never been regulators before. Another angle, which I think is important is how many of the new people coming in have been in positions where they were held publicly accountable for decisions? It's from day one been a concern of mine with regard to Secretary Kennedy that his predecessors had managed large organizations, yes, and he hadn't, but that almost all of them had been in positions where they had to report to shareholders, they were public health leaders, they ran organizations, and they had to get up in public and feel what it feels like to have your words sent back to you in maybe unflattering terms or to realize that what you did might've accounted for 50 people dying. And, that's a solemn responsibility and it's best, you do better at the second and the third time you're in it.

Jodi Scott (00:51:15):

Yeah. Steven, let me add a little bit of perspective from the device side. I think we've had a little bit more stability at the leadership level. So Michelle Tarver's been in her role since October of 2024. That's been great for the device side. I also think that the staff has been very impacted because one of the things about CDRH is the breadth of technology that it covers requires a lot of really technical reviewers. And in the last two years, the need for people in the agency who really understand AI and machine learning to be able to review those submissions because AI and ML has had more impact in two years than hardware has had in the previous 20, right? Both on the

industry and in the agency. And I think some of those, what I call the new cool technologies and the people who understand them at the agency were really most impacted by some of the changes in personnel. And so, we need them from the industry perspective, we need those people at the agency who understand the technology deeply, who are in a position to review those submissions and ask thoughtful questions, scientific-based questions so we can actually get those products approved because I'll tell you what, we knew they were coming, they're here, and the agency is grappling with how do we review these really technical technologies that have a real positive impact on patient care and health.

Zan Fleming (00:52:52):

Jodi, I'm so glad you jumped in and just to say we are delighted that you've joined us as a new panelist and what great expertise you bring in the device and diagnostic field and AI in particular. We're going to come back to those subjects in just a moment, but just terrific to have you in that great articulation. But maybe to close out here, we have maybe one more question and Emma, you can put that up can be done very quickly, and this is sort of related to the, that's number. Oh, okay.

Emma Snyder (00:53:40):

It's okay. I switched the order. We have two questions.

Zan Fleming (00:53:46):

Yeah. Alright, well how many people served as center director, including acting, at CDER and CBER combined during the calendar year 2025? And quickly put your answer. I mean, we're sorry for those who are not drug or biologics people to be dwelling on these, but okay, well, and the answer is

David Fox (00:54:15):

Nine to 10.

Zan Fleming (00:54:16):

Nine to 10. Nine to 10. Okay. So not too far off. And the follow on question? Yeah, how many people served as senior director at CDER and CBER combined in the 30 years prior from 1994 to 2024. And quickly put your first hunch in, and the answer is seven to eight. Seven to eight.

David Fox (00:54:52):

So the perspective we're trying to bring with this question is that from the beginning of PDUFO, which we mark this 1994 and conveniently 30 years even to 2024. So in that 30 year period, we had seven individuals serve in those leadership positions. It's eight if you count Janet Woodcock twice, she had two different terms as CDER Center Director, but we had fewer people over the last 30 years leading the two major therapeutic centers than we have over the last one year.

Zan Fleming (00:55:31):

That is quite remarkable. Well Dave, stay on, as we bring Frank back. We'd like to talk about this thing called CRL. First of all, for those who may not know, maybe Frank, you should tell us what a CRL is, and then let's get into this as one policy change that is of interest.

Frank Sasinowski (00:55:53):

Yeah, thanks Zan. Dave just mentioned we're talking about PDUFA. And PDUFA created this system where at the end of a review, you have two options. In the old days, you used to have three, you'd get an approval, an approvable or not approved. And with the PDUFA, it changed it, it's binary. You either get an action that's positive, an approval, or you get a Complete Response Letter. And so when you get a Complete Response Letter, those had always been kept confidential. FDA had never disclosed them until recently. The FDA made a policy change and decided to release Complete Response Letters CRLs, Dr. Mary Thanh Hai, who has succeeded Peter Stein as head of the Office of New Drugs in the Center for Drugs, that she spoke earlier this month at a regulatory science summit in San Francisco. And she said, now that we are releasing CRLs, we in the agency have to think differently about how do we craft them, how do we draft them?

(00:57:00):

So one idea I wanted to have in a poll, and so Emma can put up the question, but the idea of the poll is that, would a template help in order to have more consistency in how these are written from division to division? And in order to encourage maintaining a focus on the key messages, which should be on the deficiencies and then how to improve them, what about having a template where, for instance, the FDA CRL would have a box to say, alright, was your deficiency: manufacturing, was it safety, was it efficacy, was it risk-benefit, or something else? And then list the deficiencies and perhaps add something about how to address those deficiencies. So that was the question. So yes. Okay. Well it was a crazy idea, and I'm glad it met with a positive response.

Zan Fleming (00:58:00):

And I think Dave, you can come in here too, along with Tim even, to talk about how this is a issue that ultimately relates to the public's trust and yet balancing that against the rights of companies to have some kind of privacy about their assets. How do we make this trade off?

Frank Sasinowski (00:58:33):

Let me just say before you inviting other people in, just want to say one more thing I should have said that. I'll just put on a lawyer's hat for a nanosecond. Most people say, "Is Frank really a lawyer? He never does any lawyering." But really because of these CRLs, because they're not being publicly released, I have sponsors who are terribly afraid about shareholders' actions because the CRL is written usually in a tone that's similar to preliminary responses that the FDA gives each sponsor before a meeting. That is, it's kind of a very conservative position because the decision maker had to make a call whether to approve or not approve. And when you make a call, it's almost a human thing. When you make a call to say not approve, you're going to make sure everybody understands how that was a great decision, which means that it's going to be the same way in approval. It's not always a hundred percent certain and there's a lot of ambiguities and uncertainties, but when you write the approval letter, you are pretty positive because you want to support your decision. So because of that shareholder actions and there's lawsuits and who knows whether FDA could be dragged in, so sorry, Zan, but you were turning Tim and Dave. No,

Zan Fleming (00:59:48):

No, this is a free flowing discussion. So, jump in David and Tim or others. Go ahead Dave.

David Fox (01:00:00):

Well sure. So the CRLs, they're not definitive denial letters. They're more in the nature of an interim or intermediate articulation of where the agency stands at a moment in time. So they're part of a longer conversation. I think one of the difficulties is all you have is the CRL to go on, you're really picking up, you're jumping into a conversation that's been going on for a very, very

long time, and there's a lot of code and a lot of things that are unstated, that can't really be stated unless you turned over the entire record. I think it's interesting that the policy change to releasing CRLs has been met with little to no resistance from the industry.

(01:00:56):

There was a longstanding principle that NDA submissions, BLA submissions were inherently confidential, and therefore you couldn't release anything until there was a final approval. But since companies themselves do a lot of talking about their own applications, that confidentiality point kind of went out the window. And so I think from a legal perspective, the Agency weathered whatever storm there was going to be and gotten through that. So now I think the interesting question is what will evolve in the substance and the breadth of CRLs? And there's talk now, and I dunno if Dr. Hai's point, how that will play out, is the agency going to start writing the CRLs differently. But the other part is the agency can start releasing its action packages that are underneath the CRL, and that will get really interesting and really it's kind of like a slippery slope issue. Once you're in for a little, are you in for a lot? I think one of the other possibilities here is companies may have to start releasing their own sort of counternarrative

(01:02:09):

To the CRL, all of which is to say it will force more information into the public view sooner. And maybe that ultimately is a good thing. We all know a lot of this information does get out there early when we have advisory committees. So it's been an imperfect disclosure system so far. And so I wouldn't say this is a Yeow?! or Wow! It's a kind of a wait and see evolving story. I think it's interesting. The last piece I'll say is when the bolus of CRLs were released, the historical ones, I think the first thing I saw was instantaneously, a lot of the investment analysts put out what looked like AI crunching of them. And I thought it was very interesting when you applied AI across all of these CRLs, how little you actually learned because they're all so unique. And so to try to mush them all together and try to come up with some thematic aspects of it, you might really generally end up with mush.

Steven Grossman (01:03:17):

I add a point on this that I think because my view of the release of these is that it's good on balance over time, but that's completely instinctual and not analytic. But there is an analytic component to all of this, which is that companies have relied on input from the FDA for long periods of time, that the layoffs, the retirements, the leadership turnover all create some additional jeopardy for the companies where they have been telling their shareholders, let's assume honestly, that FDA is saying A and B and C, and suddenly there's a new review team, and they see some of the settled issues differently, and there's something that looks abrupt compared to the company's narrative that was not the company's fault. Now I don't think it changes my view of whether or not this is a good evolution, but I think there are more than the usual amount of bumps than say if this policy had been adopted three years ago

David Fox (01:04:34):

In terms of securities litigation issues. I think it's just a matter of timing. It changes the timing, but the CRLs become available through discovery anyway if somebody can plead a case. So I think it's more of a timing question. I don't think it's categorically going to change. It will get more interesting if the CRLs become more editorial and longer discussion topics. It'll add another layer of complexity to that area of litigation. But I think what's unfortunate is companies may face securities litigation earlier in their overall process before they've had a chance to respond to the CRL and remedy it and resubmit and ultimately get approval. So it might be some wasted litigation research.

Steven Grossman (01:05:27):

Right? But I see this as a narrative problem before it's a litigation problem.

Timothy Franson (01:05:32):
Yeah, I think —

Steven Grossman (01:05:33):
Companies are raising hundreds of millions of dollars based on a narrative and the presumptive honesty of them in conveying that narrative. And now things have changed abruptly, and they may not have changed abruptly for anything that was the company's fault. The stock goes down, they have troubles making points in public because, well, what are they really up to? So the litigation point is legitimate, but I think the problem created a change I favor, but a problem that's created by it is more than just litigation.

Timothy Franson (01:06:11):
So I think think there is a learning point here, and I would invoke the great philosopher Yogi Berra who said, "If it wasn't for time, everything would happen all at once." In the case of CRLs, it happened all at once without notice-and-comment rulemaking. So every sector from industry to investors and so forth did not have the opportunity to put together some kind of cohesive, what does this mean? And we're still left with whether there is a consistency or inconsistency of actions across divisions and centers. So I think it's hard to look at decisions as new precedents until some of this gets sorted out.

Zan Fleming (01:06:56):
I think that's a great way to end this particular segment. CRLs is an issue to watch and we'll keep doing that. Let's do shift gears and go to the Center for Devices and Radiologic Health and our expert Jodi Scott, who again, we're just delighted to have join us for the first time. Jodi, you bring terrific industry experience and leadership and you happen to have a specialty in AI. And boy, that is a hot topic at CDRH and FDA in general, but why don't you give us your thoughts about particularly AI looking forward?

Jodi Scott (01:07:48):
Great, thanks Zan. So thank you for having me. I think with AI, I'll start with saying everybody's doing it. It's kind of the new hot full topic. We knew it was coming, but it has clearly accelerated. In terms of on the device side, the number of 510(k) clearances has increased dramatically. There were, I think in 2025, about 295 of them with AI/ML components to them. 62 of them were software as a medical device, with some radiology component in them being about two-thirds or so of them. So it is a part of so many medical devices and I should say FDA has been reviewing products that we would probably call AI and ML going all the way back to 1985. Of course we didn't call it that back then, but they were based in AI. But there, just an incredible explosion in technology with some AI component, whether or not that is in its development of the product or actually active and live in the product itself.

(01:09:02):
It's changed a lot of the ways that FDA looks at the technology and the way that they review technology. I think we should also mention that FDA is using AI within its own organization, both for reviewing submissions, also to get the efficiencies that you get on some of the things that really don't require what I call the humans being humans to do, but sort of the administrative efficiencies. But also I think in some ways substantively as they go through their review process to sort of get through some of those applications. On that front, I should say FDA, they're learning the same way that industry is learning on how to use AI. They have the same challenges that we

have. Anytime you use it, I always tell folks that the AI, the algo, it's a sycophant. It so desperately wants to give you an answer, and sometimes it's willing to lie to you in order to do that.

(01:10:00):

And so that requires humans to continue to be humans and be the last line of defense against the algorithm. And so Agency, industry, we all have these same challenges with the use of AI, but we are definitely seeing them. They've announced that they're using ELSA within their reviews and within the agencies on the device side primarily, but also on the drug side. They are using it for their identifying signals within adverse event data. And we're definitely seeing them follow up where there may be something that looks like they're seeing something in the field. They're also using it to plan and prioritize their inspections. Where are they going to go next? Who do they need to see? Is there something going on someplace that the agency needs to check in on? So it is definitely transformative both on the agency and the industry and what the agency is having to review.

(01:10:57):

I should also say we've got coming this year, next week, the quality management system regulation goes into effect on February 2nd. And so that's a dramatically different change of thinking about quality systems. Interestingly, AI has an impact there as well because if you think about for years we've been really focused on manufacturing. Where it's hardware technology, you have a manufacturing facility that does traditional manufacturing. Now there's a lot of companies where their manufacturing facility is really just design and development and a bunch of guys in a conference room and their production process is pushing the software out into the cloud and to the patients. So lots of changes on the CDRH side, and I think it's only going to continue to increase. One other point, which is worth mentioning is that we're also seeing a huge uptake in de novo authorizations because, in between the 510(k)s and the PMAs, but a lot of these AI/ML SaMD products are moving through the de novo authorization process.

(01:12:21):

And so it can be a real strategic advantage for companies who are able to make it through that process. But it's really interesting how AI is shaping kind of everything. And one more point, I should also say, the drug and the biologics companies, they're not out of this either. Every pharma company has somebody whose job it is to think about what are they going to do with AI and ML, both from a company governance standpoint and also from a product development standpoint because the power is incredible. So it's an area that is moving fast. Everybody's in it. So I say, hold on, but pay attention because there's a lot of really good things coming.

Zan Fleming (01:13:08):

It's good advice. And wow, what a great summary of what is another very important part of FDA, and one that is particularly dynamic. I wish we could spend more time on CDRH, but let's take the opportunity to go to the F in FDA and we're delighted to have join us for the first time, Ricardo Carvajal, who brings preeminence in this area, a former FDA senior official, and now a senior partner who is a particularly well-suited expert for this next discussion. So Ricardo, so much you can talk about, but why don't you just get going.

Ricardo Carvajal (01:14:08):

Zan, thanks very much to you and your team for inviting me in for your leadership and organizing this event. So 2025 was a difficult year for the Human Foods Program or HFP. The entire program had been reorganized toward the end of 2024, was still trying to find its sea legs and then came the change in administration and DOGE and the government shut down, and the results were pretty chaotic as staff retired, were fired, resigned, or reassigned. I think it's hard to overstate the impact of that chaos. Let's recall that even in the best of times, the HFP runs pretty lean and is

almost entirely dependent on congressional appropriations, which makes it especially vulnerable to any kind of disruption. So not surprisingly, we saw very little activity in the form of new regulations or guidance documents, but much of the day-to-day work — inspections, enforcement activities, pre-market reviews — that continued us before, albeit more slowly and in some cases much, much more slowly to the chagrin of some of our clients.

(01:15:28):

If we zoom out to a policy level, we have to start by remembering that historically the HFP has focused on the twin pillars of food safety and nutrition. But much of the agenda for the past 15 years was driven by the obligation to implement the Food Safety Modernization Act of 2011, or as we so fondly refer to it, FSMA. FSMA forced FDA to focus its food resources on developing several major regulations, many new guidance documents, really dozens. And the goal of that herculean multi-year effort was to implement a regulatory system designed to prevent food contamination from any source. So food safety in the classic sense. As 2025 began much of the FSMA work had been done, and we had a new sheriff in town with other priorities. The MAHA movement took center stage, and it's pretty clear that that is going to continue into 2026 just judging by the list of priorities that the HFP published on the FDA website just a few days ago.

(01:16:40):

So to pick just a few examples, we can expect more emphasis on the role of nutrition in chronic diseases with HHS and USDA playing lead roles. And we see that in the recent issuance of the new dietary guidelines. We can also expect greater attention to the association between ultra-processed foods or UPFs and chronic diseases. And that issue, it was actually run up the flagpole toward the end of the previous administration, but I think we'll see that one take on greater prominence. And then finally, one of MAHA's animated concerns has been the safety of substances used in food, including color additives, processing aids, and direct food ingredients. And let's delve into that last one a little bit because that's where the new administration made its biggest splash and rolled out a playbook that I think could be used to target any product or any product category that falls out favor.

(01:17:43):

So to help set the stage, first a little background on FDA's regulation of color additives is in order. In essence, any use of a color additive in food has to be approved by FDA through the issuance of a regulation that establishes safe conditions of use. And because this requires a careful evaluation of safety and also requires rulemaking, approval of a color additive typically takes at least a couple of years. So conversely, any revocation of the approval of a food additive, of a color additive, is also going to require FDA to carefully reevaluate safety and to determine that the approved use of the color additive is no longer safe, followed by rulemaking. So that also typically takes at least a couple of years. Well, we are definitely not in Kansas anymore. So in April of 2025, FDA and HHS issued a press release announcing measures to phase out the use of all synthetic colors in food

(01:18:48):

by the end of 2026. The program staff at FDA seemed to have no idea the announcement was coming. The decision appears to have been made at the top and rolled out without the input of staff. And shortly thereafter, the administration began a campaign to pressure companies to abandon their use of synthetic colors. There were high level meetings between the government and company CEOs, and then FDA created a webpage that started tracking companies' pledges to remove synthetic colors from their products. Now ask yourself as a company CEO, could you afford to not have your company's pledge on that webpage? The administration also made explicit shows of support for new state laws that ban synthetic colors. For example, laws passed in West Virginia and Texas, just to name two. So in effect, if you look at that whole package, it was an end run on all of the substantive and procedural safeguards that would normally apply when FDA revokes its approval of a color additive.

(01:19:54):

I don't think any of us spends too much time day in and day out thinking about those safeguards, but some of them were built right into the Federal Food Drug Cosmetic Act by Congress. Others are built into the Administrative Procedure Act, which is a good government law that's been in place for decades and still others are built right into FDA's on regulations. And I think one in particular that I'd like to call out because it's frequently forgotten, is the good guidance practice or GGP regulation at 21 CFR 10.115. Through the GGP regulation, FDA established requirements for the issuance of guidance documents. And if you look at the definition of guidance document in the regulation, it explicitly excludes informal communications such as speeches, editorials, media interviews, press materials. The regulation then goes on to plainly state, and here I'm going to quote, "The agency may not use documents or other means of communication that are excluded from the definition of guidance document to informally communicate new or different regulatory expectations to a broad public audience for the first time." The origin of that regulation lies in the fact that some FDA officials decades ago were using speeches and press release materials to communicate new and different regulatory expectations to industry and the public. And that wreaked the kind of havoc that you'd expect.

(01:21:29):

Now, I'm not suggesting that the current incarnation of FDA is ditching procedural safeguards altogether or that the playbook that we have seen rolled out with synthetic colors could become the norm. But to the extent that that playbook succeeds, and I think the jury's still out on that one, I think the temptation to use it again may prove irresistible. That's all I have for now, and I think we go to Steve next.

Zan Fleming (01:21:54):

Wow. Well, Ricardo, that is amazing. Certainly a very compelling articulation and fascinating to us who forget that the food part of FDA gets but about 20% of the budget, but it actually regulates much a larger proportion of the consumers' spend compared to drugs and biologics and devices. So thank you so much for that. That was terrific. We are running out of time, but let's do a free-for-all here. And that will be to bring in Steven and others who are students of Congress and its oversight of FDA. Let's talk about that, about where is Congress now and all of this ultimately having a responsibility for what FDA and other agencies do.

Steven Grossman (01:23:03):

Yeah, let me do a quick, because it's like a punchline: this time is different. Well, in terms of congressional ability to function, this really is a unique situation and I don't think you understand what is and isn't happening to FDA compared to the past, relative to Congress without understanding that the House is at a record tight margin between the parties. I go back a number of decades, I remember the Senate changing because of a change of party. I don't remember the House ever being dependent on special elections as to who is in charge of the body. It is possible that if less than a handful of people were to be in a plane crash tomorrow, then suddenly the Democrats would be in charge of the House. I'm not predicting that. I'm not saying that would be good. But that's one piece.

(01:24:11):

The second is that the Senate itself is always, you need 60 votes to really do anything of any consequence. So the Senate is traditionally tied up and you have the two situations in the face of an administration that has advanced something called the unitary executive branch perspective. And so you have an aggressively ascendant executive branch in the face of Congress that's trying to figure out how to operate at any level given the historical circumstances. So within that, I think all of us look and say, "Well, it used to be that there'd be a hearing. A congressman would call up and raise a question." And a lot of that's not only not happening right now, and it's not very

effective, but that is bound up in the circumstance. It's not particularly FDA-specific. Now, that's one slice. The other is that FDA has also had two types of relationships with Congress.

(01:25:29):

One is structural and the other is personal. The structural is at least every five years, FDA policy is front and center because of the user fees. The fact that FDA is science-based means that historically Congress has been interested in what FDA does and has had a lot to say, but it always has structured it less, have you given this due process rather than saying, "You got this wrong, please do X, regardless of what you think." So all that's been good. The personal side is, but again, is handicapped by the current situation and the personal side is also kind of different. And the paradigm for this is Scott Gottlieb. In the years after he departed, we'd be doing Alliance meetings on the Hill and people would say things, staffers would say things like, "Our bosses miss Scott."

(01:26:35):

It was just like, oh, okay, why is there any difference? And the answer uniformly was, "He gave our boss his personal cell phone, and he answered it." Now, I don't think any sub-cabinet office and maybe not any cabinet officer right now actually has that capability in this administration. They just aren't supposed to talk to Congress. They're supposed to be very concerned about the chain of command. And so I think that we are in a unique situation where Congress is frustrated on a lot of levels and does not have any of the traditional avenues either structural or personal to be able to respond. That's a quick one person's view.

Zan Fleming (01:27:26):

Well, and so well said. And from a person who has been studying Congress for many decades. Very incisive, Steven. David or Frank, any follow up comments related to Congress and maybe the upcoming PDUFA negotiations?

David Fox (01:27:50):

Yeah, I was going to just say on a more sort of prosaic level, we are in PDUFA reauthorization season. Always the question: will it be a sort of clean reauthorization, PDUFA only, or will more substantive changes to the Act be tacked on, and will we get a more complete package? It's sort of every other five year cycle. We get clean-to-heavy, clean-to-heavy. We potentially set up for a heavier cycle this time. There's been a lot of conversation over the last few years about creating an ultra rare disease pathway. There was different legislation people followed — Frank nodding — Promising Pathways Act, potentially some modification to the substantial evidence standard to recognize mechanism of action and plausible pathway hypothesis as an underlying basis for getting to substantial evidence. So that's a possibility. There's some possibilities around Orange Book reform. Patent listing is always a hot topic, sort of competition issues. And then I'll just lay down a marker. I would love to see 2026 be the year of THRIVE, or 2027, so I'll leave this to Zan, but we're very, very interested in preventive healthspan, deferring onset of chronic diseases, and we think we've worked very hard on a potential legislative solution to create an FDA regulatory pathway to encourage the development of healthspan drugs, devices, foods, dietary supplements. So that's aspirational on the legislative front, but I think we're going to keep working at it.

Frank Sasinowski (01:29:44):

I think the only thing I would add, Dave, that, was a great list and the only thing I would add to it is PRV, is that that's something that many people are kind of —

Zan Fleming (01:29:53):

Pediatric vouchers.

Frank Sasinowski (01:29:56):
Yeah, the Pediatric Priority Review Voucher.

David Fox (01:29:58):
Yeah. It seems like reauthorization of that is almost an automatic. I know, it's annoying that it keeps coming up.

Frank Sasinowski (01:30:07):
I mean, we've seen it come very close sometimes.

David Fox (01:30:11):
Yeah, but I mean, yeah. Yeah.

Steven Grossman (01:30:16):
If I could just do a final thought on the user fees. It's going to be a heavy package this year. There's an inverse relationship. The more Congress has opportunities to legislate in the interim five years, the less pressure there is on the user fee package. Given my general comment about the frustration of Congress right now, I have to assume that the list has upwards of a hundred or more items on it that Congress feels strongly about. It will be after the parts that most of us are concerned about, which is how does it affect the companies and support the funding of the Agency? The list is going to be extremely long, and they're going to be a lot of people who are going to say, "If I don't catch this train, I'm going to wait five years. And that's too long."

Zan Fleming (01:31:13):
Right, well, what a great way to end. The time has just shot right by. We've left a lot of things on the table including a list of lightning round questions, and I'm going to see if we can get some responses from our panel to those, and we'll publish them, along with a transcript of our program that you'll receive, and Thomas will tell you more about that. I'm also very glad that Dave Fox mentioned the THRIVE Act. That's something that you'll hear more about. Dave is a co-author, and this is very important legislation that I hope will take centerstage soon. We've got so many things that we'd love to talk about, but let me just thank you for joining us and mention the tie that binds all of us is love and respect for, or the art and sciences of health product development, and getting these products to everybody who needs them. So let's both celebrate this calling, I would say, and keep responding to that calling. And with that, we're going to conclude our formal program with Thomas and a few quick housekeeping items. Thomas?

Thomas Seoh (01:32:54):
Sorry, had to unmute. Terrific. The discussion has been terrific. Just a reminder that all registrants will receive a link to this recording within a day or two. We do want to mention that our not-for-profit Kitalys Institute will be descending from the cloud where the COVID pandemic forced us to go to hold our first in-person conference on Targeting Healthy Longevity October 1 through 4, 2026 in Hong Kong with our partner, the APAC Longevity Medicine Society. Please watch your inbox for details. So with that, the formal portion of this event will close. And thanks to the speakers and to you, the audience for your attendance, passing the mic back to Zan for our post-panel after-party.