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# Opening Remarks

### Dr. Sam Raney:

Good morning, everybody. I'd like to welcome everyone to the fiscal year 2025 generic drug science and research Initiatives public workshop. My name is Sam Raney and it's really a pleasure to see everyone here today. The purpose of the public workshop is to provide an overview of the status of the science and research initiatives for generic drugs and to provide an opportunity for public input on these initiatives. FDA hosts this public workshop every year as part of our commitment under the Generic Drug User Fee Amendments or GDUFA. We welcome hearing any comments you have during our panel discussions. We invite you to provide your comments via one of the microphones in the aisle. For our virtual audience, we welcome your comments as well, which can be submitted to the docket for the public workshop via the QR code that you see on the screen here or via the other QR code, which is to the web page for this meeting on FDA.gov, which also has a link to provide public comments. We'll be monitoring the docket during the workshop, and we'll do our best to incorporate your comments into the discussions during the workshop as well. For people here in the Conference Center, coffee and light snacks are available in the lobby until 2:00 PM each day. No coffee is available during the afternoon breaks, which are after 2:00 PM, so you may want to get your cup of coffee before the end of the lunch break. Restrooms are around the back to the side. With that, I'd ask you to please place your phones on silent and join me in welcoming our first speaker, Doctor Susan Rosencrance, who is the Deputy Super Office director of FDA's Office of Pharmaceutical Quality, and she provides her welcome and opening remarks.

### Dr. Susan Rosencrance:

Thank you, Sam, and good morning, everyone. It's a pleasure to join you today in this public workshop focused on generic drug science and research initiatives. I'm sure you're all aware that one of FDA's top priorities is to improve the availability of high quality, safe, effective and affordable generic drugs for Americans. When it comes to the timely development and regulatory assessment of generic drugs, one of the most critical programs under GDUFA is the generic drug science and research program. That's because this program helps reduce regulatory barriers and promotes competition among drug manufacturers. It also ensures that

bioequivalence and product quality standards reflect advances in gold standard science.

The Office of Pharmaceutical Quality, or OPQ, which I represent, contributes to the assessment of new drug applications, biologics license applications and, of course, abbreviated new drug applications or ANDAs. Additionally, OPQ and the Office of Generic Drugs jointly lead many GDUFA funded research projects. Overall, though, the GDUFA science and research program involves coordination and collaboration across FDA. Some of the other collaborators include the Office of Translational Science within CDER, FDA's Center for Devices and Radiological Health, FDA's National Center for Toxicological Research and FDA's Office of Inspections and Investigations. We also work closely with research collaborators at institutions around the world and with the global generic drug industry.

GDUFA funded research improves the efficiency with which generic drugs can be developed and evaluated, and this benefits public health in two critical ways. First, it makes it more feasible for manufacturers to develop generic drugs, which facilitates competition and reduces the risk of drug shortages. Secondly, it improves the health outcomes of patients by helping to make safe, effective and high-quality drug products more widely available.

The beauty of science is that it's not static. Rather, it's dynamic and the continual advances in emerging issues in pharmaceutical science and manufacturing provide opportunities and challenges for generic product development. You can't always predict where science will take you. Consider that at the start of GDUFA II, nitrosamine impurities weren't even a topic of scientific discussion. Yet our most recent GDUFA science and research report began with methods for analyzing the growing number of nitrosamine impurities.

Furthermore, not all products are the same. Some generic products are relatively easy to develop, while others may bring great challenges for characterization or the assessment of immunogenicity, for example. The outcomes of GDUFA funded research expand our understanding of drug products and contribute to the development of state-of-the-art analytical procedures to characterize product quality and performance. New or modernized analytical procedures provide manufacturers more efficient approaches for developing generic products, leveling the playing field for greater competition.

Each year we have seen GDUFA funded research making it more feasible to develop generic products, products that were not viable as recently as just a few

years ago. We have tangible results to cite. A good example occurred on July 1st of 2024 when FDA approved the first generic bupivacaine liposome injectable, which references EXPAREL. This first generic approval was a notable achievement due to how scientifically challenging it was to develop a bioequivalence approach for this product, which uses a complex liposomal dosage form. GDUFA funded research helped to develop recommendations for the physical, chemical, and structural characterization of the product, as well as the relationship between in vitro product characterization and in vivo performance. It supported the development of a product specific guidance and prepared FDA to assess the adequacy of information submitted in the eventual application.

The approval of bupivacaine liposome injectable, a complex generic, exemplifies what can be achieved for patients with effective coordination between FDA and the generic drug industry. It goes without saying that our collaborative engagements through the GDUFA Science and research program have been highly effective at addressing scientific challenges for generic product development and assessment. Through this program, we help to ensure that the generic drug industry has and will continue to have the most efficient and modern tools needed to overcome barriers to generic drug development.

In closing, I want to note how proud we are in OPQ of our collaboration with OGD on GDUFA funded research projects.

### Dr. Iilun Murphy:

Good morning, everyone. Here at the FDA, we work every day focused on the needs of millions of American patients who rely on generic drugs. We understand the tremendous value the generic drug program brings. More than 35,000 generic drugs have been approved and more than 90% of prescription drugs are generic drugs. The program has an average of around 700 full approvals of generics every year and US generics save our healthcare more than a billion dollars a day.

FDA conducts economic analysis to understand the quantitative impact that new generic approvals bring in each year for the US public. For example, in 2022, just from the generic approvals that year, there was almost $19 billion in savings. Among those, about 20% comes from first generics, those approvals for which there are no previous generics available.

The GDUFA program has been instrumental in providing FDA needed resources to allow for more timely review of applications. Prior to 2012, there were large application backlogs and there was not an easy way for us to provide as much

guidance on the optimal ways for applicants to demonstrate bioequivalence and meet other scientific requirements. In parallel with increased efficiency in reviewing applications, GDUFA allows for advancement of scientific development of generic drugs. This is through funding dedicated to advancing research in areas where generic development has been limited.

Each fiscal year, we reach out to our stakeholders to establish research priorities for the most pressing scientific challenges they face with generic product development. Scientists and clinicians from industry, academia, and the FDA then strategically design research projects and studies so they can look at the research outcomes that enable FDA to build scientific bridges across the knowledge gaps. Similar to previous years, FDA will take the information it obtains from this public workshop into account in developing its FY 2026 GDUFA science and research initiatives.

Over the three cycles of GDUFA, there's been clear positive impacts of the GDUFA science and research program. We've been intentional in tracking research conducted and the applicability of the data obtained. Our pre-ANDA program focuses on stronger communications with applicants prior to ANDA submissions. This allows for improved development of products and applications. In addition to offering meetings with applicants, FDA's recommendations related to bioequivalence issues and product quality are communicated through continual publication of new and revised product-specific guidances as well as general guidances for industry.

In FY24, FDA issued 206 new and revised PSGs, half of which were for complex generic products. These provided recommendations for developing generic drugs and for generating the evidence to support ANDA approvals. This included 147 PSGs for products with no approved ANDAs at the time of PSG publication. The recommendations in many of these PSGs would not have been possible without the GDUFA science and research program, and the impact of research is not just for complex generics, but for all generics.

As part of FDA's commitment to expanding its collaboration and communications with industry, we work closely with the Center for Research on Complex Generics. In 2024, CRCG hosted five scientific workshops on challenging topics for generic drugs, including drug-device combination products, modern master files, immunogenicity risk for peptides and oligonucleotides, nitrosamine impurities, and the modernization of metered dose inhaler products.

We are deeply grateful to all our collaborators for the success of the GDUFA science and research program. The continual advances in pharmaceutical science and

manufacturing, the development of new therapies will be bringing ongoing challenges for generic development, but we remain confident that our collaborative engagements to advance the GDUFA research program is a key way to address the scientific challenges for generics.

In closing, we look forward with optimism, expecting that the outcomes of this research program will continue to enhance patient access to high quality, safe and effective medicines by accelerating the approval of generic drugs and promoting generic competition as a key part of FDA's drug competition action plan. Thank you so much for being here today.

### Dr. Robert Lionberger:

All right. Thank you very much, Sam.

It's a great pleasure to be here at this workshop to talk about our science and research programs and, most importantly, to listen to the input from all of you in the room, invited speakers and panelists, as well as people online who comment through our docket. We welcome input on how to make our programs more valuable for the generic industry and the American public.

To begin, I want to remind everyone why science and research are so important for the generic drug program. If you think about how FDA's new drug program works, it's really strongly based on our gold standard clinical trials demonstrating safety and efficacy for products. Those clinical programs can be very expensive to generate new evidence of safety and efficacy. To have effective generic programs, we use pharmaceutical science and clinical pharmacology to identify what aspects of these products need to be the same, with the goal of identifying products that provide the same safety and efficacy without repeating clinical trials. This is the essence of having an efficient generic drug abbreviated program - the scientific understanding that allows us to approve new versions of these products without repeating clinical studies.

This is true for everything across the generic program, even our simplest tablets and capsules where we use PK studies to look at bioequivalence. That's an alternative to clinical studies because we know that drug delivery ensures similar efficacy. So there's a strong foundation for that.

If you think about the generic industry and how it's changed over time, there are really three pillars:
1. Oral dosage forms (tablets and capsules)

2. Solution products, injectables, and topicals
3. The new emerging area of complex generics

I want to emphasize how much this has changed over the last 20 years. Twenty years ago, 70% of generic applications were for tablets and capsules, another 20% for solution products, and 10% were what we now consider complex generics. The vast majority of those (2/3) were topical and transdermal products, which have a long history. Only 3% of the space in 2004 was for other complex generic products.

Fast forward to 2024, and we've seen a decrease in submissions of oral dosage forms. These are still very important products, but if you ask the generic industry, they've become commodity products. There's been growth in solution products but also significant growth in the complex generic space, now being almost 20% of submissions. There's been a significant increase in all of those non-topical products - complex injectables, inhalation, and nasal products.

So the generic industry is changing, and the economic effects of these products are different. The tablets and capsules have become almost commodity products with very low sales prices and high demands for efficient development programs. Complex generics have become a more important part of the business model for the generic industry, as well as being the category where there are more products without generics available that are important to the public.

I'm very proud of the work we've done over the last 10 years to establish a system for complex generics that has enabled this part of the generic industry to grow and make an impact. These include both our scientific and regulatory processes. The GDUFA science program has really helped enable this, and some of the impacts include:

- Generic versions of dry powder inhalers
- Over 50 topical products approved without doing clinical studies
- Generic versions for long-acting injectables
- The possibility of generic versions of recombinant peptides (something we said could never be a generic 20 years ago)
- Significant advances in quantitative medicine approaches and modeling approaches that help our scientific work across different categories

As products people want generic versions of become more complicated, we're seeing it's not just drug delivery, but also the patient-user interface that's important. Over the past 10 years, you've seen a lot of development in our thinking around

comparing the user interface of combination products to ensure that device constituent parts can be used appropriately by patients when substituted.

Internally, we've built up our understanding through our complex products database to have a full inventory of what products are complex and why. I think one of the big impacts of the GDUFA science and research program has been how it's affected our other regulatory programs, like the scientific advice we give to applicants.

You heard in Dr. Murphy's talk about the PSG value and how important that is to generic competition. In the last 10 years, we have 300 product-specific guidances with more efficient approaches for bioequivalence. Most of those are focused on complex products, establishing ways that people can have a pathway toward a generic submission.

We've also had over 800 pre-ANDA meeting requests since GDUFA II and the introduction of those programs. And those discussions are focused on the scientific challenges. In order to be eligible for those meetings, you have to be doing something where there's not a product-specific guidance or some innovative science and research approach to develop products. Those discussions are informed by our scientific and research foundation for our scientific staff, so when you come in and meet with us on complex product development, you're talking with people who have deep expertise in those product areas.

All of these things work together to help build the foundation for that new pillar of the generic industry business model, which is complex generics - something that really didn't exist 20 years ago.

But it's not just what's happening in the past; it's what's happening in the future. Here, I just took 10 complex products that don't have generic competition and added up their sales. These 10 products alone account for about $25 billion in sales per year. All of these products have complex issues and are very challenging to develop. If you're developing a generic version of these products, there are multiple scientific and regulatory challenges you have to navigate to effectively develop a product.

If you compare this to our total investment in our GDUFA regulatory science program, which is about 5% of the generic GDUFA program (about $25 million a year), you can see the potential impact. If this research activity, our product-specific guidances, our meetings with industry, and our scientific work can just accelerate even one of these products to have generic competition even just one year faster, that's a huge return on investment for the cost of the program.

The cost of the program includes our external collaborators, our work with laboratory scientists, our work with quantitative scientists internally, and the people developing the product-specific guidances and conducting meetings. All of that is really working together toward this goal. There's a huge value that comes from this investment in our research.

The purpose of this workshop is to help us focus on the scientific challenges that will make the most impact in accelerating access to generic versions of these products, especially the products that don't have generic competition yet. We're really open to hearing that and having that discussion with you here today.

The future value of research is also important to product developers. The reality is there will be no generic products that are not economically viable. If we don't have an efficient system for generic competition, some company somewhere has to decide that they're going to invest in product development, conduct the studies, prepare the submission to FDA, and that calculation has to depend on an efficient regulatory system. This includes things like clarity about what studies are needed. This goes to the value of the product-specific guidances - to have a very clear sense of the studies needed to develop a product. Developers can then make a better determination of whether the investment is worth it.

The value of our science and research is that we are constantly attempting to improve and make the process more efficient across all different product categories. You saw last year, for oral tablets and capsules, a significant change as part of a global harmonization initiative in the ICH M13 guidance to reduce the number of fed bioequivalence studies needed. This is not just for complex generics; it's for all products - identifying the most efficient set of studies, making that available through PSGs and pre-ANDA meetings, and also feeding that into the review process. So when you submit an application with novel scientific content, you know that it will be reviewed consistently, and FDA has the expertise available to do that.

Our research program is a constant effort to make our system more efficient in terms of bioequivalence and pharmaceutical development. One of the reasons we're able to do that is the input we get from meetings like this, where stakeholders from industry and scientific experts from the community point out opportunities, challenges in product development, and scientific advances that could be applied. By bringing together this broad community, we really help move this process forward.

Today, in my overview, I want to give a sense of the whole portfolio. This is at a higher level than talking about individual research projects. We try to be extremely transparent about our research projects, so if you go to our FY24 Science and Research Report, you'll find a list of all the research projects supported by the GDUFA research funds at FDA. These include both our internal projects in modeling and data analysis in our offices, projects in our laboratories, as well as our external collaborations with experts through grants and contracts supported by the GDUFA regulatory science program.

We're trying to be completely transparent about all ongoing projects. You can look back at the priorities from last year that we're trying to update this year. We have hundreds of projects, but we try to narrow our research portfolio for this discussion into eight different areas. I'll talk about each of these eight areas to give you a sense of the whole scope of activities and what we're discussing today.

Because this portfolio is so large, we really can't go into depth on all eight topics every year. So we've developed a rotational process where each year we take a deeper dive into some of those areas and invite experts from industry and academic groups to talk about those specific areas to really refine our approach. The science and research activities aren't solved in a year; the program is generally focusing on stable areas, but we do want to continually refine it.

To give you a sense, last year we had sessions on impurities and nitrosamines, quantitative medicine and predictive models, and drug-device combination products. This year, we've picked three other areas from the portfolio to focus on:

1. Complex active ingredients
2. In vitro methods for complex generics
3. Efficiencies for IR and MR generic tablets and capsules

We're also listening through today's workshop for input on our product-specific guidances and which of those guidances should be our highest priorities. If you're not aware and want to know what product-specific guidances are coming out soon, you can look at our forecast list. Those are the ones FDA is already planning to do, and people are assigned to work on them. You can expect them to be delivered on that approximate timeline.

What we're really most interested in today, and in comments to the dockets, are product-specific guidances that are not on that forecast list. If you look at that and think, "I'm considering developing this product, and I think FDA should prioritize

guidance for this particular case," that's something we really welcome as a comment to the docket or a discussion in this meeting. That helps us identify things we might have missed in our planning when trying to analyze what's most important for us to work on.

We also accept this feedback through our controlled correspondence mailbox, where you can request product-specific guidances. We take those requests into account as we're doing our planning process as well. So there are various ways you can provide input on which product-specific guidances would be most valuable to the generic industry.

I'll talk a little bit today about the whole portfolio and how it's really important for any efforts we're making on drug pricing and competition. The scientific foundations are so important to the generic program; if you don't have them, you really undermine the possibilities of competition in the future.

Today's event is intended to be conversational and stimulate discussion. We want to encourage people to provide comments to the dockets. I really appreciate our new Commissioner and his leadership-by-podcast style, where he really has conversations about different topics. You can think of today as a two-day conversation where we'll bring FDA staff, people from industry, and academic experts to talk about the challenges in these particular areas. Hopefully, that will stimulate you in the audience to identify and comment on areas where you can help us identify the most important things for our science and research programs to work on.

You can see the project-level details in our Science and Research Report. Now, I just want to give a broad overview of the different areas, including the ones we're not talking about today, so you understand the whole portfolio and the whole scope of our research activities.

The first area, which Susan mentioned in her introduction, is about impurities. When we're talking about impurities here, the key challenge is nitrosamines. We've had several CRGC workshops on this topic, discussions last year at this workshop, and in previous years. It's challenging for the generic industry in various ways. Through the research program, some of the key accomplishments have been working in our labs to help develop analytical methods that people can use to find nitrosamines. As referenced in past workshops, some of the work that FDA labs have done shows that antioxidants and reformulation can actually reduce the formation of nitrosamines.

Once we recognized that possibility, we identified ways through this meeting to make it easier for applicants to reformulate products to reduce nitrosamines. Generally, you want to reduce any potentially toxic impurities. This led us to science and research activities to look at faster ways to reformulate products without changing their bioavailability. You can see some of these in the 2024 revisions of the nitrosamine guidances. For example, less bioequivalence data is needed for BCS class 1, 2, and 3 immediate-release products based on some of the research that came out of the GDUFA program.

Some things that may come up on our second day are risk analyses for BCS class 4 compounds, where more scientific or modeling work might be needed to help support a more efficient reformulation process for those products. We still hear from the generic industry about the importance of having efficient methods to deal with nitrosamines across the whole spectrum, from our pharm/tox work with NCTR to reformulation and the analytical methods people need to monitor and control these impurities.

The second area, which we'll be talking about today, is complex active ingredients. The goal here is to characterize and understand products that are mixtures of different molecular species. The requirement for the generic program is that generic products have the same active ingredient. So we want to make sure we have the capability to measure and set scientifically appropriate standards for products that are sometimes mixtures of different components or things like oligonucleotides and peptides that have very complex molecular structures and also potential immunogenicity risks.

Here, the two areas of scientific focus are peptides and oligonucleotides. When we began the research program, we really had a commitment to making generics available in all product categories. Over the past 10 years, we've seen a huge increase in GLP-1 peptide products, which have become a huge part of the pharmaceutical space. It's really important that we have appropriate methods for generic products for competition in that space, as those have become some of the largest-selling products. We want to make sure we have generic competition there, and we've seen in the peptides a surge in the number of ANDA submissions for many of these products.

Oligonucleotide-based drugs are an emerging category. No generics have been approved for any of these products yet, as it's still very new. We are beginning to see some submissions in these areas, but we'll talk a lot today about the challenges with developing oligonucleotide-based generic products. We had a fantastic CRGC

workshop on immunogenicity last fall, and we had the first generic approval for a liraglutide product in December of this year as well. This is an area where the demand for affordable generic products is going to have a significant public health impact.

The next category in our portfolio is complex dosage forms and formulations. This generally refers to complex injectables, as we talk separately about some of the locally acting, inhalation, and topical products. The challenges in this area are long-acting injectables and implants, where we're just beginning to see some generic products being approved. Some of the challenges here are products that don't yet have generic competition and have much longer dosing intervals, such as three to six months. This poses a significant challenge for doing even pharmacokinetic bioequivalence studies, which might need a year-long study just to compare one dosing interval.

We're looking at scientific work in these areas as well as more efficient study designs and as well as more predictive models. We have begun to approve generics for some of these release-controlled, long-acting products and are moving toward in vitro bioequivalence methods for some of the simpler drug substance products.

The fourth category is complex routes of delivery. This primarily includes inhalation, topical, ophthalmic, nasal, and GI-acting products. We've really been able to move forward in this area. We now have product-specific guidances for all inhalation products that have alternatives to clinical endpoint studies. This is one of the most important aspects of having effective generic competition - not having to repeat large-scale clinical studies to get generic products approved.

However, there are still significant challenges. If you look at my list of products without generic competition, there are still many inhalation products that don't have generic versions. Although we have approved a few generic versions of both metered-dose and dry powder inhalers, there are challenges with reformulating some metered-dose inhalers to use different propellants due to changes in the marketplace and propellant availability.

We've identified the inhalation area as probably the most important focus area because that's where we still see challenges in drug development science and the need for specific manufacturing processes and dedicated infrastructure for those products, which are limiting generic competition. We're very interested in discussion later this afternoon about some of the challenges in those areas and things we can do to move forward in the inhalation area.

I've been at FDA for 20 years, and one thing that has really emerged as a significant part of the generic program that wasn't on the radar before is drug-device combination products and device constituent parts. We see more and more products where the medical innovation comes not just from the active ingredient in the product, but from the delivery device constituent part. This poses challenges. We have a clear understanding of how to evaluate and measure drug delivery if the device is driving it, ensuring devices deliver the same amount of drug at the same rates to the site of action. But the more challenging parts are ensuring patients can use these products effectively and that differences in the device and how it's presented to the patient don't interfere with product use when there's generic substitution and there might be differences.

This has become a standard part of our ANDA review process - to look at those differences and determine if they're acceptable. From a scientific point of view, we need to determine how big of a difference is acceptable in terms of patient access and use. We recognize there's a lot of intellectual property and patents around different devices. If you require the generic product to be identical, you may introduce barriers to competition. If you allow differences, you then have to ensure those differences don't affect patient use of the product.

The focus of the scientific work here is to try and help us understand which differences should be acceptable. One of our key accomplishments this year is completing the first human factors study under our IDIQ, this is a Task Order contract that allowed us to direct human factors studies to provide data to help make these decisions. The study focused on barrel extension and gave us good insights into designing these studies efficiently. The data from the study will help inform our regulatory thinking about different areas. We now have the capability in our research program to generate new data looking at device differences and helping us understand which ones are clinically significant.

Even though complex generics are growing, a significant part of the generic space and prescriptions people receive are still oral and parenteral generic products - the non-complex products. Our goal here is to make this process efficient and reliable for these products, recognizing that many of these are commodities. We don't want to do in vivo studies when biowaivers or in vitro approaches can be used. We recognize that these commodity products are being supplied into a global supply chain, so there's a large focus on having global harmonization and ICH documents that have consistent approaches across all major markets globally. This is also very helpful for efficient development of these products.

Last year, we saw a significant impact of this through the regulatory process with the M13A finalization and implementation, which resulted in updating about 800 of our product-specific guidances to have more efficient bioequivalence approaches. We estimate that about 200 in vivo studies per year would now not be recommended under this new approach.

Even in the space of non-complex products, there are opportunities for significant efficiencies and eliminating unnecessary studies. I'm very proud of the work our whole team has done in this area. In a regulatory environment, it's often easy to ask for more information, but really going through and determining from a scientific basis whether we really need a study and can reduce that requirement is a significant accomplishment. This is not just for the US, but for global harmonization as well. There is significant scientific and regulatory wok that goes into coming up with a more efficient regulatory system and a significant amount of work is necessary to make that happen.

Behind all of these products, there are tools becoming more important to efficient generic drug development. One of these is quantitative medicine. About a little over a year ago, CDER launched the Center of Excellence in Quantitative Medicine, recognizing that these predictive model approaches are going to be more significant across development programs, both for new drugs and generics.

Through the GDUFA science program, we've been establishing foundational tools that can be used for complex generics, specifically the PBPK models for local routes of delivery. We're also developing new ways to use models. Some key accomplishments include meeting pilot programs to have additional discussions on modeling approaches and establishing a model master file process. This allows models to be submitted separately from the application, similar to a drug master file for API manufacturing. They can be submitted separately and referenced by applicants, hopefully encouraging more efficient use of quantitative medicine by the generic industry. If there is a model that’s developed that’s useful, that can be reused in multiple applications with just one review and one submission. This is really building the infrastructure for using quantitative medicine in the generic drug application.

The final area of our research priority portfolio is artificial intelligence and machine learning. The goal here is to develop AI methods that FDA can use to improve the efficiency and consistency of our scientific assessments and advice. This is an area where there will be massive changes to our whole society as these tools become

more available and integrated into workflows across all parts of our daily life. Pharmaceutical development and FDA review are no different.

Our research program's recent focus has been on using AI methods to help develop quantitative predictive models faster, better, and at a bigger scale. We're really trying to understand how AI methods can achieve very high reliability. This isn't just about asking a question to ChatGPT or similar tools, but really understanding agent-based workflows to get to high reliability, and focusing AI assistance on appropriate documentation as needed.

One example we've been working on and will be presenting publicly at different workshops is looking at maximum daily dose determination. This is something generic drug developers need to know as it affects impurity levels and levels of excipients they can use in their products. Generally, it can be done by looking at the label, but FDA has complex rules about what to do. If you just ask an AI assistant what the maximum daily dose is, maybe 1/3 of the time it'll give you the right answer. But if you develop a focused workflow, do engineering work to optimize the workflow to implement FDA's rules and guidances, and rely on certain data sources such as FDA-approved labels, then you can get to much higher reliability answers.

That's part of the engineering and research work around making AI useful within an FDA environment - looking at how to get to high reliability, what types of data controls and method approaches can do that, building on the foundation of general large language models being developed for broad societal use. This is going to be a big challenge in the future.

We're also interested in hearing about ways these tools are used in pharmaceutical development. Can AI tools help optimize formulations? Can they help your development work move faster? We also have tools that help us build and test models faster. There will be a lot of impact on pharmaceutical development and regulation from these approaches, and we want to make sure we're at the forefront of that.

As I conclude, looking toward the next 10 years of generic drug programs, it's clear that complex generics are going to be a bigger part of the industry. That's where the unmet needs for products without generic competition are, and from a business perspective, where the financial viability of the generic industry lies. We see that this will be a bigger percentage of the generic drug program's workload.

We know that complex generics are more complicated, so there are more needs for meetings or interactions around these products. There are challenges in implementing novel methods. Through our CRGC workshops on things like immunogenicity and drug-device combinations, we've seen that when you have new approaches and methods, there's an iterative process where you have to listen to stakeholders to identify the most efficient regulatory approaches.

We see drug-device combinations as being more and more of the products where more of the value of pharmaceutical products coming from the device constituent part. Quantitative medicine will be a bigger part of all types of pharmaceutical development, and we're trying to build the infrastructure for that. Quantitative medicine means reducing unneeded studies when you can predict what will happen for a particular formulation or study with high reliability you don’t have to conduct those studies. There are other opportunities for quantitative medicine as well, such as understanding how products can be used in pediatric populations or groups that were never used in bioequivalence studies. No bioequivalence studies were really ever conducted in pediatric population but we approved generic products for those indications and quantitative medicine can be different approaches to understanding and identifying what are the key attributes in different population groups as well.

Even though non-complex generics have become commodities, commodities are really important. Our whole economy runs on commodities. We want that process to be more efficient, which means eliminating unnecessary studies. We're looking at injectable products as well; we have very restrictive regulations on development of non-Q1/Q2 generic products. There are many B2 applications which just have very small changes in excipients for injectable products. These are areas where our regulations ought to follow our scientific understanding. We want to have a globally harmonized approach for our commodity products to ensure efficient markets globally.

We want to have high confidence in these products. As Dr. Murphy said, 9 out of 10 prescriptions are for generic products. We want people to be confident that if they take an FDA-approved generic product, it's going to provide high quality and effective therapeutic benefit. Susan Rosencrance mentioned drug shortages being important for non-complex injectables and tablets. We want to have a system which is very robust against shortages, making it easier for companies to adapt to changes in supply chains and make post-approval changes to their products and processes more efficiently.

Finally, in the next 10 years, there will be massive transformations driven by AI in how we do reviews and how pharmaceutical development is conducted. We hope that through our science and research program, we can help build data foundations, open environments, transparency, and clarity about best practices for the use of these tools, both in the assessment of applications and in the development of pharmaceutical products.

We continually welcome comments on our research program to identify things FDA can help facilitate the best possible use of AI in pharmaceutical product development and regulation. To conclude, without a scientific foundation, there's not going to be generic competition. You're not going to have more efficient approaches to product development unless you understand the scientific work. As part of that, we really look forward to your input. That really helps us refine and focus our research portfolio on the most important things we can do in this next year to help accelerate access to safe and effective generic products.

With that, I look forward to the rest of this workshop and the discussion over the next two days. Thank you all very much.