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CHECK UP: EXAMINING FDA REGULATION

OF DRUGS, BIOLOGICS, AND DEVICES

WEDNESDAY, MAY 22, 2024

House of Representatives,

Subcommittee on Health,

Committee on Energy and Commerce,

Washington, D.C.

The subcommittee met, pursuant to call, at 10:33 a.m. in Room 2322 of the Rayburn House Office Building, Hon. Brett Guthrie [chairman of the subcommittee] presiding.

Present: Representatives Guthrie, Burgess, Latta, Griffith, Bilirakis, Bucshon, Hudson, Carter, Dunn, Pence, Crenshaw, Joyce, Balderson, Harshbarger, Miller-Meeks, Rodgers (ex officio); Eshoo, Sarbanes, Cardenas, Ruiz, Dingell, Kuster, Kelly, Craig, Schrier, Trahan, and Pallone

(ex officio).

Also present: Representatives Castor, DeGette, and Schakowsky.

Staff Present: Jolie Brochin, Clerk, Health; Abigail Carroll, FDA Detailee; Grace Graham, Chief Counsel; Sydney Greene, Director of Operations; Emily King, Member Services Director; Chris Krepich, Press Secretary; Karli Plucker, Director of Operations (shared staff): Emma Schultheis, Staff Assistant; Lydia Abma, Minority Policy Analyst; Jennifer Black, Minority FDA Detailee; Jacquelyn Bolen, Minority Health Counsel; Waverly Gordon, Minority Deputy Staff Director and General Counsel; and Una Lee, Minority Chief Health Counsel.

*Mr. Guthrie. The subcommittee will come to order, and I will now recognize the chair. I will now recognize myself for five minutes for an opening statement.

So today three important center directors for the U.S. Food and Drug Administration are here with us to share updates about the work they oversee with their respective divisions.

And we really appreciate you being here.

With the agency now collecting the highest number of user fees on record, it is critical we hear from the center directors about the ongoing challenges the agency and industry face in getting safe and effective products to patients faster.

In addition to reauthorizing the user fee agreements, Congress granted FDA a suite of additional authorities that were signed into law in December of 2022. These include updates to ensure clinical trials are reflective of the broader patient population; greater transparency for sponsors to collaborate with payers to decrease the time from a novel product's approval to coverage; reforms to strengthen the accelerated approval pathway and streamline processes for

manufacturers to update their software without unnecessary regulatory hurdles.

I am proud of the bipartisan work this subcommittee has accomplished throughout the last user fee reauthorization. Since then, FDA has approved and cleared hundreds of new products. Our work collectively enabled the review and approval of 55 novel drugs in 2023, and the approval of almost 1,000 generic drug applications. During that same time there were 23 biologics device applications and 20 biologics license applications approved, and over 100 novel devices cleared by the FDA.

Cell and gene therapy is of particular importance and interest to me and others in Congress. We are on the precipice of a renaissance in health care in which personalized medicine can cure otherwise incurable diseases. For example, among those medicines approved in 2023 were 2 cutting-edge, potentially curative gene therapies for sickle cell disease. Just last summer CBER also approved a therapy to address underlying cause of the disease in Duchenne muscular dystrophy in boys aged four to five. Both examples illustrate the incredible value American innovation plays in

our health care system, and the value the FDA brings to help facilitate this remarkable work.

That being said, I have some concerns that I hope to have addressed today that threaten to undermine the strides we have made. Missteps by the Biden Administration have already caused uncertainty among innovators in these small biotechnology companies that could impede patients' ability to access innovative products.

The repeated attacks on the accelerated approval pathway from CMS, which is second-guessing FDA's equities to academics and payers alike, insisting that these approvals are unproven or lesser than traditional review pathways, degrades public trust and an important tool the agency has to help safely and effectively get cures to patients more quickly.

This is also a pathway that Congress -- and bipartisan Congress -- has repeatedly strengthened and supported. The recently-released 5,000-page Laboratory Developed Test, or LDT Rule, has been touted as a mechanism to drive more innovation and protect patient safety. I fear this complete overhaul of LDT regulation will have the opposite effect.

Instead of driving up costs of care and delaying patient access to lifesaving care, tests developed to treat patients at the bedside to detect early stage cancer or detect Alzheimer's sooner will be subject to onerous requirements under the new regime proposed by CDRH.

The FDA must work with Congress on a long-term solution that balances patient safety and facilitates future innovation. Last year, Ranking Member Eshoo and I wrote Dr. Marks about clinical holds. According to the Wall Street Journal, there was an average of 664 clinical holds which temporarily stopped clinical research between 2017 and 2021, up from 557 average annual holds in prior years. In response to our inquiry, we learned that 79 percent of the responses to innovators' questions about their applications and the holds associated with those application were written-only responses.

To be clear, I understand the complex nature of these applications, but providing written responses to complex questions with no chance for a true dialogue isn't acceptable. It is imperative for the agency to literally come to the table and work through these issues with

innovators, or else patients will be left without answers and without lifesaving care.

In closing, I want to thank the witnesses for being here today. I know your work is not easy. I know that our job is to -- your job is that we have safe and effective medications, but we must know that patients are counting sometimes months. If you are a parent with a child with Duchenne muscular dystrophy, the race to keep them out of a wheelchair before they get access to medicines is real. It is important. An accelerated path is real and important, and it has been bipartisan, and we want to work together. That is our pledge, to work together to bring these innovative technologies to market.

[The prepared statement of Mr. Guthrie follows:]

**********COMMITTEE INSERT**********

*Mr. Guthrie. And I will yield back and recognize the ranking member for five minutes for her opening statement.

*Ms. Eshoo. Thank you, Mr. Chairman, and good morning, colleagues.

Today we welcome leaders from the FDA to discuss the work of the Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, and the Center for Devices and Radiological Health. Dr. Cavazzoni, Marks, and Shuren, it is wonderful to see you. It is good to see you. I think this is the first time in 30-plus years that I have seen the three leaders here together, so it is extra special today.

The FDA oversees the safety of more than $3.6 trillion worth of products, including more than 6,500 medical devices, 1,600 FDA-approved animal drug products, and 20,000 FDA-approved prescription drugs. The FDA also regulates 78 percent of our nation's food supply. Overall, FDA-regulated products account for $0.21 of every dollar spent by U.S. consumers.

The FDA's mission to protect the public's health leaves no room for error, yet the FDA has a Herculean task: oversee

a huge segment of products Americans rely on with almost the same amount of money a single county in Maryland funds its schools with. Just think about that for a moment. The FDA's budget was $6.7 billion in fiscal year 2023, with over half of the funding provided by the Federal Government. The remaining funding was provided by the industries the FDA oversees in the form of user fees. Per capita, FDA's budget amounts to $10.78 per American.

Congress has not set the FDA up for success. Drug shortages are a key example. Drug shortages have for decades threatened adequate delivery of quality patient care and severely limited Americans' access to lifesaving drugs. Drug shortages are caused by long-term structural factors, including our over-reliance on foreign sources for essential medicines and Active Pharmaceutical Ingredients that are known as APIs.

Last September our subcommittee held a legislative hearing on drug shortages after months of horror stories shared by physicians and patients about shortages of lifesaving treatments for treating cancer. Included in the hearing was my Drug Origin Transparency Act to provide the

FDA with the information they have repeatedly said they need to identify where drugs and APIs are made to prevent shortages. Almost a year later, we have not advanced legislation to address drug shortages.

The stories I hear from patients and physicians, especially those treating children, have not stopped coming in. In April 20, 2024 survey by the American Society of Health-System Pharmacists found shortages of critical drugs reached another record high this year, with more than 323 drugs in shortage.

Democratic members of this subcommittee have put forward well-thought-out policies to require manufacturers to inform the FDA if there is a sustained increase in demand for a drug or ingredient, and allow the FDA to recall products from the market to prevent harm to consumers. We can't keep doing what isn't working and expect a different result. It is in our nation's best interest to ensure the FDA can comprehensively address drug shortages and other issues that touch the lives of millions of Americans.

I hope our subcommittee takes on this critical issue in earnest without delay. We can start by meeting President

Biden's request for $7.2 billion in funding for the FDA in fiscal year 2025, which is a $495 million increase over the previous year. Additional funding means faster reviews, and approvals of drugs, and more frequent inspections of foreign manufacturing facilities: two topics that our subcommittee and industry agree are needed. So I look forward to hearing from our distinguished witnesses today on how Congress can best support the FDA's work.

[The prepared statement of Ms. Eshoo follows:]

**********COMMITTEE INSERT**********

*Ms. Eshoo. And with that I yield back, Mr. Chairman.

*Mr. Guthrie. Thank you. The gentlelady yields back, and the chair recognizes Chair Rodgers for five minutes for her opening statement.

*The Chair. Thank you, Chairman Guthrie.

Dr. Cavazzoni, Dr. Marks, Dr. Shuren, thank you for joining us today.

The FDA plays a critical role in the health and well-being of the American people. If it is successful in its mission, it has the potential to save and extend people's lives. If it fails in its mission, the cost could be astronomical and devastating. The FDA is responsible for regulating more than $3.6 trillion worth of food, tobacco, and medical products, about $0.20 of every dollar spent in the United States.

Americans must have confidence that the agency is doing its job. They have to be able to trust that medical products they are relying on are safe and effective, and it is Congress's duty to ensure that the FDA is using the resources and authorities it has been given to protect and advance public health.

I am proud that America has been a leader in developing innovative treatments such as non-addictive medicines for chronic pain, so-called N-of-1 drugs, where hospitals are making drugs designed for one patient, and implantable upper airway devices for pediatric patients with Down syndrome and severe sleep apnea. All these things, which will make a meaningful difference in people's lives, were recently approved by the FDA or will be seeking review in the near future.

There are also advances that could reduce the amount of time it takes for new technology to reach patients in need. New biomarkers have been developed from advances in genetic sequencing, manufacturing techniques, and methods to generate clinical data that, if used properly, could decrease cost and time to demonstrate these new technologies meet FDA standards.

This committee worked in a bipartisan manner to give FDA new tools in the last user fee reauthorization, and we expect the agency to use these tools to pave the way for groundbreaking innovation. I firmly believe that the accelerated approval pathway should be leveraged now more

than ever, as more and more diseases can be treated or even cured because of a better understanding of their mechanisms of action and genetic signatures.

FDA approval, unfortunately, is not the final hurdle for patients, as significant problems with CMS and private coverage still persist. But it is an important first step. FDA cannot move backwards, and I am worried that we are starting to see warning signs that that may be occurring.

For example, I am disappointed to see that, according to the fiscal year 2023, PDUFA and MDUFA performance reports, all three centers here before us today have failed to meet critical performance, process, and hiring goals, despite all-time highs in funding.

In addition, the agency has been failing to adequately accommodate in-person meetings and to respond to outreach related to major clinical and scientific development decisions in a timely manner. This is especially concerning, as the FDA has unilaterally decided it can regulate, by its own estimate, 80,000 tests under the Laboratory Developed Tests Final Rule.

FDA leadership often says that the right -- says the

right things regarding speeding up innovation to patients when the benefits outweigh the risks, such as not asking nice-to-know questions if the statutory standard for approval has been met, not moving the goal post after a company has invested millions of dollars and years of time on a clinical trial FDA once said was the best path forward.

The challenge is making sure the sentiments expressed by the agency's leadership are reflected by the application reviewers. Unfortunately, I am hearing the opposite from stakeholders who are finding FDA review staff more disconnected and difficult to work with than ever before.

Everyone on this dais wants the FDA to succeed because, if the FDA succeeds, American innovation flourishes, leading to better outcomes for patients. And I am hopeful that we can have a productive conversation about what challenges the agency is facing and why, and how Congress can help the FDA streamline operations and provide clear, consistent, scientific, and regulatory information to innovators and drug manufacturers that are looking to improve the daily lives of Americans.

[The prepared statement of The Chair follows:]

**********COMMITTEE INSERT**********

*The Chair. Thank you, and I yield back.

*Mr. Guthrie. The gentlelady yields back, and the chair recognizes the ranking member of the full committee, Ranking Member Pallone, for five minutes for an opening statement.

*Mr. Pallone. Thank you, Mr. Chairman.

We are here today for an update on the hard work that the FDA does every day to ensure the safety and efficacy of drug and medical devices. Every year FDA rigorously reviews hundreds of applications for drugs and biological products at the Center for Drug Evaluation Research and the Center for Biologics Evaluation, Research, and Medical Devices at the Center for Devices and Radiological Health. And today we will hear from the centers' directors of each of these branches of the agency.

And I would like to thank all of you for being here today.

In recent years FDA's work has garnered more attention from everyday Americans, especially during the pandemic. And this attention has also brought increased scrutiny. And I think it is important for the public to know that they can trust the products available to them, and that the public

servants at FDA are working around the clock to protect their health and well-being.

I also believe it is important to discuss areas in which the agency can do more to protect public health. However, I want to note that, as we ask FDA to take on additional responsibilities, it is up to Congress to provide the agency with the tools and resources it needs to fulfill those tasks. And I have repeatedly said that Congress must come together on a bipartisan basis to give FDA the additional tools and resources it needs to provide patients and health care providers with confidence that the medical products they rely on are safe, effective, and available.

We have been asking our Republican colleagues for more than a year to advance meaningful legislation that would provide additional tools and authorities to address ongoing drug shortages, prevent future drug shortages, and strengthen the medical supply chain. However, Republicans have repeatedly declined to join Democrats to pass legislation to do so, including through the Pandemic and All-Hazards Preparedness Act, which they have still failed to reauthorize.

And it is especially frustrating that Republicans have been unwilling to put any new requirements on drug manufacturers to help address the shortages that continue to affect Americans. For example, we should know where our drugs and their critical ingredients are being made so that when a drug shortage or other supply interruption occurs, FDA and manufacturers can react quickly and appropriately.

We should also ensure that FDA is notified when an unexpected surge in demand for a drug occurs and is likely to cause a shortage.

It is also unacceptable that the agency still does not have the ability to recall unsafe, adulterated, or otherwise dangerous products, and is instead forced to rely on the goodwill and voluntary compliance of manufacturers.

Committee Democrats would also like to make progress on strengthening the pipeline for pediatric drugs, and ensuring that drug manufacturers are fulfilling their responsibilities to conduct studies in pediatric populations, as I mentioned at last week's markup. But unfortunately, Republicans, not -- Republicans have not been willing to work with Democrats to move forward on any of the meaningful proposals I

mentioned to address these important issues.

So we simply cannot expect more from an agency without providing the necessary tools and resources. It is incumbent upon Congress to provide FDA with more resources, more staff, and the appropriate authorities in order to continue to fulfill its mission. We can all agree FDA faces new and unique challenges, but they can only do what we provide them with the authority to do, and this task will only continue to become more complex and more demanding in the years ahead.

So in closing, I hope that Congress can come together to support FDA in fulfilling its mission and addressing these challenges. Democrats stand ready to work across the aisle to support the agency's tireless work to protect Americans health and well-being, and I look forward to hearing from our witnesses and thank them.

Well, I thank all of you.

[The prepared statement of Mr. Pallone follows:]

**********COMMITTEE INSERT**********

*Mr. Pallone. I yield back, Mr. Chairman.

*Mr. Guthrie. Thank you. The gentleman yields back, and now we will -- that concludes opening statements, and the committee will move into testimony from our witnesses today, and I will introduce all three of you and then call on you one at a time.

So today we have Dr. Patrizia Cavazzoni, director, Center for Drug Evaluation and Research; Dr. Peter Marks, director, Center for Biologics Evaluation and Research; and Dr. Jeff Shuren, director, Center for Devices and Radiological Health.

So thank you all for being here. It is important, as I said, that we all work together to move the innovation forward, and we look forward to hearing from you.

So now we will begin with five minutes by Dr. Cavazzoni.

STATEMENT OF PATRIZIA CAVAZZONI, M.D., DIRECTOR, CENTER FOR DRUG EVALUATION AND RESEARCH; PETER MARKS, M.D., PH.D., DIRECTOR, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH; AND JEFF SHUREN, M.D., J.D., DIRECTOR, CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

STATEMENT OF PATRIZIA CAVAZZONI

*Dr. Cavazzoni. Chair Guthrie, Ranking Member Eshoo, and members of the subcommittee, thank you for the opportunity to testify before you today.

As we are generally focusing on innovation, my testimony will focus primarily on new drug development. CDER also works on generic drugs, biosimilars, over-the-counter drugs, and drug shortages, among many other activities.

In 2023 CDER approved 55 novel drugs. Of these, about two-thirds were approved first in the United States and the third were first in class.

We are also continuing to make progress in the approval of therapies for rare diseases. Between 2013 and 2023 CDER and CBER approved 277 orphan drugs and biologics. Last year

CDER approved 28 orphan-designated drugs, representing half of the novel drug approvals.

But we can't rest on our laurels, and need to find ways to accelerate the development and approval of therapies for rare diseases because there is still a huge unmet need.

Coupled with regulatory flexibility, our regulatory tools have allowed us to make major inroads, but challenges remain when it comes to rare diseases with relatively smaller patient populations. We are witnessing unprecedented progress in the science that underpins the development of therapies for rare diseases, and better science will lead to better drugs, as we have seen in other areas.

To seize the moment we have been expanding CDER's Accelerating Rare Disease Cures program, which we launched two years ago. This program brings together expertise across CDER and beyond, and engages with the rare disease community on how to navigate drug development and the regulatory review process. Our rare disease team works to promote consistency in the review of rare disease programs and in what is communicated to drug developers in the rare disease community.

CDER and CBER have partnered in many areas of rare disease drug development. For instance, you will hear more from Dr. Marks about the START pilot program. We received numerous proposals and made our selections, and will be notifying sponsors soon.

Beyond these programs I want to discuss other activities we have underway to promote clinical trial innovation. Just last month we launched the CDER Center for Clinical Trial Innovation. This new program will serve as a hub that will support the implementation of innovative approaches to clinical trial design, as well as conduct, through enhanced communication and collaboration, and by conducting demonstration projects in areas that have historically posed challenges.

Expanding the use of real-world evidence is a crucial aspect of our push to innovate how drugs are developed. There is a long history of using real-world evidence to support regulatory decisions, primarily in the evaluation of post-market safety. The next frontier is about spurring the use of real-world evidence to evaluate the effectiveness of drug therapies. This is particularly relevant to the

development of drugs for rare diseases with relatively smaller populations, where it may not be possible to identify a sufficient number of patients to participate in clinical trials. For example, last year we relied on real-world evidence from a patient registry in conjunction with a small clinical trial to approve the first treatment for Friedreich's ataxia, a rare, inherited neurodegenerative disease.

I am going to conclude with an emphasis on rare diseases. As you will hear from Dr. Marks, we are at a turning point in our understanding of the science that is opening doors to treatment that would have been unthinkable only a few years ago, such as gene therapies and drugs that work on gene expression. But despite all the progress, there are still too many rare diseases that lack treatment options, and we need to do more to alleviate the suffering of rare disease patients and their families. For this reason, CDER and CBER are actively working to develop a shared vision and a plan for areas that are critical to rare disease drug development, such as communication with the rare disease community, novel endpoints, biomarker development, and

innovative trial designs, while maintaining our current structure in order to take full advantage of clinical and scientific expertise across both centers.

It is crucial that we have the best collaboration and coordination across the medical product centers to fulfill our goal to bring better treatments to rare disease patients and their families.

Thank you for your time today, and I look forward to answering your questions.

[The prepared statement of Dr. Cavazzoni follows:]

**********COMMITTEE INSERT**********

*Mr. Guthrie. Thank you. Thank you for your testimony, and the chair will now recognize Dr. Marks for five minutes for your opening statement.

STATEMENT OF PETER MARKS

*Dr. Marks. Chair Guthrie, Ranking Member Eshoo, and the members of the Subcommittee on Health, thank you for the opportunity to testify before you today.

The Center for Biologics Evaluation and Research focuses on advancing the development of and regulating complex biologic products including, among others, blood components, vaccines, and cell tissue, and gene therapies. The past year has brought progress in each of the areas we oversee. For example, last year we issued updated blood donor guidance that implemented an individual risk assessment strategy for all blood donors, and we are currently in the process of issuing draft guidance that will implement a similar individual risk assessment for tissue donors.

Following a second recent outbreak of tuberculosis involving multiple recipients who received bone grafts from a common donor, we will issue guidance to ensure that appropriate steps are taken to minimize the possibility of this happening in the future.

And both to protect the public from unsafe or

ineffective products, while at the same time spurring innovation, we plan to revisit our current regulatory framework for human cells, tissues, and tissue products. We realize that there are current regulatory frameworks that could potentially benefit from a more nuanced regulatory approach while still ensuring key questions of safety, effectiveness, and product quality have been addressed.

In the area of vaccines we have passed here, we approved two respiratory syncytial virus vaccines for use in older individuals, and one of them was also approved for use in pregnant women to present -- to prevent RSV in the newborn.

Staying on the topic of respiratory viruses, we remain vigilant for further evolution of the virus that causes COVID-19, and will be discussing appropriate vaccine composition with our Vaccines Advisory Committee on June 5, 2024.

We have also made significant strides over the past year in the field of gene therapy, with 6 products approved in 2023. As a hematologist who cared for many individuals suffering from the myriad complications of sickle cell disease, I greatly appreciate that these approvals included

two cell-based gene therapy products for this condition. Of note, one of these products was the first for a one that used the CRISPR technology, which may be transformative, and we are working to implement both the letter and the spirit of the platform technology provision of the 2023 omnibus, which may expedite the pace of progress, particularly in the place of gene therapy.

Gene therapy has raised many hopes, particularly for rare diseases. However, several impediments hinder its growth. These include manufacturing, clinical, and regulatory challenges. Although we may not be able to address all of these challenges through the work of the FDA, we believe that we have a central role to play in our own center and in working across centers at FDA.

At CBER we are collaborating with stakeholders to address manufacturing challenges through internal and external scientific collaboration.

Also, informed by the use of the -- excuse me, also informed by the critical medical needs of numerous rare disease patient populations, we are applying the use of accelerated approval to gene therapies when appropriate and

when there is strong scientific underpinning that indicates that they will meet our standards for quality, safety, and effectiveness.

Global regulatory convergence and collaboration should also foster the development and availability of more products for rare diseases, and we have initiated a pilot program called CoGen T with regulatory colleagues in other countries to help facilitate this.

We will also leverage what we have learned over the past several years during the pandemic to try to improve the situation for rare disease patients in this country. One specific program to highlight is the STAR communications pilot, which intends to provide at least three CBER products and three CDER products with ongoing communication as needed, in a manner similar to that which Operation Warp Speed did for the COVID-19 vaccines. We are in the process of making final selections and notifying participants, and the hope is that we can significantly reduce development time to reduce suffering and save lives.

Finally, we know that for rare diseases the only way we will accomplish our goal most rapidly, expediting progress

for patients, is if we optimally communicate, coordinate, and collaborate across the medical product centers. As Director Cavazzoni noted earlier, CDER and CBER are actively working to develop and implement a rare disease innovation agenda that will be based on a shared vision and comprehensive approach to aligning review efforts to the greatest extent possible, identifying and enabling innovative approaches, and streamlining communication internally and externally with all interested parties to ensure that rare diseases receive the concerted attention that they deserve. We very much owe this to patients.

Thank you for the opportunity to testify today. I look forward to answering your questions.

[The prepared statement of Dr. Marks follows:]

**********COMMITTEE INSERT**********

*Mr. Guthrie. Thank you for your testimony. And the chair will now recognize Dr. Shuren for five minutes for your opening statement.

STATEMENT OF JEFF SHUREN

*Dr. Shuren. Chair Guthrie, Ranking Member Eshoo, members of the subcommittee, thank you for the opportunity to testify today.

I became the director of CDRH almost 15 years ago, in September 2009. At that time no innovative technology came to the U.S. first or second or third. It went to Europe, it went to other countries. At the end of that calendar year we had only authorized 25 novel technologies. All of our stakeholders were upset with the program. We made a commitment to change that dynamic, set a new vision, changed our programs and policies and practices, got help from Congress. And so last year, excluding COVID devices, we authorized 124 novel technologies, a fivefold increase, the highest number in the almost 50-year history of our program and at a time when we received more pre-market submissions than almost a decade.

And today, over 50 percent, as much as two-thirds of the innovators for the U.S. market, do bring their novel technologies here first, or in parallel with other major

markets. We literally went from 0 to 60, and that is great, except I look at it and say, well, we have got at least another third, and we have got to make good on it, and we are working on that.

One of the ways we got there, we launched our Breakthrough Devices Program, which got codified into the law. Today we designate over 100 medical devices as breakthrough every single year. And the overwhelming majority that come to us for pre-market review we authorize.

But most of those devices that get a designation never get to patients. Sometimes they are not safe and effective, and they shouldn't be out there. But many times it is for other challenges, because there are lots of obstacles going from concept to commercialization. It is appropriately called the Valley of Death.

And so last year we launched a pilot as part of our program to change that dynamic. We created a new position, the Tap advisor. And rather than our traditional approach of a company comes to us and we react to their questions, the advisors engage proactively and strategically and in real time, working with those innovators to identify their

challenges and to work on solutions. And that may be their needs for FDA, but also incorporating the voice of patients, the evidence they may need to push adoption by providers and patients, or challenges with payers like coverage and reimbursement. The feedback has been very positive. One company noted that, by being in the program, they have already saved over a year in development time. That is real progress.

But we have other challenges. It doesn't matter if you have great technology if people don't have access to it. And today too many Americans don't have access to good care. They are disenfranchized by the health care system. Eighty million people live in primary care deserts, and that is in part because our health care system was designed around brick and mortar facilities. And to meet the needs of hospital administrators, it wasn't designed around patients and their needs. And at the same time we are seeing health care costs go up.

So to try to address that we are looking at how do we really change health care delivery. That means moving care as much as possible from those brick-and-mortar facilities to

people, to where they live, to -- into the home so they have those opportunities, with a focus on under-represented populations.

And so just a few weeks ago we launched our initiative, Home as a Health Care Hub, where we have partnered with an architectural firm with expertise in the area to create a virtual reality model, a prototype to serve as an idea lab for innovators so they can start to make what we really need: integrated, medical-grade consumer technologies that meet the needs of people. That allows the opportunity to drive down costs, provide care to more, and the opportunity to better participate in clinical trials.

We are focused on under-represented populations like rural communities and starting with diabetes. We have partnered with patient groups like the Juvenile Diabetes Research Foundation, provider groups like the American Diabetes Association, and MedTech innovators. The goal is that prototype will be out later this year for widespread use.

So that is just a few examples of the kind of innovations that we are doing at CDRH because, at the end of

the day, if we want industry to be innovative, if we want to get innovations to people who need it, then government has to be innovative, too. Thank you.

[The prepared statement of Dr. Shuren follows:]

**********COMMITTEE INSERT**********

*Mr. Guthrie. Thank you, thank you. That is excellent testimony. We concluded our opening statements, and we will move into questioning, and I will recognize myself five minutes for that purpose.

So Dr. Marks, Ranking Member Eshoo and I wrote you a letter, and I mentioned in my opening statement about the written responses. And so Monday -- I guess it was Monday, it might have been Tuesday -- I had the chance to visit where they are doing the cell therapy for diabetes, and with Dr. Felicia Paralia -- if I said that correctly -- but it was just amazing to stand there and see little cells floating in solution that implanted in a human body. It produces insulin on demand, and it is just fascinating, and just all of that that is happening here in the space.

I also saw another company that had an ALS drug that they had very promising research. They had another study, and so it wasn't as promising as they thought it was going to be, so they are regrouping and trying to figure out what the difference is in the two studies.

Having said that, I know that every bit of promising technology does take effort to make sure it is safe, it is

effective, and it is going to be -- can really move this country forward. Because you stand there talking to Dr. -- and this is a person that has changed the world, if her technology is really -- and it has been implemented, and it has been successful, and cured -- I don't know if "cured' is the right word, but people were insulin independent who have type 1 diabetes.

And so having said that, I know we all have to get to -- I know Operation Warp Speed was something that you guys did fantastically on, and I remember saying there shouldn't be another group of people in Washington with more esprit de corps than FDA, after coming together on a common mission and getting it accomplished. So these diseases, like diabetes and others, seem to be the same.

And I am not saying this specific person had issue with FDA, but just in general these innovative technologies and only getting -- and the problem isn't that we don't want FDA to rush beyond and not do stuff safe and effective, but it seems like we would have a better effort than just written responses to these kind of questions.

And so I guess my question -- I know that -- do you have

an update on what happened with the 79 percent, and what you are doing to make that better?

*Dr. Marks. Yes, so thank you for that question.

So we are working to reduce the number of written responses. They went up very significantly during the COVID-19 pandemic, when we had a tremendous number of applications and for various circumstances. They are not at a level where I want to see them at, because I do agree, fully agree, with multiple members who have already stated something like this, that dialogue, live, is very important. So we are working to reduce the number of written responses.

We are also working to reduce the number of clinical holds, and that actually -- we have made, actually, visible progress on that at our center from rates of 22 to 26 percent in 2021 and 2022. We are down in 2023 to 13 percent. And so far this year we are at about a 10 percent clinical hold rate. So that has come down significantly, in part because of active dialogue that we are having with sponsors during their 30-day review period for their Investigational New Drug application.

So I guess the sum of this is I agree with you, and we

will continue to try to enhance communication, reduce the number of written responses, and reduce the number of clinical holds so we can have innovation proceed as fast as it can.

*Mr. Guthrie. I just want to emphasize it is not -- the request isn't the shortcut. The request is to make sure that any time that is inefficient is done away with so we can get these to the marketplace quicker.

So Dr. Shuren, I know we had meetings when I first got on the committee about what was going on in the medical device -- in your area, and made commitments, and you just talked about successes that you have made. So we appreciate that. I know that we can all work together to move forward. It incredible, what is going on, as you all know, and what your scientists are involved in, making sure these come to the forefront.

The other one is artificial intelligence. I know Representative Obernolte is the leader of our special task force, and Crenshaw -- Mr. Crenshaw and Dr. Miller-Meeks sent a letter or wrote to you regarding comments you made about artificial intelligence. So I just kind of wanted to maybe

have a chance for you to clarify.

You talked about a safe space design, and maybe use third party to look at safe space design for AI. I do know that we have had some concerns from people because there is one that was mentioned, the Coalition for Health AI, and I want to -- that had major players in the space on their board. And so a lot of the smaller innovators are concerned that the major players will be reviewing their AI.

So the question is, is it going to be a voluntary to submit to this lab? And how do you make -- how do you ensure that small players can be innovative in this space?

*Dr. Shuren. So this sort of concept is called an assurance lab. You know, for innovators today, if you are making artificial intelligence-enabled medical devices, one of the challenges is you need access to large data sets to be able to design, train, and validate those technologies. And many of them don't.

So the idea of an assurance lab -- and we can't set that up at the FDA, so we are partners. What that looks like is to have more of a federated model of these data repositories that -- where they have already been evaluated, so you

understand their characteristics, fit for purpose --

*Mr. Guthrie. Thanks. I didn't leave you much time, but is it going to be voluntary, or how are you going to ensure that it is innovative --

*Dr. Shuren. It is voluntary. And actually, we are working with the VA. They are interested in setting it up. So we think we can learn from that set as a model, and put that out there as best practices.

*Mr. Guthrie. Okay, thanks. I am sorry I asked you a long question and left you a short time to answer, so I apologize.

And I will yield back and recognize the ranking member for five minutes for her questions.

*Ms. Eshoo. Thank you, Mr. Chairman.

Just before I came over to this hearing room I was down the hall in the Gold Room with the director of the National Science Foundation, and they had -- there are now 35 projects that have been launched through the NAIRR and, you know, they are all experimental, but there is a great deal that is taking place across Federal agencies, NIH being one of them, and I think that FDA could benefit from that partnership.

And also, it is my legislation to actually approve a full NAIRR, so democratizing all of this -- the effort relative to AI.

I introduced the Innovation in Pediatric Drugs Act to ensure that pediatricians and physicians have the clinical data they need to safely prescribe new drugs and therapies for children. Today drugs for rare diseases -- and the term, "rare diseases,'' has been mentioned at least maybe 75 or 100 times already this morning -- they don't have to be studied in children. And it leaves them with a rare -- it leaves them behind, relative to the rare disease. More than half of all new drugs approved by the FDA last year were for rare diseases.

So I have a series of -- I am going to ask all of my questions, and ask you to remember the questions so that you can answer them, but I want to get them all in because I feel so strongly about this area.

Would requiring post-market pediatric studies for rare disease drugs increase the number of drugs for use in children?

If a company is required to complete a pediatric study,

when is the study required, before or after a drug is on the market?

Under what circumstances does the FDA exempt companies from required pediatric studies?

And how can we make pediatric studies less burdensome for drug companies without sacrificing the need to understand how drugs impact in children?

So I think that both of these questions -- all of my questions go to Doctors Cavazzoni and Marks.

*Dr. Cavazzoni. We think that we --

*Ms. Eshoo. You need to turn your mike on.

*Mr. Guthrie. I don't think your microphone -- yes, there you go.

*Ms. Eshoo. We are all dying to hear what you are going to say.

[Laughter.]

*Dr. Cavazzoni. I am happy to get us started.

We think it is incredibly important that we study all diseases in the pediatric population, including rare diseases. And we think that the exemption to doing post-market studies for rare diseases is a problem because rare

diseases overwhelmingly occur in children. We understand that this is a cause for some trepidation by developers and sponsors.

I want to assure you that, as always, we would take a very sensible, pragmatic approach. We recognize the challenges in continuing to develop and generate safety and efficacy data, particularly for rare diseases, after they have been approved. And we would, of course, work with sponsors and developers to come up with practical and realistic ways of continuing to do that.

It is also really important for rare diseases that we be able to study the disease in children before approval. And, you know, we are concerned about a decision a couple of years ago that would -- a court decision a couple of years ago that would curtail that. And you know, we are happy to work -- to continue to work with Congress to make sure that we are continuing to have as broad a population that studies for rare diseases before the drugs are made available in the market --

*Ms. Eshoo. Except we need to go to Dr. Marks, because I want to get a quick question in with Dr. Shuren, as well.

*Dr. Marks. Very, very quickly, I would say I completely agree, and I think we can take a very thoughtful approach, as necessary, when there are diseases which don't affect children to developing policies for exemption when appropriate.

*Ms. Eshoo. Okay. And Doctor Shuren, bravo on your 15 years. That is quite a journey, and there is much to be proud of.

Your center clears AI-enabled medical devices. How does the FDA ensure AI-enabled medical devices are being used appropriately, for example, in pediatric populations so that, you know, we are ensured that the children receive safe care?

*Dr. Shuren. So one of the key things is assuring that the data that is being used to go ahead and design training --

*Ms. Eshoo. Yes, well, it is good data in, good data out.

*Dr. Shuren. That is exactly right --

*Ms. Eshoo. And if it is not, then it is -- can be lethal or deadly. Well, thank you very much for your work.

I hope members will remember my opening comment about

the FDA's budget because, as we pressure them to continue to innovate to do more, they need a budget that matches what we are requiring or requesting them to do.

So thank you, Mr. Chairman, I yield back.

*Mr. Guthrie. Thank you. The gentlelady yields back and the chair recognizes Chair Rodgers for five minutes for questions.

*The Chair. Thank you, Mr. Chairman.

I was disappointed at our hearing in April when Secretary Becerra stated that a number of drugs the FDA approved were "safe and effective, but people took them and nothing happened.’‘ This continues a dangerous trend of rhetoric around accelerated approvals being anything less than having the full FDA gold standard, which is untrue and leads to unnecessary delays in patient access to much-needed innovation.

Dr. Marks, could you please confirm that the biologics granted accelerated approval have full FDA gold standard approval?

*Dr. Marks. Chair Rodgers, yes, that is correct. When we approve something through accelerated approval, it meets

our approval standard, which is substantial evidence of effectiveness. And so we would expect it to have -- be safe, and have an effect in people. Perhaps not every last person, but it means that it has met our standard that, at least in some people, it is effective.

*The Chair. Thank you.

Dr. Cavazzoni?

*Dr. Cavazzoni. Yes, I would echo this. Accelerated approval is one of our two pathways. When we use accelerated approval, we make a determination that there is substantial evidence of effectiveness based on a surrogate endpoint or an intermediate clinical endpoint. And, you know, we stand by our standard.

*The Chair. Thank you.

The cost of getting a new drug or device is moving in the wrong direction. In fiscal year 2024, PDUFA -- the PDUFA user fee for each full application submitted with clinical data is over $4 million, which is a 25 percent increase over 2023 levels. The MDUFA fees for a standard PMA are up nearly 500,000, which is almost a 10 percent increase over fiscal year 2023 levels, all while the FDA's performance around

meeting management response times and reaching a decision on an application the first time it is submitted -- often called the first cycle approvals -- continues to fall short of expectations. All this leads to increased time and cost to get medical products to market.

Staff needs to get back in person, and patients should be allowed to testify in front of advisory committees in person. So for each of you, how do you define hybrid work?

What percentage of your employees are fully in-person, hybrid, or fully remote?

And for those that are hybrid, would you speak to accountability measures that are in place to protect against abuse and ensure productivity?

Has anyone had their ability to work in a hybrid manner revoked due to this, the abusing of the privilege?

And I will start with Dr. Cavazzoni.

*Dr. Cavazzoni. I am happy to start. So at FDA -- has taken an approach whereby staff are designated as either eligible for remote work or telework, and the latter requires a presence on campus. That designation is based on the type of work that the staff do. So to give you an example, within

CDER over three-quarters of our staff are not remote. To give you another example, within the Office of New Drug and the Office of Generic Drugs, which are the hub of where we review application, 90 percent of our staff are telework-eligible, meaning that they are not remote.

We really believe in a model that allows -- that has staff come in to be at White Oak or the office when they need to be. And obviously, the review staff have a lot of difficult things to discuss, and complex decisions to make, and so on, and so they are, obviously, more present at White Oak.

*The Chair. Okay.

*Dr. Cavazzoni. I also want to talk about the advisory committees. We have recently announced that we are --

*The Chair. Okay, thank you.

*Dr. Cavazzoni. -- transitioning back to in-person advisory committees.

*The Chair. Good. Good, good, good. I think I am going to let the other -- I would like to have more -- maybe an answer in writing on this, because I am going to run out of time.

[The answers submitted to The Chair's question follow:]

**********COMMITTEE INSERT**********

*The Chair. I wanted to address another issue. A number of members on this committee are -- have expressed interest in getting necessary medical supply chains out of adversarial nations and into nearer and friendlier to the United States. And we often hear the FDA is not a partner, and can be an impediment, and I would like to change that.

So Dr. Cavazzoni, if a generic drug company wanted to change API suppliers, would that require a fee, a pre-approval application, and what sort of timeline is required?

*Dr. Cavazzoni. So we review changes that are proposed in where a drug is manufactured and how it is manufactured. It is part of our ability to make sure that the drugs remain -- are of good quality.

We are also very concerned about the lack of redundancy, resilience, and lack of geographic diversity in the supply chain, and we are -- remain very interested in working with Congress to address those issues.

*The Chair. Okay, thank you. I have run out of time. I do want to look at how you are prioritizing those types of applications, and if you need more direction from Congress on that front.

*Dr. Cavazzoni. We would.

*The Chair. With that, I yield back.

*Mr. Guthrie. Thank you. The gentlelady yields back, the chair yields back, and the chair recognizes the ranking member of the full committee, Ranking Member Pallone, for five minutes for questions.

*Mr. Pallone. Thank you, Mr. Chairman. My questions are all of Dr. Cavazzoni.

And I am concerned that Congress has not taken action to combat drug shortage issues before they continue to worsen. Democrats have put forward common-sense proposals to strengthen FDA's authorities to address vulnerabilities in our supply chain. So let me ask you, Dr. Cavazzoni, one of the major problems that we saw last year and continue to see now is the shortage of drugs that seem to be related to increases in demand. Drug manufacturers are required to report to FDA when there is a discontinuance or interruption in the supply. However, when the shortage is driven by demand rather than supply, manufacturers are not required to report to FDA. So would the FDA be more effective if they were made aware of an unanticipated spike in demand?

*Dr. Cavazzoni. Unquestionably. We are also quite worried about drug shortages and the state of the supply chain.

Through valiant efforts, our drug shortage team have been able to prevent over 200 drug shortages last year with very limited resources and with a very small staff. We would welcome having additional authorities.

What you raise, this particular authority that you raise, which is having manufacturers require -- be required to report to us an increase in demand would be incredibly helpful to us because we would be able to intervene before the shortage starts, and ideally prevent it, rather than getting into a mitigation mode.

*Mr. Pallone. All right, thanks.

Now, another proposal that I would like to see passed into law is a requirement that drug companies report when drugs and their critical ingredients -- where drugs and their critical ingredients are being made. And when a drug shortage or other supply interruption happens, FDA manufacturers can react appropriately if they have that information.

So let me ask -- I think of the pediatric drug shortage of acetaminophen. I don't know how to pronounce acetaminophen. And you know, it seems to me we let American families down by not enabling the visibility for this. Would greater transparency into the supply chain for both prescription and OTC drugs have been useful in the pediatric shortages?

And are there other examples where transparency would have helped?

*Dr. Cavazzoni. Yes, there are -- we are also, you know, very, very interested in having more transparency on where drugs are made, and particularly how much of a drug is made in a specific facility, including API facilities.

Why is that important? Because facilities that make or plants that make APIs will distribute their API across multiple plants that make the finished drug. And when we have either a shortage or uptick due to increase in demand or natural disaster or so on, it is very important for us to understand how much of that API has actually been distributed across all the different plants, rather than scrambling and not knowing how much is placed in each facility, and then

being able to intervene specifically with specific manufacturers. So that increased transparency is very important.

It is also very important in our ability to have the best site selection model when we do inspections. And knowing how much of where and how much a drug is made, as well as the API and the finished product, is very important in guiding how much attention we pay to that facility in inspections, because we view inspections as a way to actually prevent further problems that can cause shortages.

So we are very happy to continue, and very interested to continue to work with -- on these additional authorities.

*Mr. Pallone. All right. Let me get to my last question. I have to shorten it a bit here. Mandatory recall. You know, I don't understand how mandatory recall is not, you know, one of your tools.

There was an example in November with a critical -- with eye infections that were resulting from contamination that could have resulted in vision loss or blindness. So the question: Would mandatory recall have allowed FDA to act more quickly to protect consumers and remove these products

from shelves?

*Dr. Cavazzoni. Mandatory recall is an authority that we don't have for drugs. We have it for lettuce, but not for drugs. And it would be incredibly important to protect the public.

The example that you gave is a very egregious example where we had a bad actor who introduced contaminated eye drops into -- to come into the United States. Those eyedrops cause horrible, horrible problems for patients -- for instance, blindness, sepsis, having to have an eye removed. And in those situations we cannot require a manufacturer to recall the drug promptly. And in this particular situation, it actually took quite a bit of time while all of this harm was happening among the public.

We had a similar example with hand sanitizer which was contaminated with methanol. We had deaths during the pandemic, and in those situations the same bad actors who had introduced contaminated hand sanitizer resisted voluntary recall of these drugs.

So we think that having that authority is extremely important, if not essential, to protect the American public.

*Mr. Pallone. Thank you. Thank you, Mr. Chairman.

*Mr. Bucshon. [Presiding] The gentleman yields back. I recognize Dr. Burgess for five minutes.

*Mr. Burgess. Thank you, Mr. Chairman. Let me start by just asking a question on the PDUFA.

According to your recent report that you have -- that you put out in 2022, you met 6 out of 20 procedural meeting goals in PDUFA. A problem with that is it could result in sponsors delaying study starts or proceeding without the risks -- at the risk -- without FDA alignment. So what steps is the FDA taking to address this seeming shortcoming of only 6 out of 20 performance metrics being achieved?

*Dr. Marks. Thank you for that question.

So we -- clearly, in 2022, we were still again coming off of some of the challenges from the pandemic. But to be honest, we have always had challenges making some of the -- meeting goals that we need to have. I think we are just redoubling our efforts to make sure that we have sufficient staff to be able to get to these meetings in a timely manner, and it is really staffing and attention to this that is one of the key things for us.

*Dr. Cavazzoni. I am happy to add to what Dr. Marks said.

So first, we have gone back to granting in-person meetings for all meetings. Only about -- for CDER, only about 10 percent of the meetings are requested to be in-person by sponsors. So there is also, you know, we see that sponsors also like to have the flexibility of having maybe a video conference, or a call, or sort of a hybrid meeting.

As with Dr. Marks, we take the granting of meeting very seriously. We think it is extremely important for our dialogue during development of drugs, and we are really doubling down on making sure that these meetings are granted within the timeframe that are expected, and they are -- they take place in the best possible mechanism or way that is required by the problem that needs to be discussed with the sponsor.

*Mr. Burgess. Yes, I appreciate all of that. I mean, you just simply have to do better. Companies are paying for performance here, and they -- it is reasonable for them to expect a performance.

And then we hear other discussions that the FDA wants to

vastly expand its authority into licensing laboratory-developed tests. If you don't have the staff to do this, how are you going to have the staff to do that?

Perhaps I will submit that for answer for writing.

[The question submitted for the record by Mr. Burgess follows:]

**********COMMITTEE INSERT**********

*Mr. Burgess. But on the Priority Review Voucher, which came up earlier on the cell and gene therapies, particularly curative treatments for sickle cell, one of the priority review vouchers was denied. How is the FDA ensuring that there is a consistent, predictable application of the Priority Review Voucher program?

*Dr. Marks. So I will get this right eventually on this microphone. So thank you.

So we look carefully at the Priority Review requests. In some cases it is challenging because some of these products -- it becomes a legal matter in understanding whether it is a same product or a different product. But we clearly understand how important the Priority Review Voucher program is for those innovators in this area, and so we will do our best to make sure that, when we take an action, it is very well justified.

*Mr. Burgess. Yes, we are beginning to see why the right-to-try legislation was one of the most popular bills passed in the last six years.

Let me just ask all of you, since you are here. And if there is not time, we can do a response in writing. I have

tried to get information from the FDA. I presume you have done some sort of look-back into the pandemic years. Presumably, we are at an inter-pandemic period right now. No one knows when the next one will start, but we all want to believe that we are better prepared than we were last time.

So have you done -- has the FDA done an introspective, after-action report on the COVID-19 pandemic? Have you looked at what went right and what went wrong, and what we might do to mitigate the next one?

*Dr. Marks. So thanks for that question. We have been looking at this, and we do understand certain things that went very right: issuing guidance very rapidly so that manufacturers know what to expect when they need to put new products out there, having very highly-specialized teams gather together to review --

*Mr. Burgess. I am going to run out of time. Let me just ask for all of you, could you respond to me? I will put submit that in writing.

[The answers submitted to Mr. Burgess's question follow:]

1223 **********COMMITTEE INSERT**********

1224

*Mr. Burgess. We need to know. What is the state of the art today at the FDA for last time and for next time?

Thank you, Mr. Chairman, I will yield back.

*Mr. Bucshon. The gentleman yields back. I recognize Mr. Sarbanes, five minutes.

*Mr. Sarbanes. Thanks very much, Mr. Chairman. Thank you all for being here.

Over the years, as you know, this committee has been engaged in critically important efforts to lower drug prices. I know a lot of that particular work hasn't been in FDA's purview, but there is one area where we have worked with the agency in that regard, and that relates to generic competition, as you know.

I think it is fair to say that it is well known that generic competition, as a general matter, works to reduce national drug spending, both when a generic drug initially comes to market and then, further, as more generic manufacturers enter the market. We have certainly seen that over time.

Not only that, but generic competition also has a direct impact on American patients, expanding access and

subsequently improving health outcomes and equity. So very important.

According to one HHS report, once a drug goes off patent such that generic competition can begin, prices decline by an average of 20 percent in drug markets with 3 generic competitors. In markets of 10 or more competitors, prices can decline by 70 percent in 2 years and by 80 percent in 3 years after the first generic entry. And markets that have more competitors result in larger price declines, as you would expect to see.

FDA plays an important role here, since the agency's generic approvals are truly a lifeline to many patients. Dr. Cavazzoni, can you briefly speak to how FDA facilitates generic drug entry?

*Dr. Cavazzoni. We have -- within CDER we have very large generic programs. This is an area that is critical for us, of course. The entire generic drug program is pointed towards making drugs more accessible to patients by creating competition, and therefore lowering prices. This is a program that has a, you know, that has historically had a lot of high volume.

We are increasingly focusing on what we see as coming up in the pipeline for generics, and all those are drugs that we call complex generics -- for instance, combination products where there is a drug and a device, or more complicated-to-make drugs -- because we know that that is coming up. And so we have to be ready to start to review these applications, and also increase our first cycle approval of these very complex generics. And we are making some inroads there.

There are some things that could help us in being more efficient. For instance, one of the problems that we encounter that brand drug manufacturers use to stifle competition are, you know, constraints around what we can disclose to generic manufacturers when it comes to all of the ingredients in a drug. And so we have put forward some proposals to help to see -- to the effect that we could -- to remove some of those barriers.

We are really pulling all of the stops, working also with the FTC, with the U.S. Patent and Trademark Office, because we understand how critical generic drugs are to the health care system and to access and affordability.

*Mr. Sarbanes. This question may give you a chance to

maybe expand a little bit more on your last observation, but with complexity, often, as you know, comes the opportunity for people to game the system, as well. And we often hear of gaming in the context of generic drug entry, as some product sponsors will do pretty much anything they can, as you know, to lengthen the time that their product enjoys exclusivity while others are being kept off the market. So I know that that is an arm wrestling exercise that you are going through on a daily basis.

Could you address the -- what you see as the largest gaps in the issues that currently exist in FDA's authority when it comes to promoting competition?

*Dr. Cavazzoni. Arm wrestling is a really good way to describe it.

As I mentioned earlier, the -- one of the biggest gaps that we have is the inability to disclose all of the ingredients -- for instance, a buffer that is used to determine what the acidity or the pH of a drug is. And we are constrained by trade secret laws. And so it would really help us a lot to be able to convey all of the information to the generic manufacturers, rather than trying to have -- not

being able to say anything, or getting into some kind of guess game: "There is a problem, we can't tell you what it is,'' and so on. And that can take years out of a review.

*Mr. Sarbanes. Yes.

*Dr. Cavazzoni. And I have -- certainly, there have been some examples where a complex generic has been held up for years and, of course, the savings that would go with that because of these kinds of constraints.

*Mr. Sarbanes. Well, this is the committee where we would look at what kind of authority would allow for more transparency, so thank you.

I may have some additional questions around this that we will follow up with. Thanks very much.

I yield back.

*Mr. Bucshon. The gentleman yields back. I recognize Mr. Latta for five minutes.

*Mr. Latta. Well thank you, Mr. Chairman, and thanks to our witnesses.

As probably noted a little earlier, we have two subcommittees running right now, so we have members coming between both subcommittees.

But Dr. Cavazzoni, if I could start my questions with you, Congress created the Priority Review Voucher, PRV, program to provide an important incentive for the development of drugs and biologics to prevent or treat tropical and pediatric diseases. While FDA is required to establish an updated list of rare diseases that qualify for the tropical disease program since July of 2020, my understanding is that there are at least 11 new rare diseases that are awaiting a decision by FDA.

The Further Consolidated Appropriations Act, which was recently signed into law, included report language that directs FDA to maintain the necessary resources to evaluate PRV candidates in a timely manner. Does the FDA anticipate making a decision on these diseases or on -- if these diseases qualify for the PRV this year?

*Dr. Cavazzoni. And as you heard from Dr. Marks, we are acutely aware and recognize the importance of a review by -- Priority Review Vouchers for developers of drugs for rare diseases, and we grant them in accordance with the guideposts that we have established. We endeavor to be consistent in our decisions and to be able to justify our decisions based

on that data or our regulations.

We know that there is, you know, some anxiety about the reauthorization of the rare disease -- the pediatric rare disease voucher program, and we stand ready to work with Congress to reauthorize it.

*Mr. Latta. Thank you. Dr. Marks, FDA instituted its accelerated approval program to allow for earlier approval of drugs that treat serious conditions and fill an unmet medical need based on a surrogate endpoint. A surrogate endpoint can be things like a laboratory measurement or other measure that is thought to predict clinical benefit, but it is not itself a measure of clinical benefit. The use of surrogate endpoint can considerably shorten the time required prior to receiving FDA approval, but the sponsors are still required to conduct additional clinical trials to confirm the anticipated clinical benefit.

Given that 95 percent of the 7,000 rare diseases have no approved treatment, and that it takes, on average, 15 years from pre-clinical work to FDA approval for a rare disease drug, I am hopeful that the FDA will continue its support of the accelerated approval pathway as an option for sponsors to

pursue.

I understand that many small, innovative biotechnology companies that offer commercialized products under the accelerated approval pathway face costly uncertainty around conducting post-approval confirmatory studies, even in these rare diseases -- or in these disease areas with well-established biomarkers or mechanisms or action. Could you please commit to offering more guidance to industry in this area where you have recently acknowledged that need?

*Dr. Marks. Yes, thank you for that question. So I completely understand.

We are increasingly relying on accelerated approval in this area of rare diseases where it is indicated, where we can approve high-quality, safe, and effective products. And we are committed to trying to find the most forthwith path to go from an accelerated approval to a traditional approval or full approval. And that is why sometimes we will go directly to a full approval when we can.

But we are also grateful to Congress for the regenerative medicine advanced therapy provisions which allow us to use an expanded number of methods of getting from an

accelerated to a traditional approval. So we will leverage those, as well.

*Mr. Latta. Okay. Well, thank you very much, Mr. Chairman. I am going to yield back the balance of my time.

*Mr. Bucshon. The gentleman yields back. I recognize Mr. Cardenas for five minutes.

*Mr. Cardenas. Thank you very much to Chairman Guthrie and also Ranking Member Eshoo for holding this hearing and for -- so that we can have a better understanding of the indispensable role the FDA plays in the safety and efficacy of drugs and biologics and devices.

Our health system depends on successful collaboration between the public, researchers, Congress, and the FDA. As we have fought to recover from the COVID-19 pandemic, medical innovation has been critical to the public health of our nation. I am encouraged by the strides FDA has made to advance the development of groundbreaking technologies that will benefit the American people.

We are seeing shortages across critical disease areas and populations, including patients with cancer and children with mental health conditions. These shortages are prolific.

This is an alarming trend. Constituents in my district have expressed worry as their access to treatments for ADHD and diabetes faces supply shortages and access delays. We have a responsibility to use every tool available to rapidly recover and prevent these shortages, securing lifesaving access.

In the spirit of understanding how to improve our collaboration with the FDA, Dr. Cavazzoni, can you elaborate on how effective communication with diverse stakeholders has been helpful to anticipating drug shortages?

*Dr. Cavazzoni. Yes, this is -- hearing from the public and stakeholders is very important. To that effect, we have a -- I am pleased, actually, to highlight the fact that we have launched a new sort of website that allows -- that makes it easier to report shortages or concerns about shortages, not only for manufacturers but for also the public. And so it is a one-stop-shop around shortages.

It is extremely important for us to understand where there is increasing demand or problems with production as early as possible. And so every patient, every parent, every member of the public is part of our sentinel system in watching out for shortages.

*Mr. Cardenas. Thank you very much.

As we continue to explore avenues to address these shortages and provide innovative and essential treatments, we should focus on strengthening our partnership with the FDA, not weakening it. A key component of strengthening this partnership is building trust among the increasingly diverse population of the United States.

I am proud to represent a very diverse community that deserves to have peace of mind that the treatment their doctor has prescribed has been thoroughly evaluated. By enrolling participants who reflect the diverse characteristics of those who will be ultimately using medical products, we build trust among prescribers and patients. It is essential that clinical research reaches all demographic groups to successfully modernize treatments.

As part of the recently-launched Center for Clinical Trial Innovation within CDER, one focus was around pragmatic trials as a way to lower the burden for patients to participate in clinical trials. This question is to all the witnesses: How are each of your centers working to sustain your commitment to diversity and inclusion while upholding

regulatory rigor?

*Dr. Cavazzoni. Yes, I am happy to start. For CDER we are focusing on pragmatic trials, making trials easier to conduct. We have issued guidance on decentralized clinical trials, which are very important when it comes to inclusion on underserved populations.

We are also firing on all cylinders in implementing the new authorities that Congress has given us to require diversity action plans as part of clinical trials. It should be a matter of days before we issue guidance, and this is clearly an area of great commitment.

Dr. Marks?

*Dr. Marks. Yes. So again, I think here I will just echo and say that, particularly in the area of vaccines, this need for diversity plans so that people feel confident that people like them have received the vaccine, and have received it safely is critical. And we will continue to help push that with manufacturers and through diversity plans.

*Mr. Cardenas. Thank you.

*Dr. Shuren. Just to piggyback, it is very much the same, but we are also looking at the technologies that can

make it easier for people to provide their data in the comfort of their home, because expecting people out in distant parts to go into clinical trial sites is unrealistic.

*Mr. Cardenas. So when it comes to clinical trials, for example, diversity in those individuals who are participating actually makes a difference as to how effective that would be in different demographics. Isn't that the case?

*Dr. Cavazzoni. I don't think --

*Mr. Cardenas. Not in every case. But it could, in effect, have that --

*Dr. Cavazzoni. We think that it is important that we understand the benefits and risks of a drug in the populations that are going to be taking the drug. And so our goal is to see clinical trials that reflect the makeup of the population that we have in the United States. And that is really the fundamental reason for having these diversity action plans.

*Mr. Cardenas. Wonderful. Thank you very much.

My time having expired, I yield back, Mr. Chairman.

*Mr. Bucshon. The gentleman yields back. I recognize Mr. Griffith for five minutes.

*Mr. Griffith. Thank you very much.

Dr. Cavazzoni, I was glad to hear you mention just now the benefits and risks of a drug, and making sure we know all of those. I am glad the FDA has changed its position related to medicinal marijuana. I wish it had become -- it had been the case sooner. I went public in 1998. I think the science was there when Virginia passed its law in 1979 for medicinal marijuana. The problem was it required that you have a prescription, and because it was scheduled to schedule 1 -- and I know that was you all and the DEA -- but because it was schedule 1, the research that needed to be done to use it for medicinal purposes wasn't there, and the doctors couldn't prescribe. I think we would have a more sane policy today towards using THC for medicinal purposes had we done that.

I will leave it at that. I am not looking for a comment, but I am just -- leave it at that for now. We will exchange some questions later, and do some things there, but I have more to get to. I could go on for hours about different things.

The next one I want to switch to is the ACT for ALS Act that was signed into law in 2021. It allowed for increased

research and understanding into rare, neurodegenerative, and terminal diseases. And that didn't just mean ALS. ALS was put into the title because that is one that everybody knows about. You don't have to get into a lot of explanation. But there are a lot of others that were to be -- you know, have this new increased research and understanding between the FDA, the NIH, and drug companies to try to move these treatments along.

I have spoken at previous hearings about the need for more attention to developing treatments for Huntington's disease, because there currently is no treatment. And, you know, perhaps it is a -- it is vital to me because I am -- I may be the only one here, I suspect I am -- who has the knowledge of and are friends with two different families who are affected by Huntington's. And so it is a serious issue.

So because of the ACT for ALS Act, FDA has released their action plan for these diseases, which included the first disease-specific science strategy focused on expediting development of therapies for ALS. And I support that, but that cannot be in lieu of exercising the same level of urgency for other diseases like Huntington's.

Can you commit to ensuring that you all will take a similar all-hands-on-deck approach leveraging regulatory flexibility and working with sponsors in the Huntington's space?

*Dr. Cavazzoni. So we are, of course -- share the problem with Huntington's disease. It is a terrible disease with no treatments. And we are working with sponsors and developers to bring therapies to patients.

We have made a lot of progress with the ACT for ALS. We have established a public-private partnership. We have issued grants, and we have established a strategic plan. We would very much want to -- be interested in expanding to other neurodegenerative diseases.

*Mr. Griffith. Yes.

*Dr. Cavazzoni. We need more resources. To give you an idea, the FDA and CDER did not receive any funding to contribute to the public-private --

*Mr. Griffith. But is that why Huntington's and other diseases are being slow-walked? Because I think the companies are ready to go. They just need some --

*Dr. Cavazzoni. Yes, we need to have --

*Mr. Griffith. -- direction.

*Dr. Cavazzoni. -- more resources to be able to -- within the context of the public-private partnership --

*Mr. Griffith. Yes, ma'am.

*Dr. Cavazzoni. -- and within the context of the grant program that the ACT of [sic] ALS established, we -- our ability to expand is -- only depends on our -- the resources that we have available. So we are very interested --

*Mr. Griffith. All right.

*Dr. Cavazzoni. -- in working with developers and every --

*Mr. Griffith. My time is running out. I will send you a QFR, a question for the record, so that you can give me more information on that.

[The questions submitted for the record by Mr. Griffith follow:]

**********COMMITTEE INSERT**********

*Mr. Griffith. I also want to let you know that I am concerned about foreign inspections, and we are sending a letter to Commissioner Califf in that regard. And the problem is we found a lot of violations in a lot of the countries which are producing the medicines for our folks here in the United States, and I am very concerned that we don't have enough inspectors.

I have got some ideas on that, on ways that we might be able to solve some of that inspector problem by having folks who maybe don't have the high-level training, but at least can go in and see if there is feces on the wall, because in some cases that is what we see in some of the prior inspection reports that are happening at places where people think they are getting safe medicines, but the ingredients are being shipped in from other countries, particularly Asia, and coming here, and they are not quite ready for prime time.

So my time is just about up, so I am going to have to use the questions for the record process on that, as well, and invite all of you to respond. Thank you.

*Mr. Bucshon. The gentleman yields back, I recognize Dr. Ruiz for five minutes.

*Mr. Ruiz. Thank you, Mr. Chairman.

The work FDA does to review and approve drugs and medical devices is critical to ensuring patient safety and the efficacy of new innovations. However, since FDA issued a final rule on lab-developed tests in April, I have heard concerns that FDA regulation of LDTs could slow the approval process for all drugs and devices in addition to LDTs.

While FDA will not collect user fees for LDTs for years, there is significant work that must begin now, including issuing guidance documents related to the rule. Dr. Shuren, how will FDA have the resources to implement the new rule, given the additional workload anticipated, with more tests needing pre-market review?

*Dr. Shuren. So we do have the resources to begin implementation of that rule, and we are already moving forward.

We are also looking at other opportunities for reducing costs both to test makers and to the FDA. So for example, where there is a number of things we are looking at for further streamlining pre-market review, one of the innovations is using a pre-determined change control plan,

where the developer, instead of modifications that would come to the FDA for review, can provide their plan for how they would validate it. We bless the plan, they don't have to come back in the door. We think that is going to actually play --

*Mr. Ruiz. So --

*Dr. Shuren. -- a big role.

*Mr. Ruiz. -- you say you have the resources, but can you assure us that this will not draw away resources from other important programs that FDA focuses on?

*Dr. Shuren. Yes, we will continue to make good on the MDUFA --

*Mr. Ruiz. Thank you.

*Dr. Shuren. -- commitments. And additional resources we need down the line, the phaseout is aligned with our next round of user fees, and we would fold that into those.

*Mr. Ruiz. Currently, we are seeing a record number of shortages across critical disease areas and populations, including patients with cancer and children with mental illness.

Dr. Cavazzoni, how much transparency does FDA have on

the supply chain, and what is needed in terms of mandated reporting to the agency for FDA to be able to act in a timely manner to better anticipate and address impending shortages?

*Dr. Cavazzoni. Yes. As I mentioned earlier, we would welcome having more authorities to -- that would allow us to have greater transparency on the supply chain, including how much is produced in specific facilities so that, when we have a shortage, we know where to go, we know where to -- who is making the drug, how much is being made, and then we can start talking to the manufacturers to see, you know, how they can -- may be able to supplement the shortage. So greater transparency on the supply chain is certainly an area, a tool that would really add to our limited toolbelt so far.

*Mr. Ruiz. Thank you.

In addition to safeguarding patient access to vital medications and medical devices they need to survive, we must also focus on ensuring the effectiveness and the safety of new innovations during the clinical trial process. As an emergency medicine physician, I am concerned about the potential effects that the lack of participation in clinical trials may have on the effectiveness of new medical

treatments and therapies for under-represented populations.

While FDA has attempted to increase the diversity in clinical trials that are used by the FDA to support the approval of a drug, we have not seen a consistent increase in clinical trial diversity reflecting the diversity of the United States. Notably, FDA did not ask for any new authority in this area for its budget.

So Dr. Cavazzoni, do you think the FDA has the resources and authorities it needs to achieve our collective goal of bringing in more participation of populations that traditionally lacked participation?

*Dr. Cavazzoni. Yes. This has been an area of focus for us for many years. We have made some inroads in some therapeutic areas. We publish a yearly snapshot on clinical trials, and we are making some gains.

We now have better authorities, thanks to Congress. In FDORA we acquired the authority to require diversity action plans, and that is going to be critical for us.

*Mr. Ruiz. Thank you.

*Dr. Cavazzoni. So we are working. We will see further improvement.

*Mr. Ruiz. Thank you. I would like to work with you on that. It is important that we continue working towards modernizing our clinical trials, and that is why I introduced legislation with my colleague and fellow physician, Dr. Bucshon, to address this very issue. Our bipartisan Clinical Trial Modernization Act, H.R. 8412, would improve participation in clinical trials of under-represented populations by addressing economic barriers and other outreach efforts.

This bill would help ensure clinical trial results are applicable to our nation's various populations and, in turn, lead to more effective treatments. As we look at ways to improve the safety and effectiveness of new medical innovations, I encourage this subcommittee to consider H.R. 8412 in future hearings and markups.

And so thank you, and I yield the remainder of my time.

*Mr. Bucshon. The gentleman yields back. I recognize Mr. Bilirakis for five minutes.

*Mr. Bilirakis. Thank you, Doctor. I appreciate it very much.

Dr. Marks, as you know, I co-chair the bipartisan

Congressional Rare Disease Caucus here in the House. I have heard from many rare disease -- I am the co-chair, by the way, we have -- Ms. Matsui is the co-chair on the Democrat side.

But I have heard from many rare disease companies and patient advocates who praise the creativity and flexibility of the Center for Biologics Evaluation and Research, the CBER, what it has shown under your leadership to get products safety to patients as quickly as possible. I really commend you for your vision and commitment to innovation, sir.

With that in mind, other rare disease companies, particularly those with small molecule drugs for rare indications, have explained to us that they wish their products fell under Dr. Marks's jurisdiction, rather than under the Center for Drug Evaluation and Research. Frankly, I find it unacceptable that this arbitrary distinction carries such adverse downstream impacts, and our caucus has frequently written to the FDA to ask you to apply the regulatory flexibility authorities you have already been given by Congress.

Dr. Cavazzoni, do you agree with Dr. Marks that you

would rather take the chance that the CDER will give a product accelerated approval that could occasionally make an error on efficacy and later be withdrawn from the market, rather than leave rare disease patients without any options on -- no hope for their unmet need? If you could answer that question, sir -- I mean, ma'am, I would appreciate it very much.

*Dr. Cavazzoni. Well, thank you.

*Mr. Bilirakis. Thank you.

*Dr. Cavazzoni. So accelerated approval is a very important tool for us when it comes to rare diseases beyond gene therapies, which I think you were referring to.

So when it comes to the drugs that CDER regulates, we use accelerated approval when we can. Accelerated approval requires the presence of a surrogate endpoint that allows us -- that reasonably predicts a clinical benefit. And when we are able to identify such an endpoint, we use accelerated approval.

To give you an idea, last year we approved 28 drugs for rare diseases at CDER, and a quarter of those were approved using accelerated approval, and that includes a rare disease

-- a rare bone disease, a rare kidney disease, and a very rare form of ALS. So we are -- certainly will continue to use accelerated approval when we can. When we can't, we will obviously --

*Mr. Bilirakis. Okay, let me go ahead and follow up on that.

*Dr. Cavazzoni. If I may --

*Mr. Bilirakis. I apologize, because I have limited time here.

How will you ensure that your center, and particularly your reviewers, are embracing the spirit and congressional intent of the regulatory flexibilities such as the accelerated approval pathway that we saw under Dr. Woodcock?

Again, you can briefly respond to that, and then I want to get on to my next question.

*Dr. Cavazzoni. So I am -- our reviewers are excruciatingly aware of the tremendous unmet medical need in rare diseases. And they know to exercise and they are encouraged to exercise regulatory flexibility as appropriate, based on the data that they have in front of them.

*Mr. Bilirakis. Okay, thank you. Thank you very much.

Dr. Marks, would you be willing to support a more formal process through an inter-center institute for rare disease to ensure coordination and consistency across the centers, across centers, review gaps and guidance for the smallest, ultra-rare populations, and optimize efficiencies in the review process?

*Dr. Marks. Thanks very -- thanks so much for that question.

*Mr. Bilirakis. Yes.

*Dr. Marks. The answer, for all intents and purposes, is yes. And even though we don't know what it will be called, I think, with the full support of Commissioner Califf, Doctors Cavazzoni, Shuren, and I are absolutely committed to addressing the needs of those suffering from less common diseases.

And we are actively in the process of developing an agenda -- with a capital A -- for rare diseases that will ensure that our centers are communicating and coordinating seamlessly across one another, and will put in place the cross-center collaboration that we need to, as well as, essentially, the single point of contact that we need to at

the agency for rare disease communities to engage with us.

So I think, by doing those things, we will give the rare disease community what they need to get the attention that they deserve to get towards cures.

*Mr. Bilirakis. Excellent. Thank you so very much.

And I will yield back, Doctor.

*Mr. Bucshon. The gentleman yields back. I recognize Mrs. Dingell, five minutes.

*Mrs. Dingell. Thank you, Mr. Chair, and thanks for holding this important briefing and hearing. I would like to -- and thank you to all of our experts.

I would like to begin by once again expressing my serious concerns regarding a recent outbreak of TB, tuberculosis, linked to the implementation of contaminated bone graft material. Last year the Centers for Disease Control and Prevention reported it is working to respond to tuberculosis cases appearing to be linked to bone graft material supplied by Aziyo Biologics.

Last year a Michigan patient had recently undergone a surgical procedure, and then was treated for a severe, post-surgical TB infection in an intensive care unit at the

University of Michigan Hospital. Sadly, the patient died. I have introduced two bipartisan bills with Representative Moolenaar on these issues, including the Shandra Eisinga Human Cell and Tissue Products Safety Act that was marked up in advance by this subcommittee last week.

While this bill will help to prevent the spread of tuberculosis through transplanted human cell and tissue products, it is critical we continue to do more to mitigate these outbreaks. Dr. Marks, given your agency is central to regulating these products and processing what can go wrong, what examples of harm can result from human cells, tissues, and cellular and tissue-based products?

*Dr. Marks. So, unfortunately, when these products are contaminated, we can see the full spectrum of illness, from slight sickness to death. And so that is why we take very seriously our authorities to inspect when necessary, and deal with these products to make sure that they are safe and free of transmissible infections.

*Mrs. Dingell. And unfortunately, this was not the first time the company had done it. There were more deaths a couple of years earlier. How could civil money penalties --

since there had been a previous incident -- or CMPs, help address these issues?

We hear from our Republican colleagues that CMPs would inhibit innovation. Is that the case?

*Dr. Marks. Yes, I think, by and large, this entire field is -- most of the actors here are very upstanding, and they are looking to do the right thing by making sure that their products are safe for those who receive them. That is the general. And for the few that are scofflaws here, I think civil monetary penalties would make them think twice about using less scrupulous manufacturing processes or procurement processes that can lead to this.

*Mrs. Dingell. Thank you. And since it was the second time, that is one of the reasons I ask.

Let me move to sunscreens. As you know, skin cancers and other conditions linked to sun exposure can impact individuals with all skin types and all skin tones. There is some evidence to suggest that access to a variety of broad spectrum sunscreen options, including sunscreens with different active ingredients, leads to improved appropriate sunscreen use and related health incomes [sic].

Dr. Cavazzoni, how is FDA taking into account the importance of sunscreen choice for individuals with all skin tones, all skin types, as it makes its decisions about the safety and effectiveness of the new sunscreen active ingredients, including in developing its final administrative order on existing sunscreen?

*Dr. Cavazzoni. Thank you for that question. We are very interested in seeing more sunscreen ingredients on the market. We are actually encouraged, too, by the pipeline that we see.

Sunscreens in the U.S. are regulated as drugs. That is a very fundamental difference compared to Europe and other countries. Because they are regulated at drugs, there are certain investigations and studies that need to be done, including studies that look at what might happen if the sunscreen is absorbed into the skin, to make sure that the substance does not increase the risk of cancer or cause other problems.

Having said so, we are very interested in working with manufacturers. One of the things that is going to help us is the monograph reform that Congress have given us, because it

will allow us to use orders, as opposed to lengthy rulemaking, whenever we want, if we need to make a change to a monograph, including sunscreens.

*Mrs. Dingell. Thank you. I am running out of time, and I am probably going to have to ask both of you to give me more later, but this is on drug trials.

I have a constituent named Ethan, who is a 20-year-old University of Michigan student who was recently diagnosed with brain cancer called diffuse midline glioma. As we all know, a life expectancy with the current standard of treatment is 9 to 12 months, and likely terminal.

There is good news. A company, Chimerix, has a phase three study underway with promising medication: ONC201. We know that from phase one and two studies that patients saw some well-documented extensions of life, likely due to the medicine. However, I have been told that FDA encouraged the company to include a placebo control arm into their application, since that is the gold standard of drug studies.

Dr. Cavazzoni and Dr. Marks, we are running out of time. Can you explain why that is needed here, even in a case like Ethan's?

I will ask for the record for that, Mr. Chair.

[The question submitted for the record by Mrs. Dingell follows:]

**********COMMITTEE INSERT**********

*Mr. Bucshon. Great, thank you.

*Mrs. Dingell. Thanks.

*Mr. Bucshon. The gentlelady yields back. I recognize myself for five minutes.

I want to thank the witnesses for being here today. I very much appreciate it.

And thanks to Dr. Ruiz for bringing up 8412, the Clinical Trials Modernization Act. I hope the committee will take a hard look at that legislation.

As you well know, my top FDA priority in recent years has been the VALID Act with Congresswoman DeGette. At its core, this legislation establishes a new approval pathway at FDA specific to diagnostic tests, one that will facilitate innovation through better support of continuous learning that can be applied to testing and clinical decision-making.

However, as you also know, currently the -- when it evaluates diagnostic tools in this space, the FDA has to use the medical device framework under a recent rule. Unfortunately, we have seen this framework get in the way of timely access to new types of diagnostics, since frequently FDA approval of medical devices can be tedious and time-

consuming.

There was bipartisan, serious concerns about the rule in this particular space at a recent hearing in this committee. Former FDA Commissioner Scott Gottlieb, in recent remarks to the Food and Drug Law Institute, recognized this need. He spoke about the VALID Act's potential to help approach dynamic clinical situations like those we might see when dealing with genetic treatments or quickly mutating viruses.

He advocated for the VALID Act's modern concept of supporting real-time learning environments, in which -- and I will quote -- "FDA focuses on the overall quality and compliance of a medical device company, rather than just the individual products,'' and also, I quote, "by monitoring a company's quality management systems and its post-market activities.'' He also said the FDA can allow products to reach patients while accessing their safe application in real-world settings.

Great potential exists for using technology, including AI, to address dynamic situations at the clinical level. But currently, FDA may not be able to keep up. Dr. Shuren, do you think that it would be beneficial -- and I asked you this

question before the -- way before the rule, a couple of years ago, you may not remember this -- do you think that it would be beneficial for Congress to pass legislation like the VALID Act or something similar so FDA could have a better mechanism of reviewing dynamic diagnostic tools?

*Dr. Shuren. We are certainly happy to work with Congress, and understanding that VALID would put in place a more modern framework for in vitro diagnostics.

But in the absence of it, I have got to tell you today, LDTs -- we continue to see problematic LDTs.

*Mr. Bucshon. Yes.

*Dr. Shuren. People are then not getting the right treatment. These even include with gene therapy, where we had a companion test that came in as an LDT. We reviewed the data, erroneous results being produced. The lab went back, did their root cause analysis, and found they had to redesign the test.

We continue to see these problems in cancer patients who, quite frankly, have tests out there that are not performing well, so they are not getting the right treatment. And today, if you are a cancer patient, whether or not you

get the right treatment depends more on the lab you go to than your tumor biology.

*Mr. Bucshon. Yes.

*Dr. Shuren. Not acceptable.

Rare disease patients bounce all over the place before they get a diagnosis. Why do we continue to tolerate that? We have got to fix that in this country, and it drives more inequities.

And we have disincentives for innovation by non-labs. We can fix it. The FDA is doing what we can with our current authorities because we have got to do the right thing, but we are happy to work with Congress on a modern framework.

*Mr. Bucshon. Thank you, I appreciate that. As you know, health care is critical infrastructure -- this is for Dr. Shuren also -- subject to attacks by bad actors, and medical device vulnerabilities remain alarmingly high. We are talking about cybersecurity here.

Congress included cybersecurity requirements for medical devices in the Consolidated Appropriations Act that passed at the end of 2022. Can you provide specific details on how CDRH is enforcing these requirements?

*Dr. Shuren. Well, we -- and first of all, thank you for the new legislation, the additional authorities, because we have moved forward to implement those. We have updated our policies, and we are now putting that into practice, while at the same time working with partners and industry and government and elsewhere to go ahead and deal with cybersecurity vulnerabilities.

We monitor several at any given time. One place where there is a weakness now is laboratory-developed tests, because we don't see those. And in fact, we have put out communications where we found vulnerabilities in platforms being used by non-labs and labs. Only because it was used by non-labs we found out about it. We made the manufacturer tell the labs, otherwise they would never have known there was a problem out there. This is another thing we can address with better oversight on LDTs.

*Mr. Bucshon. Thank you. I mean, so how do you hold people accountable? For example, enforce that patches are provided to biomedical departments of hospitals or their service suppliers.

*Dr. Shuren. Well, it starts -- to begin with is you

have got to design your device in a way that allows it to be patchable, and that is what we work with companies on.

*Mr. Bucshon. Okay.

*Dr. Shuren. Then assuring that they have got the right measures in place. And then, as we learn about problems and patches, we help push that out.

*Mr. Bucshon. Thank you. Thank you very much.

I yield back and recognize Ms. Kuster, five minutes.

*Ms. Kuster. Thank you very much, Mr. Chairman.

The Food and Drug Administration is responsible for regulating a wide array of products, including food, prescription drugs, and medical devices. Under the 21st Century Cures Act, Congress exempted several categories of software from being considered an FDA-regulated device. FDA has issued guidance to address when clinical decision support software would be considered an FDA regulated device.

Given how complex these programs are, I appreciate FDA's evolving approach to the issue, and would like to get further clarity. Dr. Shuren, there are scenarios where the software will only give one recommendation, such as prescribing naloxone to a patient at risk of opioid overdose. In this

scenario, would the FDA consider this software a device, and would it need pre-market approval?

*Dr. Shuren. Actually, in that scenario, it may not be a device. And just having one recommendation doesn't mean that it is what we call a non-device clinical decision support. What really matters is are we talking about patient-matched information from, like, records or reports connected to reference information like clinical guidelines?

So in your scenario, in fact, that may not be a device.

*Ms. Kuster. And does the FDA have plans to provide clarity on these issues for hospitals that use software?

*Dr. Shuren. We have provided some clarity, but if there is interest it is something we will take back. And we do want to make sure that the community is very clear on what they, you know, should be doing, or the things they don't have to do because they are not dealing with a medical device.

*Ms. Kuster. And with patient safety being the number-one concern.

*Dr. Shuren. Always.

*Ms. Kuster. Always. Turning now to prescription

drugs, the FDA's important regulatory work includes ensuring that medications are safe and effective. I think we can all agree medication is only beneficial if patients can afford it, but some drug companies have taken advantage of the patent system to delay affordable generics from coming to market.

To encourage competition and increase access to generics, I introduced the Medication Affordability and Patent Integrity Act with my colleague, Congresswoman Harshbarger. This bipartisan bill would enhance coordination between the FDA and the U.S. Patent and Trademark Office to ensure that generic drug approvals are not delayed due to patent gaming. I am hopeful this committee will include this practical, bipartisan solution in a future legislative markup.

Dr. Cavazzoni, how could coordination between the FDA and the PTO increase access to generics and actually reduce patient costs at the pharmacy counter?

*Dr. Cavazzoni. You know, the two agencies clearly have their distinct roles. Having said so, coordination is important, and collaboration is important. And to that

effect, we have a really exciting program that we have started where we work with the USPTO reviewers to show them where publicly-available data on drugs and biologics resides.

There is a lot of public-available data, and we train them to actually search it and understand it. And that information is extremely important for reviewers to determine whether, really, some obvious incremental changes to drugs really should not be patented.

*Ms. Kuster. So it seems like ensuring applicants are providing the agencies the information they need is important for successful coordination.

*Dr. Cavazzoni. That is correct. And this cross-talk and training program that we have, and this cross-training has been very, very helpful. The reviewers in the USPTO need to have -- need to understand the drugs, and what we regulate, and -- in order to make decisions as to whether these incremental, and obvious, and minor changes should be -- are eligible or should be patented.

In fact, those manufacturers take advantage of these minor changes. And if the reviewers are not sort of aware or understand drugs and biologics, it may slip through the

cracks.

*Ms. Kuster. Okay, great. Another product within FDA's regulatory authority is tobacco. Tobacco use remains the leading preventable cause of death in the United States, yet it has been nearly two decades since a new tobacco cessation product has been approved.

Earlier this year I sent a letter to Secretary Becerra with my colleague, Dr. Bucshon, and a dozen other Members of Congress on the need to expand our smoking cessation toolkit. Dr. Cavazzoni, what steps is the FDA taking to encourage the development of new tobacco cessation therapeutics?

*Dr. Cavazzoni. We are very interested and willing to work to develop with developers to make available more smoking cessation drugs.

Recently, last year, we issued a new guidance. That guidance introduces some new approaches that streamline the development, including some new endpoints and so on. And so we are very much open for business, and very motivated to work with developers.

*Ms. Kuster. Great. Thank you so much.

I yield back.

*Mr. Bucshon. The gentlelady yields back. I recognize Mr. Hudson, five minutes.

*Mr. Hudson. Thank you very much, and thank you to the witnesses for being here today. Thank you for what you do every day, very important roles.

My home state of North Carolina is a leader when it comes to innovation and manufacturing. So ensuring that those folks can thrive to produce lifesaving products is a priority for me. Too often I hear complaints about hitting walls with the FDA. Whether it is a delay in an answer, unnecessary or over burdensome demands, or an FDA oversight, it is happening too often.

The Prescription Drug User Fee, or PDUFA, imposes deadlines for FDA to review drug applications, as you know, 6 months for priority products and 10 months for all others. While most -- the most recent annual performance report shows the agency meeting many of its review goals, I am concerned that doesn't tell the whole story.

There are numerous public reports of FDA actions that delay approvals well beyond these timelines, often due to bureaucratic limbo or last-minute internal decisions. For

example, FDA can issue a complete response letter -- essentially, a rejection -- which stops the clock if the agency needs more time to review. FDA can also get an extension if the agency decides to hold an advisory committee meeting, which Commissioner Califf has noted are in serious need of reform to be useful.

I am concerned there are North Carolina companies being caught up in just this sort of mess, at risk of having to lay off employees and ultimately delaying access to these products. Dr. Marks, Dr. Cavazzoni, how do you keep track of products that are beyond their PDUFA dates or near misses within your centers?

And how can FDA, with existing resources, do better to -- at improving predictability and transparency in product review?

*Dr. Marks. Thank you very much for the question. So we have a group that actually tracks these quite closely, and provides our leadership, me included, with reports on this. And I agree with you, we can sometimes do better here.

I think we also -- I try to do, essentially, after-actions to understand why these events occurred so we can

help prevent them.

I agree with you, bureaucratic reasons for this are unacceptable. There has to be a good scientific reason why we -- why we miss things, and that is our goal, to always have it be on that, and that is where we are headed, at least in our center. Thanks.

*Dr. Cavazzoni. Yes. Similarly, we track our PDUFA goal dates very, very closely, and they are constantly scrutinized. We try to avoid missing all dates. And in fact, it is a very, very rare event.

What we try to do, for instance, is in situations where the sponsor would like to submit additional data over the course, once the review of the application has started and it is already on the clock, we extend the goal date to allow them to submit the data, allow it to be reviewed, so that we don't actually have to potentially issue a complete response and turn down the application, when in fact maybe reviewing some additional data would make it -- would help it get across the line.

So we do everything that we can to avoid situations where we have to turn down an application not having reviewed

all of the data, or certainly very rarely. And we think about it very carefully in those rare situations where we may have to miss a goal date.

*Mr. Hudson. Thank you.

Dr. Marks, Commissioner Califf has said that systemic efforts are underway to reform the advisory committee meetings, and recently reiterated his belief that it is not necessary to take a vote at most meetings.

He also stated that, "The advisory committee meeting structure needs to be changed to allow fuller and more comprehensive discussion of the issues surrounding medical products under review,'' and that meetings "should focus less on outcomes.''

Would you agree that there should be improvements made to the FDA's advisory committee process and practices?

And if so, what do you feel would be the most impactful improvements for patients?

*Dr. Marks. So thank you for that question.

I think it is nice to have the flexibility to both not take votes and to take votes when appropriate. I do think that our advisory committee process, while generally working

reasonably, could benefit from some freshening up, including the ability to have -- currently some of our conflict of interest issues sometimes actually get in the way of having the best possible experts speak to us at these advisory committees, and so we have to work through that.

I think we also want to ensure that these advisory committees are comprised of diverse members of the community of experts that can help bring a full picture, and not a stilted one of the area of interest. So we are committed to a process to improving them.

*Mr. Hudson. I appreciate that, and I am about to run out of time. I will submit a couple questions for -- in writing, if you wouldn't mind.

[The questions submitted for the record by Mr. Hudson follow:]

**********COMMITTEE INSERT**********

*Mr. Hudson. But Dr. Cavazzoni, my colleague's question about the smoking cessation products, that is a big concern, and I would love to get -- just hear kind of your update on where you think things are with the guidance you issued last year. So thank you very much.

*Dr. Cavazzoni. We would be happy to follow up.

*Mr. Hudson. Thank you.

*Mr. Bucshon. The gentleman yields back. I recognize Ms. Kelly, five minutes.

*Ms. Kelly. Thank you, Chair Guthrie and Ranking Member Eshoo, for holding today's hearing.

In recent years members of our committee, me included, have pushed for FDA action to boost diversity in clinical trials, which is crucial for accurate drug assessment across demographics. Though the FDA has made significant -- has made progress, significant gaps remain in representing all communities. Around 90 percent of pregnant women use medications, yet most lack sufficient safety data. Given HHS's common rule allowing testing for pregnant and lactating women, more must be done to ensure safe medication use based on robust evidence.

Dr. Cavazzoni, given the high maternal mortality rates among Blacks, Latinas, and indigenous mothers, can you share additional measures the agency is putting in place to ensure this population is included in this research?

*Dr. Cavazzoni. Thank you. That is a very important question.

We have issued guidance on this to really emphasize for drug developers and sponsors that it is very important to study pregnant women during -- before a drug is made available on the market.

There are some very real constraints, particularly in the very litigious environment that we live in, and there may be some -- you know, some discussions about tort reform may need to take place when it comes to this particular space.

And having said so, we think this is very important, and it is very important not only to study pregnant women before a drug is marketed, but also after it is marketed. And to that effect, you know, we require, for instance, pregnancy registries or post-market studies to continue to generate data on the safety and effectiveness of drugs, particularly the safety sort of in pregnant and lactating women.

*Ms. Kelly. Okay, then. My district encompasses rural, suburban, and urban from the Chicagoland area, which -- obesity rates range from a quarter to one-third among adults, exacerbated by food deserts limiting nutritious options. Commissioner Califf highlighted that obese patients are frequently excluded from trials due to comorbid conditions hindering safe and effective dosing data collection. FDA-approved medications may lack proper dosing or pose risks for obese patients, as post-marketing studies reveal. This highlights the need for inclusive trials and tailored dosing for this population's safety and efficacy.

Dr. Cavazzoni, again, given obesity's prevalent and associated risks, what specific steps is the agency taking to ensure adequate representation in trials?

And how does the FDA promptly update drug labels with the new dosing data?

*Dr. Cavazzoni. Yes, there is several things that we are doing.

First, it is a very important that we enroll in clinical trials a population that is representative of the population that will ultimately be taking the drug once it is marketed.

And to that effect, we have a -- we are paying a lot of attention to clinical trial diversity issue guidance and so on.

We also have issued extensive guidance for sponsors, indicating that we want -- we don't want the inclusion or exclusion criteria for trials to be so restrictive that it really impacts the generalizability of the data.

And lastly, it is very important that we find a way to actually have recruitment for clinical trials in the communities that have historically been excluded from clinical trials. And so the work that we are doing around clinical trial modernization -- writing guidance, we wrote guidance on decentralized clinical trials.

We are working on guidance for point-of-care clinical trials that would hopefully make it easier and encourage sponsors to start recruiting patients from clinical trials where they live every day, rather than having to trek to academic institution, which, of course, they will not do and, therefore, we will continue to exclude populations from clinical trials.

So very critical for us, and we are really exploring all

avenues to achieve these goals.

*Ms. Kelly. I have another question, but I will get it to you, because I am running out of time.

[The question submitted for the record by Ms. Kelly follows:]

**********COMMITTEE INSERT**********

*Ms. Kelly. So I will yield back.

*Mr. Bucshon. The gentlelady yields back. I recognize Mr. Carter, five minutes.

*Mr. Carter. Thank you, Mr. Chairman, and thank all of you for being here.

Let me go ahead and preface this by saying that I am of the opinion -- I have served 10 years in the Georgia state legislature, 10 years in Congress, and the prescription drug portion of the IRA is the very worst legislation I have ever seen in my whole life. I just want to set the stage for this, okay?

You know, we have continued to warn the other side of the aisle that this scheme is going to cause immense harm to patients by crushing drug innovation, and we have already seen it. We have already seen that there have been over 24 drugs pulled from the market, including cancer drugs, as a result of the IRAs passage, the prescription drug portion of the IRA.

I will tell you, the University of Chicago researchers found that the IRA will eliminate up to 342 cures and treatments over the next 20 years.

As you may or may not know, I am a pharmacist by profession. I started practicing pharmacy in 1980 -- I was 10 years old -- but anyway, I started practicing pharmacy in 1980. I have seen nothing short of miracles as a result of research and development. That is why this upsets me so much.

You know, regardless of whether you believe CBO, who has also said that it is going to decrease the number of new drugs coming to market, or whether you believe the University of Chicago, even if it is just one, which one is it going to be? Is it going to be the cure for Alzheimer's? Is it going to be the cure for diabetes? We shouldn't be trying to hurt research and development or deter research and development in any way at all. And this rule does that, and that is why I am so upset about it.

Dr. Marks, your deputy centers -- director's viewpoint that the Inflation Reduction Act has impacted innovation for small molecules and biologics, CBER's deputy security director for strategy, policy, and legislation stated that the IRA has had an impact on innovation. Do you agree with that? Do you share that feeling?

*Dr. Marks. You know, the way -- all I have to comment on this is that we have to foster -- and my goal is to foster -- I am not involved in the political end of it, but we have to foster innovation.

*Mr. Carter. Okay, I understand that.

*Dr. Marks. We have to -- anything that is counter to helping us innovate in this field of cell and genetic medicine is not a good thing.

*Mr. Carter. Would you think -- do you think that this is? I am just asking your opinion.

*Dr. Marks. You know what?

*Mr. Carter. I know, I know.

*Dr. Marks. I am going to stay out of the political. But I will say that we at our center will do everything we possibly can to help innovators move products forward, because having the most innovative products available to Americans is what our job is.

*Mr. Carter. It is confusing to me, though. And, you know, I admire the President's Moonshot and Cancer Moonshot program. How is this going to impact that?

*Dr. Marks. Yes, I can't -- I, unfortunately, can't

speak to that.

*Dr. Cavazzoni. I am happy to chime in, as well.

*Mr. Carter. Yes, and Dr. Cavazzoni, please.

*Dr. Cavazzoni. Yes, I am happy to chime in. You know, we -- in our roles, we really cannot speak to the decisions that manufacturers will make, as --

*Mr. Carter. Wait, wait. The manufacturers are making it as a result of the legislation that was passed.

*Dr. Cavazzoni. We really -- you know, we are not in a position to --

*Mr. Carter. But you ought to be. Come on. You are Americans, too, and you care. You care about innovation.

*Dr. Cavazzoni. We care --

*Mr. Carter. You care about research and development.

*Dr. Cavazzoni. We care about doing --

*Mr. Carter. Well, why aren't you telling the Administration, "This is not helping, this is deterring research and development'‘? You ought to be jumping up on the table, hollering it.

*Dr. Cavazzoni. If I may.

*Mr. Carter. Yes, ma'am.

*Dr. Cavazzoni. And chime in, Dr. Marks.

We care about doing everything that we can as regulators to make it easier and more efficient and more streamlined to develop drugs, and that is a contribution that we can make to innovation. And ultimately, that contribution may have an impact also on the cost --

*Mr. Carter. Okay, all right. Let me ask you this, because I have got just a few minutes left. But does the agency agree that new smoking cessation therapies are needed to help patients be more successful in their attempts to quit?

*Dr. Cavazzoni. Yes, we are --

*Mr. Carter. Do you agree with that?

*Dr. Cavazzoni. We are very interested in having more sponsors --

*Mr. Carter. Why --

*Dr. Cavazzoni. -- coming to us to develop new therapies --

*Mr. Carter. Well, then why don't --

*Dr. Cavazzoni. -- for smoking cessation.

*Mr. Carter. Why do you think we are not seeing more?

*Dr. Cavazzoni. I don't know. We are really doing everything that we can. We issued guidance --

*Mr. Carter. So you are not trying to stifle it, you are trying to help it. You are trying to encourage it.

*Dr. Cavazzoni. We are trying to encourage it, and we are trying to make it easier. In the guidance that we issued last year, we opened new ways and new approaches to developing treatments for smoking cessation. And we are really very much open for business, and want to work with developers to achieve that goal.

*Mr. Carter. Okay, look, I just respectfully disagree. You are the experts. You ought to be telling them, "This is wrong, this is not helping.''

Mr. Chairman, I yield back.

*Mr. Bucshon. The gentleman yields back. I recognize Dr. Schrier, five minutes.

*Ms. Schrier. Thank you, Mr. Chairman, and thank you to all of our FDA witnesses for taking time out of your busy schedules to be here today.

FDA, as we have heard, is entrusted with regulating medication, devices, food, vaccines, cosmetics, and many

other things that impact Americans every day. And I trust FDA to make these important decisions based on science and facts.

I just want to point out that right now the Supreme Court is considering a case to roll back FDA's approval and prescribing requirements for mifepristone, a drug that has been approved for over 20 years for medication abortion. FDA is the gold standard of safety and efficacy, and we cannot allow politics to undermine science. Not only is this way out of line for mifepristone, which is also approved for other indications, but it creates a slippery slope of political undermining of other medications and of scientific research and FDA authority. I am making this point; it is not a question.

I would like to turn to laboratory-developed tests, and I want to commend the FDA for taking action to move regulation of LDTs forward as, Dr. Shuren, you discussed. I do have some concerns, though, about the impact that will have on pediatric testing, some of which requires rapid authorization because of the importance of diagnosing many pediatric diseases early, given the risk of progression of

diseases in children.

And for some pediatric LDTs, there may be only one or two centers worldwide that have the expertise to perform and oversee those tests, given the specialized nature of pediatric health care. And this is particularly important, given the disproportionate impact of these rare diseases.

So it is not uncommon for one children's hospital to send samples to another children's hospital for rapid testing on their LDT, rather than have a family travel long distances and take that time. This is especially true for our local Seattle Children's, which has the unique challenge of being the primary children's hospital for the surrounding four-state region. So in order to reduce burden, for example, a hospital in Alaska might send to have the test done and avoid having to send a whole family to Seattle.

Dr. Shuren, under the final rule, would these situations be considered an unmet need, even though the test is not developed or used in the same geographic location?

And if not, how does the FDA plan to ensure that children with rare diseases will have access, and quick access, to these types of tests?

*Dr. Shuren. So if I am hearing the scenario correctly, then this would be tests that are being developed, used in a laboratory, integrated in a health care system, and those would fall under our enforcement discretion policy for an unmet need, and they would not need to come in for pre-market review.

*Ms. Schrier. And would that be subject to an appeal if it were not approved?

*Dr. Shuren. If it was subject to -- again, here sounds like it is not, but if it was subject to pre-market review, then yes. If there was an adverse decision, it would be subject to appeal by us.

*Ms. Schrier. Thank you very much. Thank you for considering this very specific children's indication.

I want to turn to avian flu now. This is important in my district right now, because I have a large agricultural element. And while there are only two confirmed cases of the currently circulating avian flu in humans in the United States, I am very concerned about the estimated 100,000 farm workers who are at a particularly high risk for potential infection and, of course, then the potential for human-to-

human spread, as we have seen happen.

I know FDA, CDC, and USDA are all working together to mitigate the impact of H5N1 on cows and the milk supply and on humans. And Dr. Marks, I was wondering if you could talk a little bit more about what your center is doing to develop an H5N1 vaccine for humans.

*Dr. Marks. So thanks very much for that question.

There actually are three licensed H5N1 vaccines not necessarily matching this current strain. We have plans to essentially have strain change supplements or, if necessary, use emergency use authorization, if we had to, to ensure that we could get countermeasures out as quickly as possible.

And we have already taken steps to stay ahead of this. Hopefully, we are not going to have to deploy anything, but we actually have learned a thing or two. I think this was from a question earlier from the -- from -- both from the pandemic and from the Mpox outbreaks that we can just plug and play here, so that we are ready with our partners at CDC and at ASPR, so that we can move quickly.

*Ms. Schrier. Thank you. I remember standing in a line with my newborn or six-month-old to get this the last time it

came up in humans.

I will yield back.

*Mr. Bucshon. The gentlelady yields back. I recognize Dr. Dunn for five minutes.

*Mr. Dunn. Thank you very much, Mr. Chairman, and thank you to the witnesses from the FDA for appearing here today.

Dr. Shuren, I have long been concerned about the FDA's desire to promulgate rigid regulations that seek to subject lab-developed tests to the same requirements as medical devices. I have appreciated the robust debate among the members of this committee regarding the appropriate guardrails as outlined in the VALID Act, which, as you well know, has gone through many iterations.

The VALID Act was on the right track toward creating an appropriately limited and narrow scope for FDA oversight of lab developed tests. However, I think, much to the disappointment of the bipartisan members of this Congress and this committee, the agency proposed a sort of one-size-fits-all regulation that mirrors that of commercially-produced kits that consumers, not physicians, administer themselves just with instructions.

The final rule was only slightly improved from the disastrous original proposal.

I do appreciate the unmet need exemptions, which were just mentioned, and the grandfathering of certain tests. I remain concerned, however, about risk classification and the FDA's ability to efficiently assume the task of oversight that you propose here.

So, first and foremost, Dr. Shuren, I want to -- I would like to know whether or not the FDA employs any -- any -- practicing lab professionals. So these would be pathologists, physicians, et cetera, who are actively performing labs for the FDA.

*Dr. Shuren. So we do have experts on staff who have worked in labs.

*Mr. Dunn. Okay, but they are not working in a lab currently for the FDA.

*Dr. Shuren. No, they are at the FDA.

*Mr. Dunn. Okay, so there are -- there is a fundamental, I think, real-life disconnect when people who are sitting at desks reading reports about people who actually are doing science write the regulations for the

physicians and practitioners who are doing the science. Do you agree with that?

*Dr. Shuren. No, we have, actually, the experts who have been overseeing tests for almost 50 years. There is no other place in the government that does --

*Mr. Dunn. Yes, I mean, but it is not the same as actually working on the tests, you know, recently. And they change. You know, I am out of practice myself just a few years, and it has changed dramatically.

Let me go on. Regulating lab-developed tests surely will require an expansion of expertise and personnel at the FDA. Do you have a plan in place to bring in the experts in that field for test development?

*Dr. Shuren. We have experts already, and if we need additional experts this will be part of what folds into our subsequent user fee discussion.

You know, I will say, too, New York State has been reviewing LDTs for 30 years. They have reviewed thousands of them. They are finding the same problems that we --

*Mr. Dunn. I believe in the problems, but I just think this is a heavy hammer.

And by the way, New York State, remember, got into some pretty deep trouble with their sequencing, as well, what they passed there.

Under the VALID Act, labs would be able to coordinate with trusted, third-party accreditors -- would they be able to with -- such as the College of American Pathologists, which employs practicing pathologists to assist with compliance with these new regulations?

*Dr. Shuren. And so, in the VALID, you could take advantage of third parties. But also, with our regulation, we have opened up the door so that you can work with third parties --

*Mr. Dunn. I encourage it, I encourage it.

So as we were tuning up the VALID Act, we sort of narrowed the scope quite a bit on that. Do you agree with that narrower, more narrow scope, or are you sort of back to the wider interpretation -- almost all the lab-developed tests that haven't been grandfathered?

*Dr. Shuren. I will say, for the VALID Act, one key aspect is that it is not one piece, the VALID Act, it was all the pieces together. So for example, one of the approaches,

a novel approach was on -- where you are really looking at the capabilities of the laboratory around technology, rather than each test. But that only worked because you would also have the post-market tools of reports and surveillance inspections --

*Mr. Dunn. So let me get -- dive into that real quick in our last few seconds here. Is it your position that the FDA is somehow better positioned than existing third-party accreditors of CLIA labs to assist with compliance and performance of these labs?

*Dr. Shuren. Yes, for assuring the test actually is safe and effective, yes. CLIA does not pertain to key aspects --

*Mr. Dunn. No, but the performance of the test is -- I mean, they come in and check to see are you running your lab well, are you getting -- are you meeting the standards, you know.

*Dr. Shuren. Well, CLIA oversees the lab operations, but not the test itself. And CMS has been very clear that these are different. They are complementary, but they are different in focus, purpose, and scope.

*Mr. Dunn. Okay. Let me -- with a few seconds left, I am just going to say that I do have concerns about the classifications risk -- risk classification of existing tests and the future test. And you will be hearing more from our offices on that. I will have questions, as I have over the last few years.

And with that, Mr. Chair, I yield back.

*Mr. Bucshon. The gentleman yields back. I recognize Mrs. Trahan now.

*Mrs. Trahan. Thank you to the chair.

*Mr. Bucshon. Five minutes.

*Mrs. Trahan. I am going to follow up on a point that -- a very important point that Congresswoman Schrier had made, because ensuring the safety and efficacy of the drugs approved in the United States is central to the protection of public health, and allows Americans to have faith that the prescription drugs and treatments they are prescribed by their doctors have been thoroughly reviewed and evaluated based on data, science, and clear evidence to assess the risks and the benefits.

So Dr. Cavazzoni, can you discuss why FDA's gold

standard of safety and efficacy is so critical, and what impact could undermining the gold standard have on the safety and efficacy of our drug supply chain, moving forward?

*Dr. Cavazzoni. Well, the standards that we have ensure that drugs are safe and effective by the time they are -- at the time they are made available to the public. And so those standards are important to maintain for public health and for -- to make sure that the public are not exposed to undue harms or to drugs that don't work.

*Mrs. Trahan. Yes, it is a seal of approval that we rely on in our country. That is why, like Dr. Schrier, I have deep concerns about efforts by right-wing judges and politicians who have sought to substitute their own opinions for that of the FDA's expert decision-making. We have watched as Trump-appointed Federal judges have been more than willing to override the impartial, non-partisan, scientific decision-making of FDA with their own ideological and extreme views, putting patients and the FDA gold standard at risk.

As we await the Supreme Court's decision in FDA versus Alliance for Hippocratic Medicine, I am appalled that 145 congressional Republicans have doubled down on this by

joining an amicus brief in support of the plaintiffs in this case, and made clear that they are willing to undermine the FDA by calling into question the approval of mifepristone, which has been approved by the FDA for over 20 years.

All right. I am going to switch gears now, but we have to get that out, and we have to make sure it is discussable in terms of the stakes.

BRIUS Medical, based in Billerica, Massachusetts, produces essential ventilators for home use. They have a pending 510(k) application with the FDA for a new version of their ventilator that includes an auto EPAP feature. The AE feature is particularly important for patients with conditions such as COPD. During the COVID-19 emergency the FDA permitted the use of ventilators with the AE feature under the Emergency Use Authorization, even if they weren't fully approved. But now that the emergency has ended, the FDA has ceased making these exemptions -- exceptions, excuse me.

The discontinuation of EUAs could lead to a shortage of these crucial ventilators, potentially harming patients who rely on them, and affecting companies like BRIUS Medical.

Dr. Shuren, given the critical need for home care ventilators with the AE feature for vulnerable patients, how does the FDA plan to address potential shortages and ensure that devices like those from BRIUS Medical, which are still awaiting 510(k) approval, excuse me, remain available to meet patient needs?

*Dr. Shuren. So first of all, EOAs have not -- you know, are still in place for many of the products out there. We do have enforcement discretion policies that we have pulled back, and we don't apply those if there is sufficient supply of alternative product that is out in the marketplace.

This particular company, we would be happy if they -- you know, it is confidential information for them. If they supported it, we would be happy to talk in more detail. We did actually clear their product without that feature, and we can talk about the issues with that feature.

*Mrs. Trahan. Well, that would be great. Thank you.

I yield back.

*Mr. Bucshon. The gentlelady yields back. I recognize Dr. Joyce, five minutes.

*Mr. Joyce. Thank you, Chairman and Ranking Member, for

holding this hearing today, and for our witnesses for being here. I have three very focused questions.

First, for Dr. Marks, I appreciate the FDA's focus on finding cures for patients with rare diseases. This is especially important because 95 percent of the more than 7,000 known rare diseases have no FDA-approved treatments. As you are aware, Julie Tierney, who currently serves as CBER's deputy center director for strategy, policy, and legislation, stated that the IRA penalty for seeking multiple orphan drug approvals for the same product could discourage future drug development, most acutely in rare disease.

Can you comment on the importance of developing medicines that treat multiple rare diseases to close that treatment gap?

*Dr. Marks. Yes. Well, what I can say here is that, obviously, it is an impetus to developers, if they develop a first indication, to be able to have a second or third indication to be able to move into. And being limited to one indication could be a disincentive.

*Mr. Joyce. I agree with you completely.

Moving on, first of all, Dr. Shuren, to comment publicly

on our gratitude for you and the FDA for ensuring that patient safety remains paramount when highlighting the significant ramifications that the EPA's ethylene oxide rules could have on medical device sterilization. It is a safety issue.

Going forward, do you feel as though you have an open line of communication with the EPA to ensure that medical device implications are understood from the onset when they are developing rules around PFAS or in other areas?

*Dr. Shuren. I do think that we have appreciated we have been able to work with the EPA, and we were able to provide important information that they took into account in their ethylene oxide rule. We are going to continue to monitor, though, what is happening with the sterilization facilities to see what the outcome is in practice, to try to minimize --

*Mr. Joyce. I thank you for that close attention. Dr. Shuren, I would also appreciate the opportunity to maintain an open dialogue going into the user fee negotiations.

It is a bit unclear to me why industry stakeholders are not permitted to keep up to speed about how these

negotiations are going when they are expected to authorize the agreement, particularly when novel issues are being considered or when certain agreements are delayed like last cycle. Because of this, we, as the authorizing committee, rely on your meeting minutes, which in the past were posted to FDA's website long after actual meetings had taken place.

Can you commit to a more timely publication of your meeting minutes this next go around, and would you be open to a more transparent negotiation process, including agency and industry updates to this committee as they unfold?

*Dr. Shuren. We are committed to more timely meeting minutes, and I will say that that was actually a joint responsibility for us and industry on taking more time.

We would be happy to have further discussions on how we can provide appropriate transparency in the process.

*Mr. Joyce. Thank you. I think that transparency will only aid as these developments are so necessary to move forward.

And my final question is, Dr. Cavazzoni, every hour at least two Americans die from skin cancer. And since this hearing has started, six Americans have died from skin

cancer. You are speaking to the only dermatologist in Congress. And no new sunscreen active ingredients have been approved in the United States since the 1990s.

Since then, the rest of the world has moved ahead of us, one or two generations of sunscreen ahead of us. Today the United States has only six sunscreen active ingredients available, potentially less upon the finalization of the sunscreen final administrative order. In contrast, the EU has 34 sunscreen active ingredients approved. How can the FDA's regulatory framework be streamlined for ingredients currently on the global market?

*Dr. Cavazzoni. So we are very interested in seeing more sunscreen ingredients available in the United States. And, you know, we are encouraged to see a greater interest from manufacturers.

There is a fundamental difference in the regulation of sunscreens in the U.S. Sunscreens are regulated as drugs. In Europe they are regulated as cosmetics. So in the United States that means that we need to obtain data that are not required for --

*Mr. Joyce. Do you find that 30 years without any new

active ingredients for sunscreens being formed or approved is incredibly unreasonable?

*Dr. Cavazzoni. We would certainly like to see more ingredients out there. One of the things that --

*Mr. Joyce. Would you commit to being able to work with industry to see that more ingredients are tested and approved by the FDA?

*Dr. Cavazzoni. We are very interested to do so.

One of the things that is going to help us is monograph reform that Congress have given us for -- prior to that, any changes that we made in the monograph, including sunscreens, would take issuing regulations and years and years of time to do so. So now that we can use orders, we expect that the -- to -- we expect that it will be much easier for manufacturers to --

*Mr. Joyce. I would love to see that --

*Dr. Cavazzoni. -- propose new --

*Mr. Joyce. -- it is much easier and much faster.

Mr. Chairman, my time is expired, I yield back.

*Mr. Bucshon. The gentleman yields back. I recognize Mr. Balderson, five minutes.

*Mr. Balderson. Thank you, Mr. Chairman. Thank you all for being here today. My first question is for Dr. Shuren.

Dr. Shuren, first of all, I would like to -- it is hard to -- I know, it is tough. I would like to thank you for taking the time to do the brief on the Digital Health Caucus last month that Representative Kelly and I are taking the lead on. So we appreciate your support with that.

We know that CDRH has cleared hundreds of predictive artificial intelligence products through its existing authorities under the medical device amendments. However, I am concerned by the impending influx of more complex generative AI products that the Center's existing processes cannot accommodate. How can we facilitate the approval of innovative products that are not suited to traditional FDA review?

*Dr. Shuren. We share your concern. As you noted, we have authorized now almost 900 AIML-enabled medical devices. But those particular functionalities are kind of the lower level diagnostic. We moved into generative AI.

The current framework is not fit for purpose. It is really designed around hardware. We need a model that is

more focused on the post-market setting that is going to be able to sort of monitor what is happening. Because with AI, if we want to deal with issues around understanding what it does and address and minimize risk of bias, it has got to be much more of a post-market model.

Secondly, the numbers of what is going to be produced are going to skyrocket. We are never going to have all the resources, and it is unrealistic to expect that. We need to have the ability to kind of have a third-party certification model in place, as well, but that would require help from Congress.

*Mr. Balderson. Okay, thank you. As we examine and continue to embrace AI, though, the United States must remain the global leader in innovation. There are national security implications if the U.S. restricts AI development. At the same time, we should work with other countries to prevent duplicative requirements for companies marketing devices with AI here and abroad.

What is FDA doing with respect to international harmonization on AI?

*Dr. Shuren. Well, much of our work for harmonization

occurs in a group called the International Medical Device Regulators Forum. We are actually the chair of it this year. We typically, in the AI space and even digital health, when there are needs for changes, new policies we not only start here in the U.S., we take it to this group because all the countries are struggling with the same issues.

So for example, we are working on policy on a life cycle management approach for AI. We just raised this at IMDRF, and that group of countries has agreed that we would create a globally harmonized policy to do so.

*Mr. Balderson. All right, thank you very much. I appreciate your answers. My next question is for Director Cavazzoni. I hope I did the name somewhat close.

PDUFA was started over 30 years ago to address unacceptable delays. These funds ensure that the agency has resources to keep pace with innovation of medicines that patients need. Under PDUFA, FDA commits to certain performance goals in exchange for conducting timely sponsor meetings to align data and study design expectations that would support future product approvals.

In the most recent performance report, FDA only met 13

of the 22 PDUFA meeting goals. And overall, FDA only met 15 of the 29 times in processing its goals. Without these, sponsors either delay studies or proceed at risk without FDA alignment, either of which may result in delayed access for patients. In the performance report FDA blamed these missed metrics on hiring challenges. The FDA has consistently missed the hiring goals outlined in the PDUFA agreement.

What new approaches is FDA using to address these shortfalls, and why do you have confidence that you will see improvement in recruiting rates as a result?

*Dr. Cavazzoni. So thank you for that question. We have -- we pay a lot of attention to our metrics, and we meet the overwhelming majority of our metrics. You are mentioning two areas that have historically been more challenging, meeting metrics and -- as well as hiring. We are making some inroads there. We are really doubling down on looking at, you know, the root causes of missing some of the meeting metrics.

When it comes to hiring, we have a lot of things underway. Something that has really helped us very much is the title 21 or 21st Century Cures hiring authority that has

allowed us to hire staff in a more streamlined fashion, and also be more competitive with the private industry.

So we are making gains. We are not where we want to be everywhere, but we are committed to continue to really double down in these areas. And we expect that we will make -- be making further gains.

*Mr. Balderson. All right. My time is expired. Thank you all very much.

Mr. Chairman, I yield back.

*Mr. Guthrie. [Presiding] The gentleman yields back. The chair recognizes Ms. Harshbarger from Tennessee for five minutes for questions.

*Mrs. Harshbarger. Thank you, Mr. Chairman, and thank you to the witnesses for being here today.

I want to start by asking you a question, Dr. Marks. In February of this year Chair Rodgers, Democratic Representative Juan Vargas of California, and I had a very positive meeting with FDA Commissioner Califf, where we discussed our shared goal of reducing our reliance on China and protecting and fortifying our medical supply chains through a friendshoring or nearshoring strategy. And we

discussed how that could be achieved by establishing a technical assistance FDA bureau in the Abraham Accords regions to facilitate leveraging U.S. access to the robust and growing biomedical industry in the Abraham Accords region.

This is a concept I put forward with Representative Vargas in our introducing the bipartisan U.S. Abraham Accords Cooperation and Security Act. Commissioner Califf said at our meeting he is happy to work with us on this bipartisan initiative, so long as we and Congress provide funding for it, and we are prepared to do that.

My question to you, sir, is, what are some key metrics you think we should look for in making this a successful initiative?

*Dr. Marks. Thanks very much for that question. I think, probably, if we are going to have a successful initiative, it is going to be one where we can measure the number of products that make it, essentially, forward from one jurisdiction to another, where we can share, essentially, a regulatory -- the equivalent of regulatory reliance, or cross-reference, and where we can also help alert each other

to problems that exist in the system and have a dialogue.

Probably Dr. Cavazzoni can say more in this regard.

*Dr. Cavazzoni. Yes, I would echo that, you know, this type of cross-work with other regulators is very important. We have a lot of activity in our international harmonization space.

I will give you an example of a very exciting pilot that we have been running with other regulators to facilitate the and remove bureaucratic barriers from -- in situations where sponsors are asking for manufacturing changes after a drug is approved. That is a major barrier, for instance, for -- to expanding the capacity, and the manufacturing capacity, and also to prevent shortages. So we are really very committed to continue to work in unison with other regulators.

*Mrs. Harshbarger. Great. That is what I wanted to hear. We want to get this done.

My next question, Dr. Shuren, for more than a decade the FDA has devoted extensive resources in an aggressive campaign to ban the use of an FDA-cleared medical device that is being successfully used by medical doctors and other licensed health care professionals at 1 facility to treat

approximately 50 patients in the nation, patients who exhibit the most extreme self-injurious and aggressive behaviors, and their families consider this therapy a blessing, since no other treatments have worked. And the alternatives would be restraining those patients and medicating them to the hilt so that many of these psychotropic drugs -- to the point that they are catatonic and experience alarming weight gains.

Following the FDA's previous regulatory effort in 2020 to ban this specific intended use of an otherwise legal medical device, a Federal court struck down your regulation as violating the Food, Drug, and Cosmetic Act, which bars the FDA from regulating the practice of medicine. Then, through aggressive lobbying by the FDA to get around this court decision, 19 lines of legislative text to give FDA this authority were stealthily airdropped and buried into a 4,000-page omnibus appropriations bill hastily enacted in 2022 to avoid a government shutdown. No hearing or formal congressional debate was even held on this provision, which represents a seismic shift in FDA's authority. And now the FDA has again issued a proposed rule to ban this specific intended use of an otherwise legal medical device.

So my question to you, sir, is, how is this not the FDA regulating the practice of medicine?

And how is this not a dangerous precedent for the FDA to now seek banning other off-label prescribing?

*Dr. Shuren. So this is a medical device. It is an electric shock --

*Mrs. Harshbarger. Yes.

*Dr. Shuren. -- device. They shock the patient.

*Mrs. Harshbarger. It is a last resort.

*Dr. Shuren. Yes, and we have looked at it. The data isn't there. We have gone forward with the regs. A lot of groups have weighed in.

That said, we are -- currently have an open comment period. I encourage everyone who has a perspective on it, have the comments into the docket by the time --

*Mrs. Harshbarger. To me, it is like a right to trial. Why would you ban that for patients who are successfully getting treated with a treatment that -- where nothing else has worked?

*Dr. Shuren. Yes.

*Mrs. Harshbarger. And, I mean, it is unconscionable.

But, you know, it is like I said. To me it is regulating the practice of medicine, which you shouldn't be in charge of.

And I just want to make you aware that this committee and many of us in Congress are going to be watching this situation very closely, and not only because of the way that this major policy was inserted last minute into a humongous appropriations bill, which is the kind of back-room deceit that the American public hates, bottom line, and it is just the way Washington works, but also because the FDA, in this saga, apparently ignored real-world evidence. So we will be watching that one.

Dr. Cavazzoni --

*Mr. Guthrie. Sorry, your time --

*Mrs. Harshbarger. Oh, well, I have got more questions. I will just submit them for the record. Thank you.

[The questions submitted for the record by Mrs. Harshbarger follows:]

**********COMMITTEE INSERT**********

*Mr. Guthrie. Thank you.

*Dr. Cavazzoni. We would be happy to follow up with you.

*Mr. Guthrie. Thank you, Mrs. Harshbarger. She yields back, the -- Dr. Miller-Meeks is recognized for five minutes for questions.

[Pause.]

*Mrs. Miller-Meeks. Thank you for not starting my time. Thank you, Mr. Chairman, and thank you to the witnesses for testifying before the subcommittee today. And I will probably follow up a little bit on what Dr. Harshbarger was talking about.

Dr. Shuren, you may recall the letter that I sent you in December of last year with Chairman Guthrie and Representatives Crenshaw and Obernolte, highlighting our concerns with assurance labs for the development and post-market regulation of AI-enabled medical devices. As I outlined, I believe it is important for the FDA to facilitate the development and utilization of AI in our medical system in a way that is both safe and effective for patients.

In your May 8 response to me you stated that your vision

for a voluntary AI assurance lab is to provide comprehensive and representative health care data for product development, training, testing, and analysis, and that such labs would be run by a third party, preferably a non-profit institution that would be responsible for the technical infrastructure design and implementation, as well as the management and controls of the Federation of Qualified Health Care Data Repositories.

Do you intend to outsource third-party regulation and post-market review to the Coalition for Health AI, CHAI?

*Dr. Shuren. Oh, no.

*Mrs. Miller-Meeks. Okay. Because let me also note that Google and Microsoft are founding members of the CHAI. The board chair of the coalition is a representative from the Mayo Clinic, which recently reported it has over 200 algorithms currently under development for deployment at Health AI, and has an active business model around AI validation.

So can you understand how organizations like CHAI advocating for involvement in reviewing additional layers of safety at FDA and ONC does not pass the smell test, and shows

clear signs of attempt at regulatory capture?

*Dr. Shuren. Yes, so CHAI is not a reviewer for us. They are a private coalition. We engage as a Federal liaison purely to provide the FDA's centered expertise in that. We participate in several coalitions with the idea of having representation from broad stakeholder groups.

We have told CHAI, too, they need to expand their membership, as well, to have more representation in the med tech side.

But we do this. If they produce anything in terms of deliverables that is useful, we may take it into consideration. But they don't work for us, we don't work for them.

*Mrs. Miller-Meeks. And so, given your earlier testimony, do you support innovation, Dr. Shuren?

*Dr. Shuren. Yes, we support innovation.

*Mrs. Miller-Meeks. And I do, too, but that is also why I oppose your Center's LDT rule. A 528-page rule is, by definition, only accessible to large corporations who can hire lawyers and consultants here in the swamp. We want bottom-up innovation. We want the pathologists to invent a

new test when they are frustrated with existing options, as we saw what happened with the COVID-19 testing debacle early on in the pandemic.

We want innovation to emerge organically, and governments sometimes should get out of the way, which is why I am concerned with the direction your Center is taking us, which leads to what Dr. Harshbarger started, and an article in the Wall Street Journal from January 12, 2023, "The FDA Wants to Interfere in the Practice of Medicine,'' and this goes back to this case and what was put in the 2022 omnibus bill, which gives the FDA the authority to ban some of these off-label uses of otherwise approved products.

This unwarranted intrusion into the physician-patient relationship -- and let me say, I am a doctor, so I am very sensitive to the patient-physician relationship -- threatens to undermine medical innovation and patient care. This is a problem for many reasons.

The statute gives the FDA the power without any public input to prevent patients' access to off-label therapies, even though their physicians and patients have found the treatments to be beneficial or even essential. And we

certainly saw this in the pandemic. We also saw that the FDA, which has touted -- and your department specifically -- touted using real-world data and real-world evidence -- we, as members of the Doctors Caucus, pleaded with the FDA to look at real-world evidence, real-world data when it came to vaccines, the timing of COVID-19 vaccines, and the uses of vaccines in children.

So it is of no surprise to us, then, that the FDA is refusing to use, as Mrs. Harshbarger said, real-world data, real-world evidence when it comes to a device, and you referred to the device in a derogatory fashion. So to me, it seems like the FDA and your department specifically doesn't want to use innovation when no other treatments work and the treatment, the risk profile for things that potentially could work is much worse and much greater.

So I think we recognize that challenge, and I would like the FDA to come up with its promise and look at real-world evidence, real-world data, and what are benefits, what are risks, certainly, as you are doing. But when nothing else is available, I think that it becomes a bias on the part of the FDA.

Thank you, I yield back.

*Dr. Shuren. We do look at real-world evidence. In fact, today we are authorizing roughly over 50 medical devices a year that is leveraging real-world evidence in support of it.

There is a --

*Mrs. Miller-Meeks. Mr. Chair, I would like to enter these articles into the record, and thank you so much.

*Mr. Guthrie. Okay. Without objection -- we have -- end of the hearing record, so we will consider those at the end of the hearing record. So thank you for offering those.

The gentlelady yields back. The chair recognizes Mr. Pence for five minutes for questions.

*Mr. Pence. Thank you, Chairman Guthrie and Ranking Member Eshoo, for holding this. And thanks to all the witnesses for still being here. I hope you had lunch before you came.

I am proud that innovators in the Hoosier State, such as Eli Lilly, are leading the charge to develop and manufacture critical drugs and therapeutics. The PDUFA was enacted in 1992 to help innovate innovators such as Eli Lilly to receive

faster approvals for their breakthrough medicines. While the PDUFA program has helped reduce the overall drug review times, there is still work to be done, as we have discussed today.

Recently, there has been concerning trends regarding the efficiency of the program. While the Administration's budget is calling for a bump in FDA funding to keep pace with innovation, there has been a recent decrease in FDA first cycle approval rates, with an increasing number of CRLs being sent to sponsors.

Dr. Cavazzoni for rare diseases, small populations, and patient heterogeneity -- that is a word over my pay grade -- in disease progression and severity can make it very difficult to interpret trial data. Please talk about how FDA is working with stakeholders to develop artificial intelligence machine learning tools, including digital twins and synthetic control arms, to advance our ability to accelerate rare disease drug development.

*Dr. Cavazzoni. Thank you for that question. We have seen an exponential increase in the number of applications that contain artificial intelligence elements, and we expect

to see that even more.

And one of the areas that we know is of great interest is this idea of in-silico comparisons in real-world data, data sets, and so on. So we are very interested in these applications.

The three medical product centers recently issued a paper, a discussion paper on how we intend to work together to advance the use of -- to make sure that -- the advanced use of artificial intelligence in medical product development. And we are really interested in continuing to work with sponsors when they present some new ideas.

*Mr. Pence. Yes. So just personally, this kind of interests me. So how are you going to validate the AI conclusion? Have you had conversations about that? Are you going to offset it against other AI validations?

*Dr. Cavazzoni. These are discussions that we are having now. I am happy to turn over to Dr. Shuren, since the Center of Excellence is -- really, the nexus for center of excellence --

*Mr. Pence. Okay.

*Dr. Cavazzoni. -- at FDA is at --

*Mr. Pence. Sure.

*Dr. Cavazzoni. -- CDRH. But we are getting ready to evaluate the models that underpin sort of the algorithms. We are having discussions on how we are going to --

*Mr. Pence. So if I may --

*Dr. Cavazzoni. -- access them, and so on.

*Mr. Pence. So do you think you have the technical skills internally --

*Dr. Cavazzoni. No --

*Mr. Pence. -- to be able to evaluate their models?

*Dr. Cavazzoni. We --

*Mr. Pence. Because that is big data, isn't it?

*Dr. Cavazzoni. Yes, we do have the technical skills in-house. And as I said, CDRH is really the hub, the center of excellence for the medical product centers.

Where we need to do some work is when it comes to infrastructure. For instance, having a enough space where -- to ingest all of these huge data sets, and the ability to review them without making it more cumbersome, too cumbersome for sponsors and for us. So there is some work to be done when it comes to the infrastructure side. When it comes to

the expertise to actually understand the algorithms, we are in good shape.

*Mr. Pence. So is that internal infrastructure data centers, or is that third-party --

*Dr. Cavazzoni. It is a little bit of both.

First it is internal infrastructure. It may entail third parties. To give you an idea, it is extremely costly to find -- to acquire the high-computing capabilities, the very fast computing capabilities to be able to review these algorithms and these AI models. And we are having discussions internally on how --

*Mr. Pence. So if I may -- I am running out of --

*Dr. Cavazzoni. Sure.

*Mr. Pence. Fascinating. Thanks. Great answers. But in the interim, what do you do with the AI information if you don't have the capability to analyze the data?

*Dr. Cavazzoni. Well, in the interim -- we are finding ways in the interim. But what we are also discussing is how are we going to upscale once more --

*Mr. Pence. Are using it.

*Dr. Cavazzoni. -- more and more and more applications

will contain the elements. So there is a component of the present and then getting ready for the future.

*Mr. Pence. Okay. Thank you, Doctor.

And I yield back.

*Mr. Guthrie. The gentleman yields back, and the chair recognizes Mr. Crenshaw for five minutes for questions.

*Mr. Crenshaw. Thank you, Mr. Chairman. Thank you all for being here.

I do want to address something that was said earlier, you know, effectively accusing Republicans of being a bunch of right wing nut jobs just because we have some problems with the drug mifepristone. You know, mifepristone is a pill that kills babies. So I don't think it is crazy that we are against that, first of all. It is not a crazy position to take.

And it should also be said that we are asking the FDA to follow their own risk evaluation processes for a post-approval process, especially when we see adverse health effects in women that take mifepristone, the pill that kills babies. That doesn't make us crazy.

Let's go to some questions here. Again, I appreciate

you all being here. One thing I am extremely interested in is regenerative medicine, and I think the value that that can bring to the public. Top of mind is some of these treatments that, quite literally, use the patient's own body, you know, their own cells to cure disease. It is one of the great miracles of our time, using autologous cell therapies. But there is a lot of regulatory uncertainty surrounding that.

Dr. Marks, you have talked about an intermediate pathway to approval for novel products that don't neatly fit into the biologic versus cell and tissue pathways. Will you commit to continuing to work with us and the industry on academic -- and academic innovators to ensure regulatory modernization that works for everyone and gives us that certainty so that we can have that innovation?

*Dr. Marks. Very much so. We absolutely commit to that.

*Mr. Crenshaw. Okay.

*Dr. Marks. I mean, it is an important area where I think we realize that there are products that are quite nuanced here, and that we want to facilitate the innovation, getting to patients without, essentially, at times, perhaps,

what could be seen as undue regulatory burden.

*Mr. Crenshaw. Great to hear. One of the things that has also come to my attention in meeting with, you know, really interesting innovators in all the health care spaces is the lack of communication with FDA. They often feel like it is sort of a black hole of communication. They don't know what they are doing wrong, they are just told to, oh, do it again, try it differently. Well, differently how? Oh, you will figure it out. I hear that kind of feedback sometimes.

So can you discuss how FDA plans to enhance communication and support for sponsors during the review process, particularly for these smaller companies that don't have the legions of lawyers and people to help them with the process?

*Dr. Marks. Thanks again. Thanks very much for this -- for that question.

So we recognize that many of the sponsors working in regenerative medicine, or even some of the small gene therapy companies, they do not have the experience dealing with FDA, and they need someone to be very able to listen to their concerns and respond. So we have a number of programs.

We have a program that people can come in very early on with just a platform approach. It may be not a specific product, but a set of products that they are intending to develop, and they can have a very informal meeting with some of our -- my colleagues about manufacturing or clinical development.

I know there is -- I will let Dr. Cavazzoni speak about a similar product, a similar program in CDER.

We also have an early regulatory meeting called an interact meeting where, without having to submit the investigational new drug application, a sponsor can come in with just a couple-page write-up of what they are planning to develop, and we can have a dialogue, as well. And it is a no-fault dialogue. We don't hold the sponsor to taking our advice, but it allows them to get feedback.

And we will continue to try to interact as much as we can in informal settings appropriately with those, trying to develop products in this area.

*Mr. Crenshaw. Okay, Doctor, I appreciate it. I only have one minute left, though, so I want to shift real quick.

I am very interested in the use of psychedelics for

treatment of PTSD. We were able to push through some legislation that will tell DoD to fund the clinical trials. FDA has leaned forward on this, I think almost a year ago proposed guidelines for frameworks for what those clinical trials would look like. Can you commit to ensuring that those will be finalized soon? I think by June is the date we are looking for.

*Dr. Cavazzoni. You know, we have issues -- issued guidance on -- for developers on the type of trials and development plans that we expect if they are interested in studying psychedelics as drugs.

And as with in all areas, we are very, very open and interested in working with developers. I cannot speak for programs that are currently under review, but, obviously, there is a lot of interest in this space, and we want to be there to guide developers and give them advice at the right time.

*Mr. Crenshaw. The guidelines were -- we saw draft reviews, and the guidelines are finalized at this point, or --

*Dr. Cavazzoni. Yes, we issued draft guidance. We want

to get a little bit more experience from the current programs before issuing final guidance, and we also want to make sure that we review all of the public input that is given, you know, that was provided to us --

*Mr. Crenshaw. Do you have a --

*Dr. Cavazzoni. -- on the issue of guidance. So --

*Mr. Crenshaw. Do you have a timeline on that?

*Dr. Cavazzoni. Yes.

*Mr. Crenshaw. Do you have a timeline?

*Dr. Cavazzoni. We want to be very thoughtful when we issue final guidance.

*Mr. Crenshaw. Understood, but do you have a timeline on that?

*Dr. Cavazzoni. I can't give you a timeline today, but I am -- we are happy to follow up.

*Mr. Crenshaw. Okay, thank you.

*Mr. Guthrie. Thank you. The gentleman's time has expired and yields back.

We now have completed subcommittee members. We have a few members of the full committee that have asked to ask questions. And so we will alternate between the both sides

of the aisle, and we will start with Ms. DeGette of Colorado.

You are recognized for five minutes for questions.

*Ms. DeGette. Thank you so much, Mr. Chairman. I know that, in my absence for a little while, there was some conversation about the new FDA rules on laboratory-developed tests, or LDTs, and I want to probe that a little bit more with you if I can.

And everybody here knows that the character of LDTs has really changed since FDA first instituted the enforcement discretion for LDTs nearly 50 years ago. In 1976 the model sort of was the simple, manual tests being performed in local labs. But now LDTs use complex software, developing technologies, and people are using them to inform extremely sensitive life implications, the decisions they are making. And so the change in character of LDTs necessitates a change in their oversight. And a balanced system that promotes public health and encourages innovation is critical.

Now, so I know after the FDA issued its recent rule, there was a lot of concern, and many of my colleagues on this committee disagreed with the approach of regulating LDTs through the medical device regulations. And I, frankly,

agree with that. I think that FDA did what it could in terms of trying to regulate LDTs, but I also think that Congress should create a better oversight framework not just for LDTs, but for in vitro clinical tests in general.

And so the FDA rule has been finalized, and so I think that everybody who is thinking about this now has to realize it is not like the option is, do we regulate LDTs or don't we regulate LDTs, because we are regulating LDTs now. The question is, how do we want to accomplish that regulation? Do we want to do it through the medical device regulation, or do we want to create a modernized, tailored approach to in vitro clinical tests?

So Dr. Shuren, I just want to ask you. Now, FDA published the rule in the Federal Register on May 6, just a couple of weeks ago. Is that right?

*Dr. Shuren. Yes.

*Ms. DeGette. Yes. So some people have said we could have a Congressional Review Act resolution here that would solve this problem. But since it has been published like this, there is not going to be a CRA this Congress, and it would be irresponsible to do one without a legislative

alternative.

Based on the majority leader's calendar, the CRA lookback window for next Congress will only extend to rules that are published this week. So the only two options that we have are the implementation of the rule that was just published, or if we pass a legislative solution.

A CRA, in my opinion, is a waste of time, especially because we have discussed in this very subcommittee the VALID Act, a vetted, balanced, and bipartisan, and rational framework for regulation of in vitro clinical tests in general. And so I am hoping that we can all work together on this.

Now, some people said that oversight of LDTs should be taken through reforms to CLIA, which is a framework through which CMS oversees clinical laboratory operations. However, both FDA and CMS have said that idea is ill-advised. Dr. Shuren, can you explain why that idea doesn't work?

*Dr. Shuren. Well, CLIA doesn't pertain to key aspects on test design and validation like clinical validity. It doesn't have reporting for problems or surveillance, or even tracking the LDTs that are out there.

And so we have been on record -- I actually testified before this committee nine years ago with the deputy administrator from CMS, and we said the same thing back there. And as -- and more recently -- and CMS has said, if you expanded it, they don't have the expertise to go ahead and do it, it sits with the FDA. And putting in place a duplicative system would only create more bureaucracy and more inconsistency.

*Ms. DeGette. Thank you. I want to turn to something else that FDA simply cannot do under its current authorities. And so I am wondering if you can briefly tell us about the concept of technology certification that we have in the VALID Act, and how it would relieve the burden from both test developers and FDA reviewers.

*Dr. Shuren. No, we couldn't do it with our current authority.

*Ms. DeGette. That is right.

*Dr. Shuren. Right. And so that novel approach is more about focus on the sort of capabilities of the developer, regardless if it is non-lab or lab, but it works when you have married it to really strong post-market authorities,

because you need that with reporting and surveillance inspections.

So one of the things with the VALID Act, it is not one little piece, it is all the parts working holistically together.

*Ms. DeGette. Great. Thank you very much.

Thank you, Mr. Chairman.

*Mr. Guthrie. Thank you. The gentlelady yields back. The chair recognizes the gentleman from Texas, Mr. Pfluger, for five minutes for questions.

[Pause.]

*Mr. Pfluger. Thank you, Mr. Chairman. I had problems turning the microphone on, and I appreciate you letting me waive on.

And Dr. Cavazzoni, I will start with you. I want to talk about price setting, and want to talk about competition, and specifically the IRA. So, you know, when we look at understanding the IRA lets some biosimilar manufacturers have a chance to "compete'' by allowing a pause before a brand biologic product's price is set, and especially if a biosimilar is likely to enter the market within two years,

but just kind of -- you know, I have some questions in my head about the timelines and the criteria, and whether those are still insufficient.

And so, given the uncertainty that I believe has been created by the IRA, how is the FDA planning to provide predictability for biosimilar manufacturers to ensure continued investment and development in this market?

*Dr. Cavazzoni. Yes, yes. We are very committed to continuing to work with the biosimilar manufacturers. Our biosimilar program is a success. We have approved the fiftieth biosimilar a couple of weeks ago.

There is two areas that I think we think would be particularly important. Number one, we really want to find ways to develop biosimilars with less clinical data using the analytical methods and the structure of the biosimilars. So we have a lot of work there. The second one is that we think that the statutory differentiation between a biosimilar and an interchangeable biosimilar is not needed. And we think that, by removing that, removing that statutory difference, we would really make some inroads in making biosimilar easier to access, allowing substitution at the time of prescription

and so on. And we would be very happy to work with Congress to address those barriers.

*Mr. Pfluger. Do these measures include -- in the nature of streamlining, do they include updates from FDA to CMS on those biosimilar products that are currently in the process, in the pipeline?

*Dr. Cavazzoni. Yes, we talk to CMS along these lines, we communicate when it is needed. Our focus in our program is really to make it easier, less expensive, and less cumbersome to develop biosimilars so that we have more out there, and more that are interchangeable and that can be substituted.

*Mr. Pfluger. Would you say that the competition between these manufacturers has led to the savings, billions of dollars of savings? Is that a good thing?

*Dr. Cavazzoni. There is data that support that, that the biosimilar program --

*Mr. Pfluger. Do you believe that data?

*Dr. Cavazzoni. The biosimilar -- we would be happy to follow up.

*Mr. Pfluger. Do you believe that data?

*Dr. Cavazzoni. I do believe it, yes, absolutely.

*Mr. Pfluger. I will move on to ethylene oxide and talk to you, Dr. Shuren, about this. I am very worried about the EPA's decisions on ethylene oxide, and I want to know kind of what the FDA is doing to work with EPA to ensure that we don't have shortages in the surgical products and, you know, biosimilar products or any in the value chain that are affected by this. Obviously, it is something that is used to sterilize a lot of different pharmaceutical, surgical, emergency room products.

*Dr. Shuren. Look, we appreciate the important work that EPA does, and our role was to try to inform that to minimize disruptions for important medical devices. And so we did work with the EPA to provide important feedback on the impact of their proposed rule. They made changes. We are still working with the EPA, and we are monitoring those sterilization facilities to see what happens during implementation to, again, try to minimize the likelihood for device shortages.

*Mr. Pfluger. Could I characterize it by saying that the FDA has concerns over EPA's rule regarding ethylene

oxide?

*Dr. Shuren. I think it would be fair to say we appreciate the changes they made in their final rule, which were helpful, and --

*Mr. Pfluger. More changes still need to be made?

*Dr. Shuren. At this point our sense is that we may be in a good place, and we will monitor to see what the real impact is.

*Mr. Pfluger. Patient safety, our supply chain, the overall health of our health care system kind of resides on you working with them to get to a better place.

*Dr. Shuren. Yes. And I will put a plug in. We also need help from Congress on authorities to prevent device shortages. We heard a lot about drugs, but we need help on devices because they are happening every day, and we don't have all the tools we need to prevent that.

*Mr. Pfluger. Lastly, for any of you -- Dr. Marks, you can take a shot at this or Dr. Cavazzoni -- is FDA approving things in a timely manner that allows safety, but also innovation to happen?

*Dr. Marks. Yes, I would say that we are trying to move

things through as rapidly as we can, while maintaining what somebody already said here was our gold standard.

*Mr. Pfluger. You are trying, and I get that. Can we do better?

*Dr. Marks. Listen, we are always trying to do better, and I think that is something that continuous improvement will continue to try to do, and that is a commitment we have.

*Mr. Pfluger. That is a lot of continues. I like that.

I will yield back. Thank you.

*Mr. Guthrie. Thank you. The gentleman yields back. The chair recognizes the gentlelady from Illinois for five minutes for questions.

*Ms. Castor. That is you, Jan. You are up first.

*Ms. Schakowsky. Okay, sorry.

[Pause.]

*Ms. Schakowsky. Okay, sorry, Madam Chair, Mr. Chair, whoever, all of you. Sorry.

Okay. So Dr. Shuren -- is that right? Yes, okay.

*Dr. Shuren. Yes.

*Ms. Schakowsky. So I am concerned about the process that you have to make sure that people who rely on a safe

product, that it is left to the manufacturer to decide if -- whether or not something should be -- if the manufacturer decides that there needs to be a recall of a product, rather than having you make that decision. And I am just very, very concerned.

In May there was a problem with an insulin pump that actually affected about 200 people. But it wasn't until that happened that we were able to get your agency to take action. And so I wanted to ask you if there was some way that Congress could do something to make sure that you have more authority for recalls, and not have to be dependent on the manufacturer to decide it is time to act.

*Dr. Shuren. No, I appreciate that, and we would be happy to have the discussion regarding our oversight with recalls.

I will say one of the challenges that we do face is that we will decide -- you know, there are standards in place as to what would constitute for recall that companies have to follow. But we are dependent today on their identifying often times those problems, and then reporting it to us. And I think you have seen some fairly high-profile instances

where a company had recalls, and they did not tell us about it.

*Ms. Schakowsky. Well, that has to be fixed.

*Dr. Shuren. Yes.

*Ms. Schakowsky. I mean, it absolutely seems to me that the government ought to be in charge of figuring out whether there has to be a connection or not, and a correction or not.

The other issue that I wanted to talk to you about, which is very similar, about hospitals, that right now hospitals are -- there is -- a letter goes out that says that there is some need to do a correction, a change in the hospitals. But it can be months before that letter gets sent out.

So I have a piece of legislation that would actually -- the -- it is called the -- let me see, the Medicare Device Responsibility Act that would require that you would have to announce that there is this problem to the hospitals, and to make a change in what happens in the hospitals, and not have to wait for this letter to come that could take months, and that -- so we want to make sure that you will get that information out right away.

*Dr. Shuren. Yes. No, I appreciate it, and that is something we would like to continue the conversation and work with you on.

I think there are two challenges here. One is the company is not identifying there is a problem and getting that reported to us. The second is reporting out to the public on a problem. We will often times put out a communication. We held a public meeting. We had our patient engagement advisory committee. They would like to shorten the time from -- it is usually sometimes 30 days -- get that to 2 weeks. We are actually working on that and more standardized information, and we are looking to actually roll out a pilot later this year on that aspect. But we still have to deal with shortening that timeframe when a company may be coming aware of something and we find out about it and can deal with it.

*Ms. Schakowsky. Well, so why does -- why are companies ahead of you to decide whether there is a problem, and whether or not there is some sort of a recall?

*Dr. Shuren. Yes, because in some of those cases, they are the ones who become aware of it. Other times, though, we

are the ones who go in the door, we do an inspection, we find a problem, and we will tell them this is -- "You need to recall this product and take action,'' and then we will enforce that.

*Ms. Schakowsky. Okay. I would like to work with you on this, and I do have legislation.

And with that I yield back.

*Mr. Guthrie. Thank you. The gentlelady yields back. The chair recognizes Ms. Castor for five minutes for questions.

*Ms. Castor. Well, thank you, Mr. Chairman and Ranking Member Eshoo, for the opportunity to waive on today. And thank you to our witnesses for being here to discuss FDA and the important work going on at your centers.

For many years I have focused on improving the health of pregnant and lactating women who have historically been excluded from research and clinical trials. Their exclusion has led to significant evidence gaps that negatively impact the health outcomes of mothers and infants. Of the more than 3.5 million women in the U.S. who give birth each year, 89 percent take at least one prescription medication during

pregnancy. Yet 70 percent of FDA-approved medications have no human pregnancy data, and 98 percent have insufficient data to determine the risk to an infant. And that lack of data creates challenges for families and providers, excludes pregnant and lactating women from research. It doesn't really make them safer, it just means that medical decisions will be made without sufficient information on safety and effectiveness.

Last month the National Academies released a congressionally-requested report called, "Advancing Clinical Research with Pregnant and Lactating Populations: Overcoming Real and Perceived Liability Risks.'' In it the Academies recommends that FDA release guidance making clear that pregnant and lactating women should be included as early as possible in studies.

Dr. Cavazzoni, HHS removed pregnant women as vulnerable populations in 2018. FDA put out a proposed rule in 2022 to finally harmonize with the rest of the department, but we have now been waiting almost two years for the final rule, and patients and providers and manufacturers are eager for clear guidance, and we should be encouraging researchers to

pursue this work and ultimately improve patient care.

What are the next steps for the final rule? What can you tell us?

*Dr. Cavazzoni. Well, this is something that is underway. We understand that there is a lot of interest in this, and there is a lot of interest in sort of in clarifying the -- when data should be collected in pregnant and lactating women.

Our stance has been that it is important that we generate data before a drug is approved, and also after a drug is approved. You know, we very often ask for registries, pregnancy registries, and that the pregnant and -- pregnant women be included at the appropriate stages of development. Obviously, there are some very early stages of development where it would not be advisable to expose pregnant women to -- and do risk when we know nothing about a drug.

So we are here to work with developers. I have to say that one of the major issues that we are not all, I am sure, are aware of is that in our very litigious society there may be a opportunity to talk about tort reform that may make it

easier for developers to assume the, you know, the potential risk of sort of litigation when vulnerable populations such as pregnant women are included in clinical trials.

But certainly, from our standpoint, we have issued guidance that emphasizes the importance of collecting, generating data in pregnant and lactating women pre and post-market.

*Ms. Castor. And you will continue to update that as expeditiously as possible?

*Dr. Cavazzoni. We are continuing to work on this, yes.

*Ms. Castor. Okay, okay, thank you.

Dr. Shuren, I was pleased to hear you raise the medical device shortage there a couple of members ago, because the update to the Pandemic All-Hazards Preparedness Act really provides us with the opportunity to apply the lessons learned from COVID-19. Unfortunately, committee Republicans refused to include critical legislation, including my bill on medical devices. I know during the pandemic you had the authorities to require medical device manufacturers to submit information related to the shortages. And by the end of 2022 the agency had received over 455 potential and actual shortage signals,

and that was very helpful to you.

So you would like this authority to be continued so that we can tackle medical device shortages, is that right?

*Dr. Shuren. That is correct because we are dealing with device shortages all the time, but now we essentially went dark to some respects, not getting those notifications. And we have those authority for drugs, but we don't have it for devices. And so we are talking about --

*Ms. Castor. Give us an example.

*Dr. Shuren. Yes, so we are talking about catheters for pediatric hemodialysis and, you know, infant duodenoscopes. I mean, those are the kinds of things they matter.

We talk about availability of tests for kids. Why don't we care about the availability to do hemodialysis for them, too? It really does make a difference. And that information, when we used it in the pandemic, helped us prevent a lot of shortages. Why we are not able to do it in peace time I don't understand because patients care what happens to them at any time in their life.

*Ms. Castor. And there should be bipartisan agreement on this.

Thank you very much. I yield back.

*Mr. Guthrie. Thank you. The gentlelady yields back, and that includes -- that concludes everyone present to ask questions.

And I will ask unanimous consent to insert in the record the documents included on the staff hearing documents list.

And without objection, that will --

*Ms. Eshoo. No objection, Mr. Chairman.

[The information follows:]

**********COMMITTEE INSERT**********

*Ms. Eshoo. But I would like to ask you to give me a minute, minute-and-a-half to say something.

*Mr. Guthrie. Okay, good, because we do have another committee coming in the room, but yes, absolutely, I will.

*Ms. Eshoo. Mr. Chairman, our colleague, Mr. Crenshaw, in my view, said some disturbing things about a drug. The FDA approved mifeprex more than 20 years ago. And it was based on a very thorough, comprehensive review of scientific evidence that determined it is safe and effective for its use. FDA has continued its periodic reviews of post-marketing data of mifeprex, and has not identified any new safety concerns.

There is an alarming precedent in the court case that the Supreme Court is taking up. It is an alarming precedent that calls into question the authority of the FDA. This is all based on science. And for at least some of my Republican colleagues, entering into some of the most private, private decisions that a -- in a woman's life, the devastating choice to consider ending a pregnancy, I really take exception to this because, again, this drug is also used in the treatment of other conditions, including Rushing's syndrome, uterine

fibroids, abnormal uterine bleeding, gynecological cancers. It can also be used, in some cases, to treat depression and post-traumatic stress disorder.

So when ideology really ends up trumping science, I think that is dangerous for our country. Should we be going down the rabbit hole of doing away with challenging vasectomies for men because they are prevented from producing children? I mean, what is happening to us here?

So this case is really based on mock science, in my view, and I think that that is one of the most dangerous rabbit holes that we could ever go down. Here, we have had a hearing with the top people from the FDA, and the perfection of all of our systems and practices so that we produce the best and the safest for the American people.

So I appreciate your giving me this time. It is deeply unsettling to have that layer of ideology, and it is like water and oil. They don't mix. We are talking about science here, and the science that has been proven to stand up to the scientific evidence and its effectiveness for decades. So thank you, Mr. Chairman.

*Mr. Guthrie. We have got to clear the room, yes, and I

thought you were going to do concluding remarks.

[Laughter.]

*Mr. Guthrie. It is not fair for Mr. Crenshaw not to be able to respond outside of time, but we will find an opportunity for that to happen in the future.

But I just want to remind members that they have 10 business days to submit questions for the record, and I ask the witness to respond to the questions promptly.

Members should submit their questions by the close of business on June the 6th.

Without objection, the subcommittee is adjourned.

[Whereupon, at 1:51 p.m., the subcommittee was adjourned.]